In Memorium

If I try to think of a single instance, where Professor Faisal left an indelible mark on my life, I end up defeated, because such instances were innumerable. I will, therefore, focus on my first meeting with him: it was an extraordinary encounter.

The first time I met Professor Sahib was almost thirty years ago. It was in our fourth year at KE, and our batch was attached to the South Medical Ward, Mayo Hospital. For some reason, only four of us had turned up for the ward, and we were not considered important enough to merit any attention from anyone. We were therefore standing around a bed, practicing doing tendon reflexes in a desultory manner. Quite unexpectedly, we were joined by a doctor we had not encountered before. He was quite young, despite his salt and pepper hair, and seemed to be full of a restless energy. One could somehow sense that despite his youth, he was someone important. Despite this fact, he was very informal in his approach to a group of lowly fourth year students. He joined us at the bedside and asked us what we were doing. On hearing that we were practicing ankle jerks (with questionable success), he spent the next hour teaching us how to elicit a tendon reflex (neutral position, muscle exposed, freefall strike the tendon, look at the muscle not the jerk). The way he held our hands and taught us each how to elicit the tendon reflexes left a lifelong impression: here was a teacher who was truly passionate about teaching. Along the way, he talked to us about his remarkable medical college days: he had never attended wards as a student, yet won medals in every clinical subject. He had a truly magnetic personality and had us all fascinated by unconventional approach to education and life. I had never met someone like him before, and have never since. Over the years, he held the hand of hundreds of students and taught how to palpate the thyroid or the liver or teach some other clinical skill. He was a teacher like no other, and although I got to know him in many other roles over the years, to me he was always my teacher and more, a mentor and a surrogate father, and his passing left me bereft of all three. My association with him spanned many decades, during which he mentored me and guided through every step in my career, and I can say with absolute honesty that all I have achieved over the years was only possible because of his support and guidance.

May Allah grant him the highest rank in Jannah.

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EDITORIAL

To Sir, With Love.
Messages from the Heart

Dr. Saira Burney

Oh, the irony of life! How it teaches us things that we do not want to learn otherwise. It takes us through times of deep sadness to reveal the meaning of true happiness. It brings upon us days of utter chaos so we can appreciate and be grateful for peaceful times. And it takes away from us people we love and hold so dear to make us understand what their presence truly meant to us.

Professor Faisal Masud, otherwise so reverently and lovingly referred to by all as 'Sir', was also taken away from us suddenly. There was no warning…we got no time to prepare for a life without him. Just like that, one august afternoon, two months shy of his 65th birthday, Sir left us for his eternal abode leaving a void that, I know, will never be filled. It's been a little over a month now but my friends and I, who'd been closest to him, still live in a disassociated state, functioning robotically, trying our best to grapple our way through the fog that surrounds us. That fateful day and the events that followed seem etched in our minds forever and it takes very little to bring it all back. We are still reeling from the suddenness of it all and keep playing, in our minds, the hours and days leading up to his death, searching for clues that could have indicated what was to come. There have been countless agonizing moments of self-reproach for perhaps failing to recognize signs of ill-health or not being mindful enough towards his personal health while forever nagging him with our own problems and ailments.

Sir's passing away was unexpected, to say the least, and we have yet to fully process it. What pains us the most is not having had the chance to say goodbye, the wish that we could somehow have known of things to come in order to say and do what we wanted to; that we could have just had one more brief moment with Sir to tell him how much we loved him and held him dear, apologise for the many times we might have hurt him, let him know what he truly meant to us and how profoundly lost and insecure we feel, now that we no longer have his sheltering presence in our lives.

This article is meant to serve as a very small tribute of love and respect to Professor Faisal Masud: a giant of a man with remarkable intellect, a mentor to thousands and a great soul of matchless courage and confidence who worked hard his entire life and used his position and influence for the good of his country. He lived a life of dignity and integrity; he died in the same manner. Sir, here are some of the heartfelt things we wanted to say to you but never got the chance. I know you won't be able to read it in this life but we are firm in our belief that our actions in this life have a mark in the next. I hope we can tell you when, God-willing, we see you in the hereafter.

You left as quietly as you had said you would, as you had wished, as you must have prayed for. You didn't wish to cause anyone trouble and you didn't. You are gone and the world is bereft. I am bereft. How do you live in a world without your mentor? Who do you turn to for counsel and advice? I need to talk to you, to listen to your voice of reason, but I can't. You taught us everything under the sun except how to cope with your loss.

Your workplace is now silent and in darkness. How busy and noisy it had been. I just have to close my eyes and I can see it, can see you sitting upright in your chair, hands crossed in front of you, talking to patients, laughing with some, admonishing others, sharing anecdotes, dispensing wisdom that people remembered even decades later. That is how I remember you best. That is how I want to remember you always.

In these early days, grief can at times be unbearable and faith is the only thing that keeps me from crumbling. So I pray to Allah to give me patience at times when I'm overwhelmed, to give me strength that I can measure up to you as a role model of devotion, compassion, work ethic, dignity and dedication to my work and country. For now, I will pray for your well-being in the grave and for your eternal peace. I will wait for the time when, God-willing, we will meet again; and for me, there is comfort in that.'

Dr. Saira Burney

'Faisal Endocrine Associates": I never thought this title would become a source of pride and such a cherishable asset for me, one I would hold dear to my heart for times to come.
My association with Sir has been a long one, but unfortunately not long enough.
It was a tumultuous, unpredictable roller coaster ride on the path of knowledge, unmatchable intellect and clinical acumen, where I stumbled at every step, trying to catch up with him but was only able to acquire a wisp from the treasure-trove of knowledge, he so readily shared with me.
Never-the-less I feel blessed to have been a part of Sir's professional life, to have had him as my teacher and mentor, and more than anything, I am grateful for the countless precious memories that I can hold close, for years to come. Today, all that I am in my capacity as a doctor: my knowledge of medicine, every prescription I write and whatever honours I have achieved, after Allah's support and mercy, it is all due to Sir's constant guidance and incredible teaching. This is something which I can never stop acknowledging and can never thank him enough.
So, for whatever little I'm worth, I will always bear his torch, spread knowledge like he did, and try to heal like he wanted us to. He was magnanimous in his teachings and never kept anything back. I choose a line from one of his favourite movies to address him today as: "O' Captain my Captain!"
Our association with you was special, we will always consider ourselves as "Faisal Endocrine Associates". This name is our privilege and an honor you bestowed upon us. Even though I feel I did not deserve it fully, I will always remain proud of the fact that you deemed me worthy to be a part of your world. Adieu Sir, you left us in a hurry to go to your eternal abode. Rest In Peace!
We miss you loads, but the journey you began does not end here; it continues.'

Dr. Fehmeda Khan

'What do you say to your life-coach? To that mentor who did much more than simply provide guidance, who held your hand as you took baby-steps into the medical world and who never let go. The one who shaped you into who you are, taught you to seek with your heart and not just the mind. Scolded you like a parent one minute and didn't bat an eyelid the next when you messed things up terribly. The tower of wisdom and strength we had all learned to rely on; the one who, when he told you 'I've got your back', meant it; who strove to give you ALL he had, which was a lot. That living definition of commitment, passion, wisdom and toil.
What do you say to such a huge presence in your life? A mentor for thousands of people: students, colleagues, friends and patients, alike. What do you say?
Nothing! You say nothing. You just raise your hands in prayer and bless him immensely for all he did for you and for countless others. You stay quiet, you remain steadfast and you carry on; just like your mentor taught you. May Allah be with us all. Aameen.'

Dr. Aziz Fatima

'Sir, I could find no words special enough to do you justice so I will use the simplest of words to say thank you for being my teacher, a mentor and my spiritual father in the true sense. You always led your students by the hand, and even when you let go to allow them to walk alone, you would always be right behind them to offer support in case they fell. You were my rock. You made me the professional I am today and I pray to God that I can always make you proud. You were an inspiration, an institution, a magician in the field of medicine and above all the most amazing father to all your students. May you have the highest place in Jannah.'

Dr. Ambreen Butt

'You were not only our teacher, you were our guide and mentor, a friend, a fatherly figure all rolled into one person. You taught us the art of medicine and alongside that trained us in the art of living with meaning and purpose. We will always be grateful to you for the generosity with which you shared your wisdom, for your kindness and for your constant support towards us. Although you are no longer with us, your legacy will continue through us and your words of wisdom will always keep us enlightened.'

Dr. Hafeeza Naz

'I have known Sir since the time of my house job. It seems impossible for me to express my true feelings while paying tribute to such a great man who I always looked up to as my teacher and mentor. Albert Einstein once said, "It is the supreme art of the teacher to awaken joy in creative expression and knowledge." This holds very true for you, Sir. My only wish is that I could have told you in this life just how much I valued your wisdom and guidance in the course of my own personal and professional life. You were and always will remain a symbol of wisdom, integrity, precision and complete confidence in your knowledge and commitment. You will always be alive in our hearts as a role model for teaching and dedication towards your students, while upholding qualities of faith and honesty.

I am grateful to Allah Almighty for having had the opportunity of knowing you and for the privilege of working with a great human being like you. You will be missed forever, Sir!'

Dr. Mehwish Iftikhar

'Living with grief is like living two lives simultaneously. One is where you pretend everything is all right and keep pushing yourself forward one step at a time and the other is where your heart silently sheds tears. Sir, you left without saying goodbye and your absence now haunts me and hurts me every day. How I miss you and wish you were here! There are so many instances during the day when I so desperately want to call you and hear your voice only to check myself, remembering that I can no longer do that. All of my work life I tried to emulate and follow you as best as I could. I was there the day that you left us but how was I to know, that you were going somewhere that I couldn't follow. Rest in peace, dear Sir. Thank you for everything. I will miss you always.'

Dr. Khushroo Minhas

We are now into October. The days are shorter and evenings rather chilly. Just like any major occurrence in one's life, there are days where it feels like it was just yesterday that Sir was here and there are days where it seems like it is decades since he's been gone. In a few days, the 16th will be upon us when it would have been Sir's 65th birthday. It breaks my heart to think that we will not be celebrating it with him, like we did every year, without fail. Now all we have are his memories. Everywhere, family and friends, alike, will be remembering and reminiscing about an incredible man who left too soon. We, his students, will be doing the same. Sir may not be here in physical form with us but he is most certainly here in every way that truly matters to us; in our hearts forever.

Happy 65th, Sir. On this day, we will honour you! We will honour your strength, your passion and commitment for work. We will honour the legacy you left behind: a legacy of excellence and of diligent commitment to maintaining high standards and professionalism in all you did in life. There is a deep void in our lives, yet we are fully aware of the enormity of the task ahead: protecting your formidable legacy and carrying it forward. May Allah help us to do that to the best of our abilities.

Our lives go on without you
But nothing is the same
We have to hide our heartaches
When someone speaks your name
Sad are the hearts that love you
Silent the tears that fall
Living our hearts without you
Is the hardest part of all
You did so many things for us
Your heart was kind and true
And when we needed someone
We could always count on you.
The special years will not return
When we were all together,
But with the love within our hearts
You will walk with us forever'.

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Original Article

Preventive Role of Folic Acid in Artemether-Induced Teratogenicity on Fetal Heart in Albino Mice

Muhammad Shahid Akhtar, Fatima Inam and Muhammad Amin

Objective: To determine the role of folic acid in preventing the adverse effects of artemether, on fetal heart in Albino mice.

Methods: Eighteen pregnant Albino mice were randomly divided into three groups A, B and C each consisting of six mice. The control group A was given intramuscular injection of solvent Arachis oil 10.7mg/kg, group B was given intramuscular injection of artemether 10.7mg/kg and group C was given intramuscular injection of artemether, 10.7mg/kg and folic acid 4.93 mg/kg, dissolved in 0.1 ml. of distilled water orally, from 6th to 10th day of pregnancy. On 18th gestational day, the mice were sacrificed, dissected to deliver the fetuses; the heart of each fetus was isolated and fixed in 10% formalin. The macroscopic features and cardiac weight were noted. Then it is processed in a usual way for histological examination with the light microscope after H&E staining, using X4, X10 and X40 objectives. The sections were evaluated for any histological changes and septal defects. For statistical analysis, SPSS version 18 was used.

Results: Gross examination of the heart revealed no structural malformation. Post-Hoc Tukey's test indicated statistically significant difference in mean cardiac weight between groups A and B (p=<0.001), groups B and C (p=<0.001) and between groups A and C (p=<0.001). No atrial and ventricular septal defects observed. Histological examination showed myocardial development in current study was delayed in groups B and C, showing presence of mesenchymal cells.

Conclusions: Folic acid prevented the adverse effects of artemether on the development of heart.

Keywords: artemether, cardiac weight.

Introduction

Any agent that induces structural malformations and abnormal development or increase the incidence of an anomaly in the population is called a teratogen.[1] Malformations caused by drugs and other therapeutic agents are important, however, we should be careful in prescribing these drugs during pregnancy, which cause teratogenicity.[2]

For DNA and RNA synthesis, folic acid, a component of vitamin B complex is required. It promotes erythropoiesis and is used commercially in food supplements.[3] It is a dietary requirement, since it cannot be synthesized by the body and only 10 percent or less of folic acid in active form is present in the normal diet.[4] The risk of congenital anomalies, like cardiac anomalies induced by retinoic acid (Vitamin A), craniofacial deformities, neonatal mortality from neural tube defects, cleft lip and palate and imperforate anus are reduced by periconceptional use of folic acid.[5-8]

New antimalarial drugs like artemether and other derivatives of artemisinin, artesunate, dihydro artemisinin and arteether are now used commonly for the treatment of malaria due to emergence of malarial parasites, resistant to drugs, like chloroquine and quinine. The mechanism of action of artemether and other artemisinins against malaria is not well understood, despite the extensive research. It is suggested that production of the free oxygen radicals are responsible for killing the parasite.[9]

As resistance to quinine is common in Asia and decrease of sensitivity to quinine has been reported in Africa, intramuscular artemether appears to be an excellent alternative to intravenous quinine.[10]

Pregnant women are highly susceptible to malaria infestation. Malaria during pregnancy, causes severe maternal complications like abortion, premature labour and still-births which are higher in Plasmodium falciparum infestation.[11] Severe maternal anemia due to malaria is a leading cause of maternal mortality.[12,13]

A study was conducted in New Halfa Hospital eastern Sudan, from October 1997 to February 2001; twenty-eight pregnant women infested with Plasmodium falciparum, after failure of chloroquine and quinine therapy, were given artemether intramuscularly (six injections, a total of 480 mg) during three different periods of gestation. One patient was treated with

twelve patients received the drug during the second trimester and fifteen patients during the third trimester. The patients were free of symptoms within three days as the parasite was eliminated from the blood and the drug was well tolerated. Only one patient (3.5%) delivered at 32 weeks and six hours after birth the baby died. There were no abortion, stillbirth and congenital anomalies in the newborn and there was no mortality reported among the pregnant women.[10] When artemether and other derivatives of artemisinin were given orally or by injection, during vulnerable period of organogenesis, caused death of the embryo, blood vessels anomalies, ventricular septal defects, malformed ribs, shortened or bent long bones, defects in scapulae and incompletely ossified pelvic bones in rodents. These embryotoxic effects were due to destruction of primitive erythroblasts, which are present early in the developing embryo, by artemether and other derivatives of artemisinin, resulting in transient deficiency of the primitive erythroblasts.[14] Artemether and other derivatives of artemisinin are not recommended in the first trimester of pregnancy due to limited safety data on its use in human, although these can be given during second and third trimesters. Various studies showed that artemether caused miscarriage and cardiac anomalies like ventricular septal defect when given during vulnerable period of gestation in animals, whereas preventive role of folic acid on cardiac anomalies induced by it has not been previously investigated. The present study was therefore designed to investigate the preventive role of folic acid on the adverse effects of artemether on development of heart in Albino mice.

Methods

It was a randomized controlled experimental study conducted at the Department of Anatomy, University of Health Sciences, Lahore. Twenty four adult BALB/c strain Albino mice (eighteen females and six males) 6 - 8 weeks old, weighing from 30 to 35 grams were kept under control conditions of temperature 23 ± 2 0C, humidity 50 ± 5 % with regular 12 hours light/dark cycles. Male and female mice were put together in a ratio of 1:3 in a single cage for mating. Females were examined early morning everyday for the presence of vaginal plug; its presence indicated that mating had occurred, the day was considered as day 0 of gestation. The pregnant mice were separated, housed in a separate cage and randomly divided into three groups; A, B and C having six female mice each. Commercially available preparations of artemether, folic acid 97% and Arachis oil, the solvent for preparation of artemether injection were used. Group A was treated with single intramuscular injection of solvent, Arachis oil 10.7mg/kg, Group B was given artemether, 10.7mg/kg once daily by intramuscular injection and Group C was treated with artemether, 10.7mg/kg by intramuscular injection and folic acid 4.93 mg/kg in 0.1 ml. of distilled water once daily, from 6th to 10th day of pregnancy.

The pregnant mice were sacrificed on the 18th gestational day to deliver the fetuses.14 All live male and female fetuses were included in the study. The live fetuses were then euthanized with chloroform, examined for any gross malformations under dissecting stereo microscope and fixed in 10% formalin solution for 72 hours after decapitation. The thoracic cavity of the fetuses was opened by midline thoracoabdominal incision; heart was identified and observed under dissecting microscope for its position and that of the great vessels and any visible gross anomalies. The heart was carefully dissected and removed with the root of great vessels for histological examination. The heart was isolated immediately after the animal was sacrificed and rapidly washed with distilled water to clear its blood contaminants, weighed and fixed in 10 % formalin for 48 hours. The fixed complete fetal hearts were processed in automatic tissue processor. The tissue blocks were made; sections were cut at 5µm thickness and mounted on the albumenized glass slides, which were allowed to dry on a slide warmer. These sections were stained with Hematoxylin and Eosin (H&E) for histological study.15 The stained sections were studied under light microscope using X4, X10 and X40 objectives. These sections were evaluated for presence of the atrial and ventricular septal defects. The collected information of the study groups was analyzed using Statistical Package for Social Sciences (SPSS) version 18. The difference in the quantitative measurement was tested by one way ANOVA. Post-Hoc Tukey's test was applied to identify which group mean differed. Relevant descriptive statistics was mean and Standard deviation. The p-value of ≤0.05 was considered statistically significant.

Results

1. Macroscopic features of the heart:

The heart of each animal in control and experimental groups were light brown in colour. The position of

control and treated groups. The origin of the aorta and pulmonary trunk were normal in all groups. Gross examination of the heart revealed no structural malformation.

2. Cardiac Weight:

Cardiac weight ranged between 7.9-12.5, 5.4-9.2 and 7.4-10.6 mg in groups A, B and C respectively; mean cardiac weight was 10.31±1.38, 6.98±1.22 and 8.98 ± 0.78 in groups A, B and C respectively **(Table-1).**

One way ANOVA showed statistically significant difference in the mean cardiac weight when compared among groups (p-value =<0.001**. (Table 2).**

Table-1: Shows comparison of cardiac weight in milligrams among groups.

Variable	Group-A Mean±SD(n=46)	Group-B Mean±SD(n=16)	Group-C Mean±SD(n=20)	P-value
Cardiac Weight (mg)	10.31±1.38	6.98±1.22	8.98±0.78	<0.001*

** p value ≤ 0.05 is statistically significant.*

Table-2: Shows comparison of cardiac weight in milligrams among groups.

(I) Group	(J) Group	Mean difference (I-J)	Std. Error	P-value
A	B	3.3318	0.3578	<0.001*
	C	1.3330	0.3302	<0.001*
B	A	-3.3318	0.3578	<0.001*
	C	1.9988	0.4135	<0.001*
C	A	-1.3330	0.3302	<0.001*
	B	1.9988	0.4135	<0.001*

** p value ≤ 0.05 is statistically significant.*

Post-Hoc Tukey test indicated statistically significant difference in mean cardiac weight between group A and group B (p-value =<0.001), group B and group C (p-value = <0.001) and group A and group C p-value=<0.001) showing significant decreased in cardiac weight in group B and group C.

3- Histological examination of the myocardium of the heart. On histological examination, fetal myocardium was well developed in group A, showing mature myocardial cells with central round to ovoid nuclei and striated cytoplasm **(Fig-1).**

In group B, myocardium was underdeveloped. Myocardial cells were immature with central nuclei, oval to elongated in shape, giving the appearance of being multinucleated and had unstriated cytoplasm. Myocardium was arranged in the form of multinucleated cords of cells. Mesenchymal cells with elongated nuclei, apparently changing to fibroblasts were present **(Fig-2).**

In group C, myocardium was underdeveloped. Myoca- rdial cells were partially mature had branching pattern, oval to elongated nuclei and unstriated c a **3**

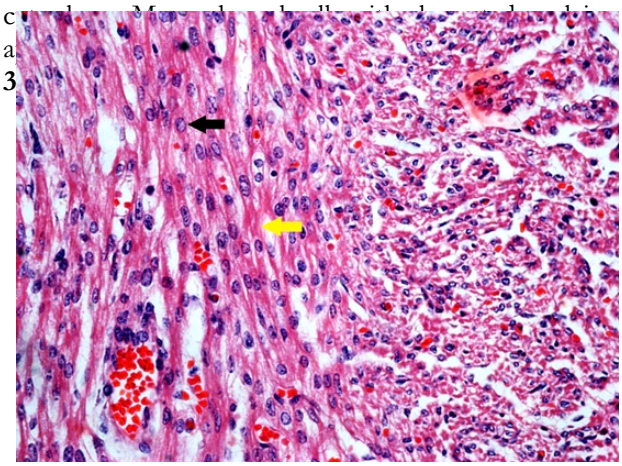

Fig-1: Photomicrograph of myocardium of ventricular wall of group A; showing mature myocardial cells with central oval nuclei (black arrow) and striated cytoplasm (yellow arrow) (Stain H&E. X400).

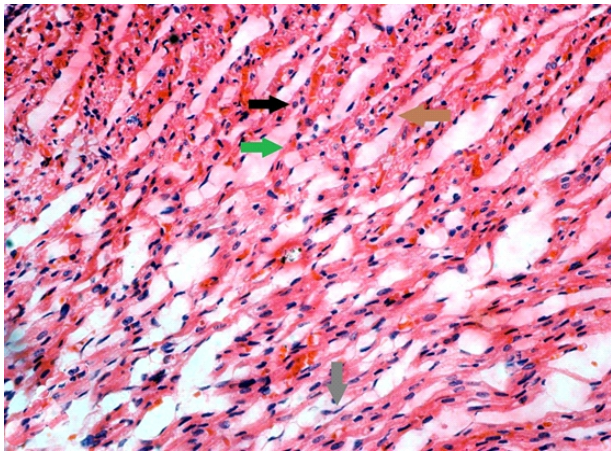

Fig-2: Photomicrograph of myocardium of ventricular wall of group B; showing underdeveloped myocardium, intercon nected cords (brown arrow) of immature myocardial cells with central nuclei (black arrow), giving the appearance of being multinucleated and unstriated cytoplasm (green arrow) mesenchymal cells (gray arrow) with elongated nuclei, apparently changing to fibrocytes (Stain H&E,X400).

Discussion

In the current investigation, the hearts appeared light

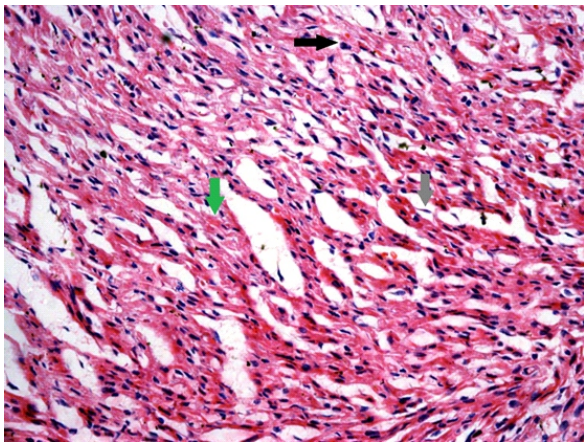

Fig-3: Photomicrograph of myocardium of ventricular wall of group C; myocardial cells are partially mature having branching pattern, with oval to elongated nuclei (black arrow), unstriated cytoplasm (green arrow) and having mesenchymal cells (gray arrow) (Stain H&E. X400).

groups. Gross examination of the heart revealed no structural malformation. Histological examination showed myocardial development in current study was delayed in groups B and C, showing presence of mesenchymal cells (Fig. 2 and 3). This observation had not been reported earlier as an effect of artemether and other derivatives of artemisinin on myocardium. Cardiac weight of animals were reduced in groups B and C and were reduced statistically significant when compared to group A. There were statistically significant decrease in cardiac weight, in group B when compared with group C **(Table 1 and 2).**

The first system which develops in embryo is cardiovascular system, which provides nutrients to the developing embryo. In mouse it begins on 7th day of gestation.[16, 17] Ventricular septal defects and various defects of skeleton, like malformed ribs, cleft sternebrae, shortened or bent long bones were seen in orally administered artesunate, a derivative of artemisinin, in pregnant rats, at doses of 6, 10 and 16.7 mg/kg, once daily, starting from Day 6 of gestation for 12 days throughout, the period of organogenesis. In rabbits, however doses of 5, 7 and 12 mg/kg once daily, starting from Day 6 of gestation for 13 days produced comparable results.[18, 19] There was an increased incidence of anomalies, when a single oral dose of 17 mg/kg of artesunate was given on day 10 of gestation to rats; in rabbits the embryolethal effect was observed as abortions and total loss of litter. These developmental effects were seen without any evidence of maternal toxicity.[18,19] It has been observed that, abnormalities of heart appeared in the rat embryo, after a single oral administration of 17 mg/kg of artesunate on day 10 of gestation; these changes are manifested in the form of reduced thickness of ventricular and atrial walls and cardiac cavity due to thin trabeculae carneae which became more evident over the next few days. The heart showed signs of recovery in the rat embryo that survived to day 14 of gestation, but its development got retarded.[20]

As evident from various studies, supporting the conclusion that periconceptional multivitamin supplementation containing folic acid may reduce the risk of congenital heart defects; the Hungarian randomized clinical trials in 1984-1991 have demonstrated that the risk for congenital anomalies of cardiovascular system and urinary system was reduced significantly after the periconceptional multivitamin supplementation containing folic acid.[21]

Conclusion

This study investigated the preventive role of folic acid on the adverse effects of artemether on the developing heart of the mouse. Cardiac weight was significantly decreased in artemether treated group. The statistically significant improvement in cardiac weight was observed in folic acid treated group. The values of the parameters were nearly comparable to those in the control group and maturation of myocardial cells on histological examination is evident indication of preventive effect of folic acid on heart.

Department of Anatomy

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Original Article

Consequences of Different Solid Malignancies in Stage I and II on The Level of Antithrombin III A Natural Anticoagulant

Beenish Ejaz, Hira Kareem, Faiza Bashir, Mehwish Farhan, Afnan Naeem and Ayesha Samad Dogar

Objective: To elaborate the association between the levels of natural anticoagulant antithrombin III (AT) in already diagnosed cases of different solid malignancies at stage I or II.

Methods: A cross sectional study was carried out in the Department of Pathology, Lahore General Hospital and Sheikh Zaid Hospital Lahore. Diagnosed cases of solid malignancies were selected from INMOL Hospital Lahore. 52 subjects of already diagnosed cases of solid malignancies were selected according to the selection criteria. They were divided in 2 groups, group 1 encompassed 26 subjects of stage I solid malignancy, while group 2 comprised of subjects who were diagnosed as stage II solid malignancy. Automated Coagulometer Sysmex CA 600 was used to measure AT levels and the subsequent data was recorded. Data was statistically analyzed using SPSS 20.

Results: The mean AT level in group I was 128.1±16.4 and in group II was 111.6±12 respectively. Results reveal that there was significant difference in mean AT level between the two groups (p value < 0.001).

Conclusions: It was concluded that the AT level is decreased in solid malignancies even in initial stages. Mean AT in subjects of group II was significantly lower (p value <0.001) as compared to subjects of group I. So, as the stage of malignancy advances AT level decreases and number of AT deficient subjects increases.

Keywords: antithrombin III (AT), solid malignancies, stage I and II.

Introduction

Cancer is a major public health problem worldwide. Among the cancer prevalence, maximum is due to solid tumors.[1] A solid tumor is an abnormal mass of tissue that usually does not contain cystic or liquid areas. Solid tumors can be benign in nature or they can be malignant.[2] Malignancy can be classified according to their primary site of origin or by histologic or tissue types. Grading of tumor is determined by the abnormality of the cells with respect to the surrounding normal tissues. Similarly malignancies can be staged by different staging methods. The most frequently used method is called TNM staging method which classifies according to tumor size (T), degree of nodal involvement or regional spread (N) and distant metastasis (M). In our study we used malignancies in stage I and in stage II, as stage I signify tumor that is limited to the tissue of origin and stage II shows limited local spread only.[3]

Malignancy is a well-known hypercoagulable state. All the patients with malignancy display a hypercoagulable state, which includes platelet activation, blood coagulation, complement activation, vasodilation and inflammation. Malignant cells can activate the clotting system directly thereby generating thrombin or indirectly by stimulating mononuclear cells to synthesize and express a variety of procoagulants. This often results in thrombosis, the second leading cause of death in patients with malignancies.[4] A thrombus that is formed is a result of alterations in the blood products especially platelets, clotting factors, the endothelium and turbulence and stasis of blood flow.[5]

A vital naturally produced thrombin inhibitor is Antithrombin III (AT). It forms thrombin-antithrombin TAT complexes through irreversible reaction with resultant inactivation of thrombin.[6,7] In malignancy the hemostatic balance of clotting and fibrinolysis is shifted to thrombosis due to the deficiency in the inhibitor molecules AT, PC and PS.[8]

Coagulation of blood is extremely coordinated so that it is constantly altered and impacted by procoagulants and anticoagulants. It is really essential to maintain a balance between the different components of coagulation so they work in harmony. So this study was conducted in order to evaluate the plasma levels of AT at stage I and II in patients of solid malignancies. It may lead to early detection or primary prevention of the complications such as thrombosis, which might be helpful in decreasing the morbidity as well as mortality of these patients by prompt

assessment of fall in the level of AT.
However, the literature is still insufficient to indicate if AT level can be used in screening programs for early detection or primary prevention of the complications.

Method

A cross sectional study has been performed. The study was performed on 52 subjects. There were 2 groups each comprising of 26 subjects. Group 1included already diagnosed cases of solid malignancies in Stage I and group 2 encompassed diagnosed cases of solid carcinomas in stage II. Cases were classified on the basis of imaging and histopathology according to the tissue type. This study incorporated Breast CA (42.3%), Lymphoma (17.3%), Female Genital Tract CA (9.6%), Gastrointestinal CA (7.7%), Bone Tumor (6.7%) and Male genital tract CA (6.7%) as presented in figure 1. Group 1: 26 diagnosed cases of stage I solid malignancy that has neither entered deeply into adjacent tissues nor has it spread into other parts or lymph nodes, also known as early stage cancer. Group 2: 26 diagnosed cases of stage II malignancy indicating limited local spread. This stage shows malignancies which are localized and not spread to the other parts of the body.
Subjects were selected with the age range of 19-85 years. Patients already having deep venous thrombosis and pulmonary embolism, hemostatic disorders, inflammatory bowel disease, severe acute infectious disease, connective tissue disorders and diabetes mellitus were excluded. Patients with known inherited thrombophilia on the basis of history and any past evidence of thrombosis were also excluded as well as patients on oral contraceptive pills (OCPs) or anticoagulants, pregnant females and those with history of stroke and /or neurosurgery within past 6 months were not included in the study.
Venous blood was drawn aseptically in a light blue top vacutainer that contains 3.2% sodium citrate anticoagulant. 2.7 ml blood in 0.3ml sodium citrate solution was taken in 9:1 ratio and centrifuged immediately to separate plasma. Samples were centrifuged for 15 minutes at 2000. Sera were stored at -80oC in freezer. Frozen plasma was thawed within 10 minutes at 37oC and homogenized by carefully mixing without foam formation. Test was carried out for AT within hours after thawing.
AT was measured applying Innovance AT kit on Siemen's fully automated Blood Coagulation Analyzer Sysmex CA 600 as per the standard procedure written in the literature of the kit by optical detection and percentage detection method.

Results

Shapiro Wilk test was applied to confirm the normality of the data. The data was not of normal distribution so Kruskal Wallis test was applied to compare the mean AT among groups. Results revealed that difference appeared significant in mean levels of AT among study groups. Mean AT in group 2

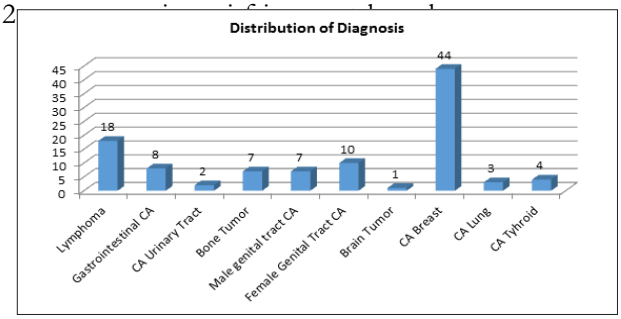

Fig-1: Malignant neoplasm distribution in study groups.

Table-1: Percentage of at deficient subjects in the study groups.

Deficiency AT	Group-I	Group-II
Yes	13 (50.0%)	23 (88.5%)
No	13 (50.0%)	3 (11.5%)
Total	26 (100%)	26 (1000%)

Key: using Chi-square test, p value <0.001 (significant)

Table-2: Showing results of study groups.

ANTITHROMBIN III					
Group	Mean±SD	Median (Inter-quartile rage)	Minimum	Maximum	p-value
Goup-1	128.1±16.4	126.1 (122.1 - 131.2)	107.0	195.3	<0.001
Goup-2	111.6±12.8	112.3 (101.1 - 121.7)	88.9	134.6	<0.001

**. The mean difference is taken as significant at 0.05 level.*

Table-3: Showing comparison of at level between two groups.

COMPARISION					
Sr. No	Groups		Mean difference	Std. Error	p-value
1	1	2	16.47308*	5.91234	0.003*

**. The mean difference is taken as significant at 0.05 level.*

compared to group 1. As the stage of malignancy increases Antithrombin III level decreases. **(Table-1)** The study participants were divided into two groups according to tumor stage. Out of 26 patients in stage II, 23 (88.5%) were found AT deficient. Out of 26 patients 13 (50.0%) were found AT deficient in stage I. Chi-square test showed a distribution difference in AT deficiency among study groups. As the stage of tumor advances number of AT deficient subjects increases. **(Table-2)** The mean AT level in group1 and 2 was 128.1 ± 16.4 and 111.6 ± 12.8 respectively. p value was calculated < 0.001 which was significant.**(Table-3)**Detailed comparison between the two groups is given in the table mentioned below. The mean difference in the level of AT between two groups was found to be significant (p value 0.003).

Discussion

Purpose of the current study was finding out deficiency in AT level, a natural anticoagulant and a core inhibitor of coagulation cascade in initial stages of solid malignancies as it is substantially increasing the risk of thrombosis that can affect the morbidity and mortality. In the current study 23 (88.5%) patients were found AT deficient in stage II and 13(50.0%) patients were found AT deficient in stage I with p value <0.001 (significant). The balance between the fibrinolytic system and coagulation cascade can shift to a prothrombotic state in malignancy due to deficiency in the inhibitory molecules such as AT.[8-12] The patients of cancer experience an elevated risk of developing thrombosis mostly in the initial three months after diagnosis.[13] AT is one of the major factors that inhibit the tumor progression and it is down regulated in tumors, so promoting their progression.[14] The plasma levels of AT correlate with tumor prognosis, aggressiveness and staging of various neoplasias.[15] AT deficient individuals have the highest risk of developing first venous thrombosis.[16] The mean level in plasma of various natural anticoagulants including AT are significantly lower in carcinoma.[11,16-18] T he current study strongly indicates a direct association between falling levels of AT with the increasing stage of solid malignancies. Further research is required in the line that antithrombin III level may be assessed for screening and prognostic purposes as this cannot only prevent disease progression but will be helpful to reduce economical burden of the diagnosis and treatment.

Conclusion

50.0% cases of group 1 i.e., 13 out of 26 cases were AT deficient and 88.5% patients of group 2 i.e., 23 out of 26 were found AT deficient. Among 52 patients of solid malignancies in stage I and II, 36 were AT deficient. This study proves that level of AT is decreased even in initial stages of solid malignancies. As the stage of solid malignancy advances, AT level decreases and number of AT deficient subjects increases.

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Original Article

Assessment of Thyroid Hormone Status of Undernourished Children of District Okara, Punjab

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Objective: To assess thyroid hormone status of undernourished children and compare with that of adequately nourished children.

Methods: Seventy one subjects with required weight, height and age were recruited for this study and were divided into two groups: Malnourished group and adequately nourished group. After taking informed consent, relevant data was collected on the proforma, blood sample was taken for estimation of thyroid function test which includes serum thyroid stimulating hormone (TSH), total thyroxine (T4) and total triiodothyronine (T3). Data was analysed by IBM SPSS version 21.p value < 0.05 was considered statistically significant.

Results: Levels of thyroid stimulating hormone (TSH) were higher in undernourished children (2.36 ± 0.30 µIU/ml) as compared to normal (1.3 µIU/ml) whereas levels of total triiodothyronine and total thyroxine, were lower in undernourished children as compared to normal.

Conclusions: These results strongly predict that in protein and energy malnutrition thyroid gland has to do extra effort to combat this condition as depicted by higher TSH levels and lower levels of T3 and T4.

Keywords: thyroid function test, malnutrition in children.

Introduction

Protein energy malnutrition (PEM) is surprisingly common in children and has a significant impact on physical and mental growth of a child. [1]According to WHO estimates, worldwide prevalence of malnutrition is 17.6% with 113.4 million children of less than 5 years of age are affected by low weight for age.[2] The WHO estimates that nearly half of all deaths, occurring among children aged less than five years in the developing countries, can be attributed to malnutrition.[3] Malnutrition is still a challenge for Pakistan as 14% of children less than 5 years of age were found to be wasted, 31% were reported underweight and 42% were found to be stunted.[4] Nutrition and endocrinology are linked from time ancient with the premise that adequate nutrition is required for statural growth. Nutritional endocrine disorders are characterized by alteration in the function or structure of the endocrine glands with resulting clinical consequences due to the deficiency or excess of a dietary compound.[4]

Thyroid hormone plays an important role in regulation of lipid and carbohydrate metabolism and is necessary for normal growth and maturation.[5] Absence of thyroid hormone causes mental and physical slowing, mental retardation and dwarfism.[6] Alterations in nutritional state, whether short term or chronic, affect physiology of the thyroid hormone, especially peripheral hormone metabolism. The changes in thyroid homeostasis have not been enough focused.[7] In PEM, there are marked changes in secretion and metabolism of thyroid hormones and in the structure of thyroid gland. This results in reduction of the activity of the gland, as the body tries to adapt to low calorie intake.[8] In cases of severely malnourished wasted children, serum total protein and albumin are reduced whereas increased globulin level is expected since malnutrition is commonly associated with infections.[19,20]

Thyroid hormone is very important for normal growth and development as it help in cell differentiation and maturation. It plays important role in all stage of aging including pregnancy, infancy, childhood and even post-menopause. Fall in thyroxine level in first trimester of pregnancy cause psychomotor and mental derangements in affected children.[9] Thus thyroid studies are of greater importance in malnutrition because inadequate functioning of thyroid serious negative implications not only on the individual but also on the family and society. This study will help us to assess the thyroid hormone status of malnourished children so that we can plan out the strategies to maintain thyroid level within normal functioning state in the affected population.

Methods

This cross-sectional study was carried out in lowest social status population locality in the outer fringes of

Okara, Punjab. Children were approached at their homes and primary education centre. Total 71 children were included in the study and divided into two groups. Out of which 40 children were undernourished and belong to undernourished group and 31 were adequately nourished and belong to adequately nourished group. After taking informed consent from children parents or guardians, following measurements were done. Each child's weight, height and MUAC were measured and compared with Z measurements score chart (CMAM protocol) for grading of their nutritional status. The weight was recorded on an electronic weighing scale to the nearest of 5 g. Four ml venous blood sample was drawn from antecubital vein of each subject and added in serum tube i.e. red top vacutainer Blood in red vacutainer was centrifuged (1600rpm for 15 minutes), serum was separated, divided into aliquots and frozen at -80 °C to be used later for analysis. Serum Thyroid stimulating hormone (TSH), total triidothyroine (T3) and total thyroxine (T_4) was measured by AccuBind ELISA microwells (product code 1225-300) of Monobind Inc. CA, USA. Data was analysed through IBM SPSS version 23. Groups are compared by measuring means and standard of means. Significance of difference was determined with two sample test and ANOVA. p-value<0.05 was considered statistically significant.

Results

To assess thyroid hormone status, serum TSH, T3 and T4 levels were estimated in both groups.Levels of serum TSH were found to be significantly higher (2.36±0.30μIU/ml) in undernourished group as compare to (1.588±0.17μIU/ml) in adequately nourished group (p-value=0.288) as shown in **(Table-1).** The mean concentration of T4 in undernourished children group was 1.963±0.087μg/dl and it was significantly lower (p-value = 0.05) than its value in adequately nourished children group (2.69±0.36 μg/dl) as shown in **(Table-2)**.

The mean concentration of T3 in undernourished children group was 8.78±0.66ng/dl and it was significantly lower (p-value=0.01) than its value in adequately nourished children group (13.37±0.74ng/dl) as shown in **(Table-3)**.

Discussion

Protein energy malnutrition is an important health problem for under developing country like Pakistan. In this study, we researched the effect of malnutrition on thyroid hormone of undernourished children of

Table-1: Comparison of serum thyroid stimulating hormone between undernourished (group1) and adequately nourished children (group-2).

Marker	Groups	N	Mean±SEM μg/dl	P-value
Serum TSH	Group-1 Undernourished children	36	2.36±0.30	0.028
	Group-2 Adequately nourished children	27	1.588±0.17	

Table-2: Comparison of serum total thyroxine between undernourished (group1) and adequately nourished children (group 2).

Marker	Groups	N	Mean±SEM μg/dl	P-value
Serum total Thyroxine	Group-1 Undernourished children	36	1.963±0.087	0.05
	Group-2 Adequately nourished children	30	2.69±0.36	

Table-3: Comparison of serum total triiodothyronine between undernourished (group1) and adequately nourished children (group 2).

Marker	Groups	N	Mean±SEM μg/dl	P-value
Serum total Triiodothyronine	Group-1 Undernourished children	36	8.87±0.66	0.01
	Group-2 Adequately nourished children	30	13.37±0.74	

Pakistan. For this purpose, we compared thyroid function test among undernourished and adequately nourished children.

Nutrition is defined as the replacement of consumed chemistry of the metabolizing body. Therefore adequate nutrition maintains the health of the individual and inadequate nutrition failing to replenish chemicals adversely affects physiological mechanism of the body.

When we compared levels of thyroid stimulating hormone (TSH) in between undernourished and adequately nourished group. It was found to be significantly higher in undernourished group (p-value = 0.028) as compare to adequately nourished group. These results were similar with research conducted by Dhanjal and Singh, 2017 in Haryana,[6] India where they found higher levels of serum TSH in malnourished controls (p-value < 0.001). But in contrary to our study, Abrol et al.[4] and Turkay S et al.[10] in their study found no significant difference in TSH when PEM children were compared to healthy controls.

This elevated level of serum TSH in undernourished children is due to the decreased secretory capacity of thyroid hormone specifically T4 which inhibits negative feedback mechanism.[11] Shahjadi et al, 2011 reported that in chronic severe PEM, the reserves are depleted which causes decrease secretion of thyroid and adaptation of thyroid may fail thus raising TSH level.[12]

Serum T3 and serum T4 levels were found to significantly lower in the malnourished group as compare to the adequately nourished group (p value < 0.001). The result of our study were similar to that seen in other studies. In the study done by Shaheen B et al. the mean fT3 value in cases was 1.5 pg /ml±0.3 and in controls was 2.3 pg /ml±0.5 (p <0.0001)[13] while there was a significant decrease in the mean T3 and T4 values in PEM patients in the study done by Shahjadi S et al. [12]when compared to control group but there was no statistically significant difference within subgroups of cases. These resulst are attributed to the fact of decerase protein uptake and reduced biosynthesis.[18] Lazarus et al have also reported decreased T4 levels in the malnourished children in India.[14] Studies from Turkey and Bangladesh reported that mean T3 and T4 levels were extremely low in PEM cases as compared to controls.[16] It is found in animal studies that during starvation, the activity of enzyme 5-deiodinase, uptake of T4 by liver are decreased. This probability is also considered above in argument of marked lower levels of T3 in undernourished group than controls. Similarly, Valinjikar et al compared the levels between children of severe and moderate malnourished children and reported results comparable to ours.[17]

The present study strongly suggests that the state in particular and society in general must address PEM to avoid the increasing population of subjects with deficient intellectual and cognitive abilities.

Conclusion

These results strongly predict that in protein and energy malnutrition thyroid gland has to do extra effort to combat this condition as depicted by higher TSH levels and lower levels of T3 and T4.

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Original Article

Comparison of Caudal Block and Local Bupivacaine in Children for Post-operative Pain

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Objective: To compare efficacy of caudal block with Bupivacaine and local infiltration of wound with Bupivacaine in children after inguinal herniotomy so as to replace narcotic analgesics with other alternatives particularly in daycare surgeries.

Methods: Present randomized controlled trial conducted in Paediatric Surgery Unit, Services Hospital, Lahore for a period one year. Patients were randomly divided in two groups by lottery method. Group A: Caudal group, Group B: Local Bupivacaine. Postoperatively patients were assessed for pain using Wong Bakers Faces pain scale. The intensity of the pain was recorded at 0, 1, 2, 4, 6 and 8 hours. Statistical analysis was done using SPSS version 20.

Results: A total of 150 patients were included in the study, fulfilling the inclusion and exclusion criteria. In group A 12 while 9 patients while in group B 9 were postponed due to low hemoglobin or other causes like respiratory tract infection. Remaining patients who completed the study were 63 in group A and 66 in group B. P value was significant (<0.005) in both groups at 0 hour but at 1, 2,4 and 8 hour it was not significant. Mean pain scores in group A were less than group B at all readings. In group A, 21 patients (33.33 %) needed rescue analgesic while in group B, 24 patients (36.33%) needed rescue analgesic (P=0.698). Mean time for requirement of rescue analgesic was 4.66 ± 2.105hours in group A while 5.000±2.043hours in group B (P=0.169).

Conclusions: Present study showed caudal with bupivacaine is slightly superior, however both techniques are effective for post operative pain control in children after inguinal herniotomy.

Keywords: caudal block; local bupivacaine; children; post-operative pain.

Introduction

Post-operative pain control has been a major concern for the surgeons in general and particularly in children. Most commonly paediatric surgeons had been using opioid analgesics which are associated with certain side effects including nausea, pruritis and respiratory depression. In order to avoid such effects in children particularly for daycare procedures like inguinal herniotomy, a search for alternative technique had been under discussion for a long period.[1] Caudal block for inguinal surgeries in children was first introduced by Cambell in 1933 and is being practiced widely with different combinations of drugs, Bupivacaine being most commonly used. It was found an alternative to opioid analgesics as it was found reducing requirement of inhalational anesthetics and post-operative analgesics in children. However it is also not without side effects and most commonly encountered are urinary hesitancy, motor weakness of limbs and postural hypotension.[2] Also because of well-developed blood vessels in sacral area, there had been reports that the possibility of systemic toxicity is always there if no blood draw on aspiration even needle is within the vessel.[3] Local infiltration of Bupivacaine is also being used for post-operative pain management in children effectively and many trials have ascertained its efficacy in small procedure.[4] The aim of the study was to compare efficacy of caudal block with Bupivacaine and local infiltration of wound with Bupivacaine in children after inguinal herniotomy so as to replace narcotic analgesics with other alternatives particularly in daycare surgeries.

Methods

This was a randomized controlled trial conducted in Paediatric Surgery Unit, Services Hospital, Lahore for a period one year from Jan, 2014 to Dec, 2014. After getting approval from ethical committee, all male and female patients between ages of 1 to 12 years undergoing elective inguinal herniotomy were included in the study. Patients of American society of Anesthesiologists (ASA) class≥III, those on analgesics, obstructed inguinal hernia and those with other associated problems were excluded from the study. A total of 150 patients fulfilling the inclusion and exclusion criteria were included in the study. Patients were randomly divided in two groups by lottery method. Group A: Caudal group, Group B: Local Bupivacaine. For inclusion in the study consent was taken from by guardian of each child. All the patients were operated electively by Paediatric surgical team of the same hospital. All the patients were

provided with the anesthesia in a standard manner which included midazolam (0.05 mg/kg), Ketorolac (0.5mg/kg) Propofol at 1.5 to 2 mg/kg used for induction. While 1.0 mg/kg Suxamethonium chloride used before intubation. Isoflurane 0.7 to 1.5% & low flow oxygen used for anesthesia maintenance. Additionally, Atracurium 0.5mg/kg as bolus dose was given and if needed was repeated as 0.1mg/kg to facilitate artificial ventilation. Three lead electrocardiograph & pulse oximetry was used to monitor the vital during surgery. Isoflurane was replaced with 100 percent O_2 about 5 min before completion of procedure. While Neostigmine & Atropine used as reversal drugs. Patients were extubated according to the standard train-of-four criteria. At the end of the procedure, patients in group A were given caudal block with 0.7 $ml.kg^{-1}$ of 0.25% Bupivacaine while patients in group B patents, injection Bupivacaine was locally infiltrated in the wound. Postoperatively patients were assessed for pain using Wong Bakers Faces pain scale. The intensity of the pain was recorded for all patients using Faces Pain Scale **(Fig-1)** at 0, 1, 2, 4, 6 and 8 hours after surgery by on duty doctor, who was not aware of the drug given to the patient. If the patient develops pain score ≥4, patient was given intravenous Nalbuphine 0.2 mg/kg and it was recorded. After 8 hours of surgery, patients were given oral Ibuprophen (10mg/kg) and were discharged after assessment by senior team member on duty. All the data including demographic details were recorded in the proforma. Statistical analysis was done using SPSS version 20, arithmetic mean and standard deviation values for different variables were calculated and statistical analyses were performed for each group. Independent sample t-test was used to compare continuous variables exhibiting normal distribution, and Chi-squared or Fisher exact test for non-continuous variables. *P*<0.05 is considered significant.

Results

A total of 150 patients were included in the study, fulfilling the inclusion and exclusion criteria. They were randomly divided into group, 75 patients being in each group. However 12 patients in group A while 9 patients in group B were postponed due to low hemoglobin or other causes like respiratory tract infection. Remaining patients who completed the study were 63 in group A and 66 in group B [Table 2]. Demographic details including age, gender distribution and site of inguinal hernia were comparable in both groups as tabulated in **Table-1.** Pain scores of the patients noted at 0 hour, 1 hour, 2 hour, 4 hour and 8 hours are given in table 2 along with P value. P value was significant (<0.005) in both groups at 0 hour but at 1, 2,4 and 8 hour it was not significant. Also mean pain scores in group A were less than group B at all readings. In group A, 21 patients (33.33 %) needed rescue analgesic while in group B, 24 patients (36.33%) needed rescue analgesic (P=0.698). Mean time for requirement of rescue analgesic was 4.666±2.105hours in group A while 5.000±2.043hours in group B (P=0.169).

Table-1: Demographic details of patients in both groups.

		Group A (Caudal Block)	Group B (Local Bupivacaine)
Age (in years)	(Mean±SD)	4.166±3.36	3.56±2.74
Gender	Male	49	54
	Female	14	12
Side Involved	Right	42	32
	Left	14	12
	Bilateral	7	13

Table-2: Comparison of Pain score in both groups.

	Group A (Caudal Block)	Group A (Caudal Block)	P-value
0 Hour	1.8±1.972	2.666±2.168	0.026
1 Hour	2.666±2.094	3.142±1.891	0.164
2 Hour	3.238±3.415	3.111±1.893	0.797
4 Hour	3.269±2.671	3.619±3.695	0.552
8 Hour	2.222±2.275	2.031±2.77	0.670

Fig-1: FACES Pain scale

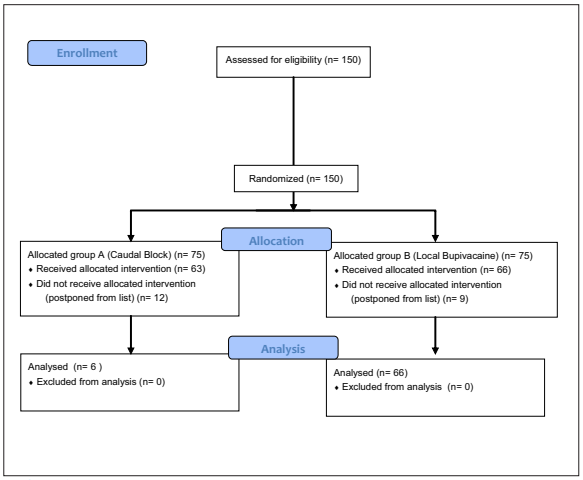

Fig-2: Consort flow diagram.

Discussion

Greek Philosopher; Aristotle proposed that pain was a passion of the soul.[5] There is much debate about what therapeutic modality is appropriate for pain control after different types of procedures. Which is the best technique of regional anesthesia is still unknown.[6] We compare caudal block efficacy with bupivacaine and local infiltration of bupivacaine. Bupivacaine is the most commonly used agent for caudal block.[7] Toxicity of local bupivacaine can be avoided if only recommended dose is given.[8] We used volume & concentration range same as Gavrilovska et al, mention for their study i.e. 0.7ml /kg of 0.25% for caudal block & local infiltration.[9]

In our study pain score was noted at 5 points and P value was found significant (<0.005) in both groups at 0 hour but it was not significant during rest of the readings. Seyed Abbas HJ et al compared three agents (I) acetaminophen suppository (II) wound infiltration of bupivacaine (III) caudal block with bupivacaine and they noted that there is no significant differences at any of recorded reading in the bupivacaine wound infiltration and caudal block groups (P=0.848), how're they reported significant statistical differences between these two groups and the acetaminophen group (P<0.05).[10]

In another study, the postoperative analgesic effect of suppository paracetamol was compared with the combination of paracetamol suppository and bupivacaine wound infiltration for inguinal herniorrhaphy in pediatric patients & author found that combination of these two methods produced better analgesia than suppository paracetamol alone.[12] Razavi and colleagues found that the caudal anesthesia in relieving pain after pediatric inguinal surgery was more effective than acetaminophen suppository.[12] We observed that mean pain scores in group A were less than group B at all readings. Conroy et al also reported higher mean pain score for bupivacaine infiltration group as compared to caudal block group.[13] Machotta A compared caudal block and wound infiltration and found no significant difference of pain score between two groups.[14] But Petersen et al., reported that during inguinal hernia repair in children, wound infiltration is as good as ilioinguinal-iliohypogastric nerve block or caudal block up to a couple of hours following surgery. Many other studies have examined postoperative analgesia following infiltration of bupivacaine into the wound after herniorrhaphy and found a beneficial effect.[1]

Need for rescue analgesia in our study was seen in 33.33% & 36.33 in caudal block and local infiltration group respectively. Conroy et al. reported that in caudal block group patient required supplemental analgesia was 37.14% while 55% patients in infiltration group.[13]

We found that Mean time for requirement of rescue analgesic was 4.666±2.105 hours in group A while 5.000 ± 2.043hours in group B. Laiq N et, al. compared caudal bupivacaine & bupivacaine plus tramadol and found that caudal block group needed rescues analgesia in 50% and 66% patients at 4 & 6 postoperative hour respectively.[16]

Seyed Abbas HJ et al compared three agents and found that duration of analgesia for caudal group was 5.37±1.79 and bupivacaine local infiltration was 5.40± 1.73 while 4.407 in acetaminophen suppositories group and p valve was not significant for caudal block and infiltration group comparison.[10]

Conclusion

Present study showed caudal with bupivacaine is slightly superior at 0 hour & in rescue analgesia requirement; however both techniques are effective for post operative pain control in children after inguinal herniotomy.

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Original Article

Effect of Cinnamomum cassia Bark Extract, Pyridoxine and Pitavastatin on Diet-Induced Murine Hypertriglyceridemia and Obesity

Maryam Mansoor, Saadia Shahzad Alam, Iram Imran, Talha Laique and Kamran Dawood Ahmad

Objective: To compare effects of aqueous Cinnamomum cassia bark extract (ACCE), pyridoxine (PYR) and pitavastatin (PIT) and dietary prevention on TG and body weight of rats.

Methods: Sixty albino male rats: sorted into 10 groups (Group 1 - control). Group 2 (dietary preventive) and Groups 3-10 (therapeutic) were induced using HFD for 30 days (HFD continued throughout). Group 2 was later reverted to normal diet. They were treated post-induction for 30 days, once daily: Group 3 (PIT 0.3mg/kg); Group 4 (PYR 18mg/kg), Group 5 (ACCE 200mg/kg), Group 6 (PIT 0.3mg/kg + PYR 18mg/kg), Group 7 (PYR 18mg/kg + ACCE 200mg/kg), Group 8 (PIT 0.3mg/kg + ACCE 200mg/kg), Group 9 (PIT 0.3mg/kg + PYR 18mg/kg + ACCE 200mg/kg) and Group 10 (PIT 0.15mg/kg + PYR 9mg/kg + ACCE 100mg/kg). TG and weight was checked (Day 0, Day 30, Day 60) and data analyzed using SPSS 20.0 ($P \leq 0.05$).

Results: Rats showed significant reduction in serum TG after treatment. Maximum effect was seen in Group 7 (PYR 18mg/kg + ACCE 200mg/kg) where TG levels decreased to 94.667 ± 20.077 mg/dL. Dietary alteration in Group 2 resulted in only marginal improvement. Weight reduction of 23 gm was seen in Group 4 (ACCE 200mg/kg).

Conclusions: Cinnamon, pyridoxine and pitavastatin showed remarkable TG-lowering activity. PYR and ACCE exhibited additive effect (39%), endorsing the need for "integrated" approach. Cinnamon can treat obesity in humans.

Keywords: hypertriglyceridemia, cinnamon, pyridoxine, pitavastatin, high-fat diet.

Introduction

Hypertriglyceridemia (HTG), known as "hyperlipemia", a common disorder all over the world, is a condition of raised serum triglycerides. In experimental and epidemiologic studies, hyperlipemia is a strong risk factor for cardiovascular disorders especially ischemic heart diseases (IHDs) especially coronary artery diseases (CAD).[1] It can be classified into primary and secondary hypertriglyceridemia. Primary hypertriglyceridemia is mostly genetic.[2] Secondary hypertriglyceridemia is however, acquired: caused or exacerbated by obesity, diabetes mellitus, endocrine disorders, diet and lifestyle, all are prevalent in more modernized societies.[1] Based on NCEP (National Cholesterol Education Program) ATIII Guidelines, HTG is defined as a fasting serum triglyceride level greater than 200 mg/dL.[3] Obesity has been found to be linked to HTG. Both are often found together in an ominous picture of "metabolic syndrome", together with other disorders. Obesity is a complex multi-factorial (genetics, environment) chronic metabolic disorder. Its prevalence is increasing day by day, making it the second leading cause of morbidity and mortality globally. It has been estimated to cause approximately 2.6 million deaths worldwide.[4] Mild HTG can be controlled by lifestyle modification: dietary counselling and increasing physical activity to achieve weight reduction in overweight/obese patients, linking it to obesity. Severe HTG has an underlying etiology of commonly, an amalgam of both factors: genetic and secondary. Family history of dyslipidemia and cardiovascular diseases for future risk assessment,[5,6] history of alcoholism and use of notorious medications should be probed. Physical findings pan across multi-organ systems and hospital admission for aggressive medical treatment is necessary (abdominal pain/pancreatitis).[6]

Treatment of severe HTG necessitates the use of pharmacologic agents. Intravenous insulin and rarely, plasma exchange may be needed if oral therapy fails. Patients should be assessed for other CV risk factors e.g. central obesity, hypertension, glucose metabolism abnormalities and liver disorders. Niacin, fibrates and omega-3 fatty acids with or without statins (reductase inhibitors) are routinely used. Statins can thus be useful in treating mild-moderate HTG alone, especially when indicated to decrease cardiovascular risk.[5] The model of HTG used in this study comes under mild HTG. Hence they are prescribed worldwide for risk reduction of CVDs. Thus we have

and lower serum lipids especially TC, LDL-C and TGs.[7] Pharmacological treatment has its advantages and disadvantages, both. So, emphasis has been made on the utilization of phyto-alternatives for treatment of various ailments.[8] Plants and plant products are becoming first choice of masses of the developing world owing to their reputation of being effective, safe and affordable.[10] Their use has also been penned down in various pharmacopoeias.[9] Experimentation with plants have shown promising results in rats, e.g. Brassica compestris (mustard), Trigonella feonum-graecum (fenugreek) and Cinnamomum cassia (Cinnamon), etc. lower serum TGs.[11] Cinnamomum cassia especially bark extracts, have traditionally been used in treating lipid-related disorders due to its anti-hyperlipidemic activity.[12]

Researchers have claimed that it reduces lipid levels notably total cholesterol, TGs and LDL substantially in experimental animals as well as humans; treats diabetes and obesity, and stabilizes blood pressure.[12,13] Several micronutrients have also been found useful in the treatment of dyslipidemia especially niacin, cobalamin,[14,15] lysine, pyridoxine and more.[11] Pyridoxine (Vitamin B_6)is present in the body in interconvertible "alcohol", "aldehyde" and "amine" forms.[16] It shows pronounced effect in decreasing TGs by affecting mobilization of unsaturated FAs from TGs to phospholipids.[17]

There is a need to find out about which approach to the treatment of hypertriglyceridemia (HTG) and obesity is more beneficial: pharmacotherapy, phytotherapy or micronutrient approach. Also, more studies are needed be conducted to find out whether they could or couldn't be used in combination and that which combination would be the most efficacious. Keeping this in view, the study was designed to investigate the most efficacious options out of pitavastatin, cinnamon or pyridoxine in treating HTG and obesity in rats.

Methods

Quasi-experimental animal trial & simple random sampling; n=6. Pitavastatin (2mg) tablets, Pyridoxine (25mg) tablets were purchased from Clinix Pharmacy, Lahore. Cinnamon bark was purchased from Hamdard Dawakhana, Lahore.1kg Cinnamomum cassia bark was cleaned, dried in a shady place and extracted with 4L of distilled water at 90°C for 16 hours, twice. Extract was filtered and then freeze-dried for storage and preservation at room temperature till use; ready to be diluted in normal saline (0.9%) and orally administered at 200mg/kg. Dry yield was 8% (w/w).[18] The extract was prepared at Pharmacology Laboratory, UHS, Lahore. 60 healthy young male albino rats (6 weeks of age), weighing 150-170 grams, were purchased from UHS, Lahore and were kept in polypropylene cages at UHS under standard lighting & housing conditions; were fed laboratory prepared diet and tap water, ad libitum. Controls received normal diet. In experimental groups, High-Fat Diet (HFD) was used for induction of hypertriglyceridemia and obesity for 30 days. HFD **(Table-1)** was purchased from University of Veterinary and Animal Sciences, Lahore. Group 2 received HFD for only 30 days and was later on, reverted to normal laboratory diet from Day 30-Day 60 (end of the study period) and left untreated to study preventive role of dietary modification. The rest of the groups 3-10 were continued on HFD throughout along with treatment.[19] In this study, 10 groups of 6 animals each were used **(Table -1)**. Body weight and TGs of the rats were checked at Day 0, Day 30 and Day 60; data analyzed using SPSS 20.0 ($P \leq 0.05$). Weight was estimated using electronic weighing balance. Blood samples for TGs were collected via cardiac puncture technique into serum v

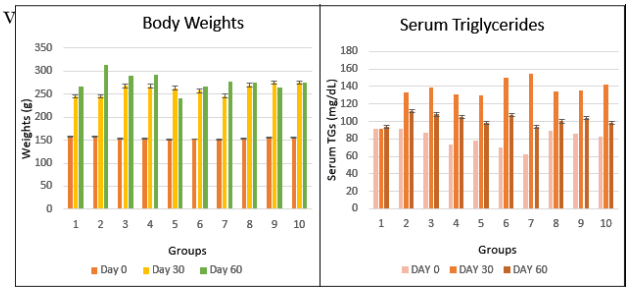

Fig-1: Comparison of weights& triglycerides at day 0, 30 and 60.

Table-1: Groups Distribution and constituents of HFD.

Group	Distribution
Group 1	Control
Group 2	(Preventive Model - HFD + Normal Diet)
Group 3	(HFD + 0.3mg/kg Pitavastatin)
Group 4	(HFD + 18mg/kg Pyridoxine)
Group 5	(HFD + 200mg/kg aqueous cinnamon extract - ACCE)
Group 6	(HFD + 0.3mg/kg Pitvastatin + 18mg/kg Pyridoxine)
Group 7	(HFD + 18mg/kg Pyridoxine + 200mg/kg ACCE)
Group 8	(HFD + 0.3mg/kg Pitavastatin + 200mg/kg ACCE)
Group 9	(HFD + 0.3mg/kg Pitavastatin + 18mg/kg Pyridoxine + 200mg/kg ACCE)
Group 10	(HFD + 0.15mg/kg Pitavastatin + 9mg/kg Pyridoxine + 100mg/kg ACCE)

Constituents of HFD: Casein: 120g; Corn starch: 549.6g: Soybean oil: 250g; Cholesterol: 10; Choline: 0.4g; Salt mixture: 50g; Vitamin mixture: 10g; Cellulose: 10g; Total calories (Kcal)-5018.4/1000g of diet

anticoagulant, centrifuged at 3000 RPM for 15 mins and stored at -20±2 °C in Eppendorf tubes, later estimated using kits at Biochemistry Laboratory of Shaikh Zayed Hospital, Lahore.

Results

Table-2: Results of body weights of rats

Group	n	Body Weight (g) Day 0 Mean±SD	Day 30 (After induction) Mean±SD	Day 60 (after treatment) Mean±SD
01	6	158.00±7.155	245.67±13.171	267.67±9.750
02	6	157.33±8.914	245.67±14.459	314.67±21.119
03	6	153.67±5.279	268.67±14.459	289.00±21.119
04	6	154.00±2.828	267.33±14.459	291.67±25.089
05	6	151.67±1.966	263.67±11.130	240.00±20.861
06	6	152.00±2.191	157.00±14.464	267.67±26.726
07	6	151.67±1.966	246.67±1.482	277.00±28.362
08	6	153.67±6.250	269.00±12.442	275.33±22.438
09	6	155.67±62.250	275.67±18.435	264.33±27.259
10	6	155.00±4.336	275.67±26.964	256.00±19.799

ANOVA Day 60 = 0.002

Legend:	
Group 1	Controls
Group 2	HFD + Self-recovery
Group 3	HFD + 0.54mg/kg PIT
Group 4	HFD + 18mg/kg PYR
Group 5	HFD + 200mg/kg ACCE
Group 6	HFD + 0.3mg/kg PIT + 18mg/kg PYR
Group 7	HFD + 18mg/kg PYR + 200mg/kg ACCE
Group 8	FD + 0.3mg/kg PIT + 200mg/kg ACCE
Group 9	HFD + 0.3mg/kg PIT + 18mg/kg PYR + 200mg/kg ACCE
Group 10	HFD + 0.15mg/kg PIT + 9mg/kg PYR + 100mg/kg ACCE

Table-3: Results of serum triglycerides of rats

Group	n	Serum triglyscerides (mg/dL) Day 0 Mean±SD	Day 30 (After induction) Mean±SD	Day 60 (after treatment) Mean±SD
01	6	91.500±14.039	92.167±11.427	94.500±13.635
02	6	91.167±17.093	133.333±9.791	112.000±11.662
03	6	87.167±12.123	139.500±36.259	108.500±13.323
04	6	73.167±8.519	131.000±21.587	105.333±6.055
05	6	78.000±8.509	130.333±12.242	98.667±11.308
06	6	70.333±3.724	15.833±15.407	107.500±18.918
07	6	62.333±6.593	155.167±11.321	94.667±20.077
08	6	89.500±8.689	134.167±13.977	100.000±4.427
09	6	86.000±9.890	135.667±10.985	104.333±8.595
10	6	83667±5.465	142.333±13.277	98.333±8.779

ANOVA Day 60 = 0.230 Reference Range: 55-75 (65 ± 14) mg/dL

Discussion

Hypertriglyceridemia (HTG) is an established risk factor for coronary artery diseases. Pharmacological treatment is rendered essential. Phyto-alternatives and micronutrients have also garnered support recently. This study determines the role of dietary prevention and also compares the triglyceride (TG)-lowering & anti-obesity effects of aqueous Cinnamomum cassia bark extract (ACCE) and pyridoxine (PYR): alone and in combinations. Body weight was checked at Day 0, Day 30 and Day 60 to see whether dietary factors, individual drugs or their combinations were helpful in reducing weight. Healthy controls were maintained on standard lab diet throughout and weight increased from a mean of 158g to 267g, as the rats were in growing phase and could gain 2-3 grams weight per day.[20] At Day 30 after induction, weight in all the experimental groups increased. At the end of the study, Group 2 showed a net weight gain of 28% despite reverting to normal diet (without therapeutic intervention), signifying the impossibility of weight loss in the absence of treatment. Therapeutic groups' results showed significant (P: 0.002) difference in weight amongst the groups. Overall, only 3 groups showed weight reduction, among which the most significant result was shown by Group 5 (ACCE 200mg/kg) of 9.6% (240g from 263g) which was also supported by many previous studies. Cinnamon may exert anti-obesity action by enhancing insulin sensitivity,[21] altering fat storage and utilization,[22] anti-oxidant mechanisms,[23] affecting ghrelin secretion and stomach emptying and releasing "catechins"- which increase thermogenesis and fat oxidation . The current study also authenticates cinnamon's role in reducing weight without making significant dietary modifications. Weight reduction in Groups 9 (PIT 0.3mg/kg + PYR 18mg/kg +ACCE 200mg/kg) and Group 10 (PIT 0.15mg/kg + PYR 9mg/kg + ACCE 100mg/kg) was 4.7% (264g from 275g)and 6.9% (256g from 275g),respectively, despite being continued on HFD for 30 days, highlighting the additive weight-lowering effect in Group 9 and synergistic in Group 10 (half-doses).Statins can help in reducing weight due to their enhancement of rapid clearance of lipids especially LDL-C. Also they increase the reverse transport of lipids which discourages their storage in the adipose tissue by raising HDL-C (2). Pyridoxine is also involved in overall lipid metabolism and reduces storage of fats as well as their rise in blood.[24]

Consuming HFD for 30 days resulted in significantly raised TGs in experimental groups. At Day 60,TGs

lowering effect seen in Group 2 (preventive) validating the inadequacy of preventive strategy alone in handling hyperlipemia. Groups 6(PIT 0.3mg/kg+PYR 18mg/kg), Group 7(PYR 18mg/kg+ACCE 200mg/kg) and Group10(PIT 0.15mg/kg+PYR 9mg/kg+ACCE 100mg/kg) revealed the most favorable hypotriglyceridemic effect of 28.6% (107mg/dL from 150mg/dL), 39% (94mg/dL from 155mg/dL) and 31% (98mg/dL from 142mg/dL),respectively. As pyridoxine was found constant in every group, it can be deduced that pyridoxine showed a "synergistic" effect on serum TGs in each combination with statin and cinnamon, even when their doses were halved (Group 10). No previous study exists to support their synergism. The potent TG-lowering effect of these agents, individually, was also supported by previous studies especially pyridoxine. Pyridoxine is known to affect methylation of phospholipids, desaturation and elongation of FAs and mobilization of unsaturated FAs from TGs to phospholipids.[17] Cinnamon acts like a dual activator of PPAR-ɣ and PPAR-α,[25] which regulate metabolism of blood glucose and lipids, respectively. As a vital part of its effect on metabolism of carbohydrates, it enhances insulin sensitivity. And one of the important actions of insulin is to promote deposition of lipids into the stores (as TGs) and increase their clearance from the blood. That is why TG levels fall rapidly when cinnamon is administered.[26]

So, it can be summarized that pyridoxine and cinnamon, both have beneficial anti-obesity and TG-lowering effects comparable to any standard pharmacological treatment (pitavastatin in this case). As recently, people's trust on plant products and micronutrients seems to be regained, other beneficial outcomes of the use of these agents need to be explored and assayed with routinely used pharmacological agents

Conclusion

Cinnamon, pyridoxine and pitavastatin remarkably decreased serum triglycerides, individually as well as in combinations, which signify their additive effects. Dietary prevention in the absence of treatment also plays a minor role. Cinnamon's beneficial role in treating obesity has also been evident as it alone reduced body weight of the rats, despite their consumption of high-fat diet throughout the study period. Hence, micronutrients and phyto-alternatives can also be utilized for the treatment of hypertriglyceridemia and obesity in humans along with pharmacological agents

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Original Article

The Comparision of Outcome of Microscopic Versus Endoscopic Trans-sphenoidal Surgery for Pituitary Adenoma

Muhammad Adnan, Muhammad Jahangir Khan, Attique ur Rehman, Shahzad Shams, Hassaan Zahid and Sami Mumtaz

Objective: To compare the efficacy of endoscopic transsphenoidal surgery with microscopic transsphenoidal surgery among patients who were operated for pituitary adenomas.

Methods: This randomized control trial was carried out in Neurosurgery Department, Sir Ganga Ram Hospital Lahore from September 2011 till September 2015. Sample size of 140 (70 in each group) was estimated and non-probability purposive sampling technique was used. Patients of pituitary adenomas were randomly selected for each of the procedure and an informed consent was taken. Two groups of patients were made. Group A patients underwent endoscopic surgery for pituitary tumor and Group B patients were operated by microscopic technique. After 48 hours of surgery, patients where be evaluated for radiological evidence of respectability and visual recovery by undergoing post-operative MRI and visual assessment by ophthalmologist. All the informations were entered in a structured performa. The data was analyzed by using SPSS version 25. All qualitative variable like gender, outcome in terms of complete resection and visual field defects were presented by frequency and percentage. Quantitative data like age was presented by mean and standard deviation. The groups were compared for outcome using chisquare test. P values were considered statistically significant if < 0.05.

Results: Out of 140 pituitary adenoma patients, 45% had microadenomas, while 55% macroadenomas. Mean patients age was 35±10 years. 57% patients were female. Among our study population, 29.2% patients had visual field defects at the time of presentation. Among 70 patients whose pituitary tumors were resected by endoscopic technique, 70% got complete resection of tumour, while among 70 patients whose pituitary tumors were resected by microscopic surgical technique, only 48% got complete tumor resection. (p=0.003). Among 41 patients who had visual field defects, 21 underwent endoscopic resection and 100% (i.e. all 21) patients showed improvement in visual field defects postoperatively. While 20 patients with visual field defects underwent microscopic resection, where 80% patients showed improvement in visual field defects postoperatively (p=0.04).

Conclusions: Our study concluded that endoscopic trans-sphenoidal surgery for pituitary adenoma is much more efficacious than microscopic trans-sphenoidal surgery, as determined by respectability of the tumor and correction or improvement in visual field defects postoperatively. Complete resection will be of value as it will correct other sign and symptoms and hence morbidity and mortality in operated patients as well.

Keywords: Pituitary adenoma, Trans-sphenoidal surgery. Microscopic resection, Endoscopic resection, Complete resection, Visual field defects.

Introduction

Pituitary adenomas arise primarily from the anterior pituitary gland (adenohypophysis)[1] whereas posterior pituitary adenomas known as neurohypophyseal tumors are very rare.[2,3] On the basis of size, these tumors are classified as microadenomas if less than 1cm and macroadenomas if more than 1cm.[4,5] Schloffer was the first who resected pituitary tumor via transsphenoidal surgery in 1907. [6] Major complications of transsphenoidal pituitary surgery include CSF Leak, intracranial major vessels injury, endocrine abnormalities and few minor nasal complications.[7] Two modes are utilized for this transsphenoidal excision: one conventional microscopic and second newly advented endoscopic. Microscopic approach provides direct access to the floor of the sella with minimal dissection of the posterior nasal mucosa or septectomy.[8] While in endoscopic approach, after posterior septectomy a high-speed drill is used to create a wide opening in the rostrum for the endoscope and instruments. After tumor removal, cavity is inspected for residual tumor. using 308 and 458 angled endoscopes.[9,10] Jankowski

Was who first time introduced endoscopic approach for pituitary tumor in 1992.[11] Literature suggests that endoscopic approach provides broader surgical field, better outcome, lesser operative time, and lower complication rate comparted to microscopic trans-sphenoidal approach.[12-14]

The novel approach for pituitary adenoma surgery in the tertiary care centres of our country is the microscopic transsphenoidal one while in the rest of the world with the introduction of newer transsphenoidal endoscopic approach the management of pituitary tumours has been changed grossly. When judging any new surgical technique, it must be compared with the current gold standard based on important key indicators (outcome variables). If we hypothesize that endoscopy is safer than microscopy in some aspects like tumor respectability, as the previous literature showed. It was pertinent to conduct a study comparing these two procedures and to direct the resources to more efficacious one, and from patient's aspect if it is proved then patients can always opt for more safe and efficacious procedure. Hence the objective of our study was to compare the efficacy of endoscopic transsphenoidal surgery with microscopic transsphenoidal surgery for pituitary adenomas among patients who presented at Neurosurgery Department, Sir Ganga Ram Hospital Lahore, Pakistan.

Methods

This randomized control trial was carried out in Neurosurgery Department, Sir Ganga Ram Hospital Lahore from September 2011 till September 2015. Sample size of 140 (70 in each group) was estimated using 95% confidence level, 80% power of test with an excepted efficacy in terms of complete resection in 49.2% in microscopic group and 70.6% in endoscopic group. For sampling, non-probability purposive technique was used. Both genders, age more than 10 years, and both types of pituitary adenomas, microadenomas < 1cm and macroadenoma >1cm, as assessed on MRI, were the inclusion criterias. While patients diagnosed as having craniopharyngiomas, recurrent pituitary adenoma operated before by transs- phenoidal approach, and patients with complete vision loss were excluded from study

Preoperative data such as age sex, presenting symptoms and visual status was evaluated. Before surgery all patients underwent neuroradiological assessment which includes CT, MRI and CT Angio/ MR Angio, while ophthalmological evaluation consists of fundoscopy, visual acquity and perimetry if patient is seemed to be having visual field defects. Patients were randomly selected for each of the procedure and an informed consent was taken. Two groups of patients were made. Group A patients underwent endoscopic surgery for pituitary tumor and Group B patients were operated by microscopic technique. After 48 hours of surgery, patients where be evaluated for radiological evidence of respectability and visual recovery by undergoing post-operative MRI and visual assessment by ophthalmologist.

During Postoperative period visual assessment was done in patients who previously had visual field defects as per perimetry and results in terms of measurable decibel of light required to stimulate retina were recorded. Outcome was assessed based on the following parameters i.e complete resection of tumour, improvement in visual field defects. No radiological evidence of residual tumor after 2 days of surgery (as per Post op MRI) defined the complete resection of tumor. If any evidence of residual tumor present than it would be incomplete resection. Improvement in the visual fields defect (if present pre operatively) was considered if there was one db increase or more in light to stimulate retina after surgery from baseline assessed by perimetry (Humphrey visual field analyzer 30-2 program) method after 2 days of surgery. All the informations were entered in a structured performa.

The data was analyzed by using SPSS version 25. All qualitative variable like gender, outcome in terms of complete resection and visual field defects were presented by frequency and percentage. Quantitative data like age was presented by mean and standard deviation. The groups were compared for outcome using chi-square test. p-values were considered statistically significant if < 0.05.

Results

Out of total of 140 patients suffering pituitary adenoma, 70(50%) patients underwent endoscopic trans-sphenoidal resection while 70(50%) underwent microscopic trans-sphenoidal resection. 60(43%) patients were male while 80 (57%) patients were female. Mean age of the patients was 35±10 years. 45% of the total number of patients (63 out of 140) presented with microadenomas (i.e.<1cm), while

59.3% (n=83) patients of total population had complete tumour resection, while 40.7%(n=57) patients had incomplete tumour resection. Among 70 patients whose pituitary tumor was resected by endoscopic technique, 70% (n=49) got complete resection of tumour, while among 70 patients whose pituitary tumor was resected by microscopic surgical technique, only 48% (n=34) got complete tumor resection. The complete resectibility of tumor was achieved significantly more via endoscopic technique as compared to microscopic technique (p=0.003) **(Table-1)**. Among 41 patients who had visual field defects, 21 underwent endoscopic resection and 100% (i.e. all 21) patients showed improvement in visual field defects postoperatively. While 20 patients with visual field defects underwent microscopic resection, where 80% (i.e. 16 out of 20) patients showed improvement in visual field defects postoperatively.

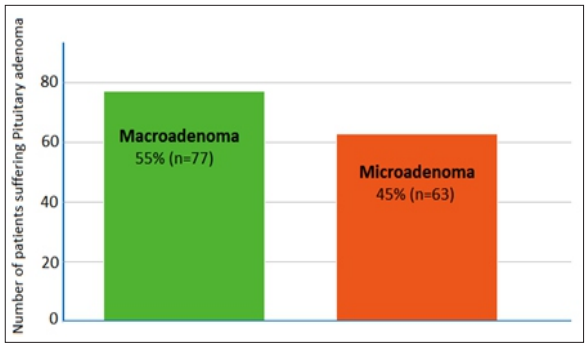

Fig-1: Types of pituitary adenomas among our studied patients.

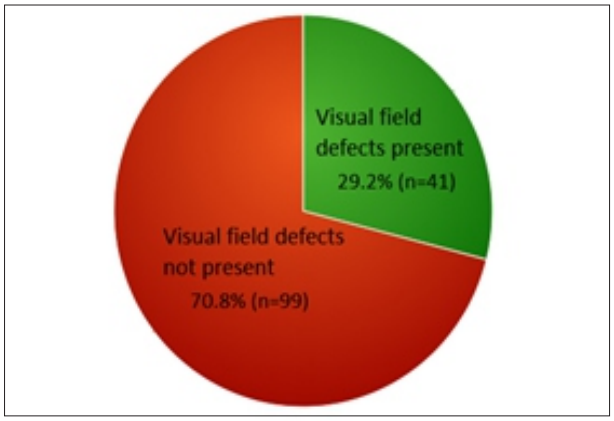

Fig-2: Prevalence of visual field defects in patients who presented with pituitary adenoma.

This improvement in visual field defects after endoscopic resection was significantly higher in comparison to that after microscopic resection technique (p=0.04) **(Table-2).**

Discussion

The aim of the study was to compare the outcome of the two surgical technique i.e. endoscopic and microscopic, for the resection of pituitary adenoma. The present study aimed at comparing outcome in terms of completeness of resection and improvement in visual field defects if any present, as analyzed by clinical evaluation and preoperative visual field assessment by perimetry. A recent increase in use of endoscopic transsphenoidal technique in past decade has made it very essential to get its comparison

Table-1: Comparison of outcome (resectibility) of endoscopic pituitary surgery vs microscopic pituitary surgical technique (n=140).

Surgical Technique	Resection Achieved		Total	P-value
	Complete	Incomplete		
Endoscopic	70% (n=49)	70% (n=49)	70	
Microscopic	48% (n=34)	52% (n=36)	70	0.003
Total	59.3%% (n=83)	40.7% (n=57)	140	

Table-2: Comparison of outcome (improvement in visual field defects) of endoscopic pituitary surgery vs microscopic pituitary surgical technique (n=41).

Surgical Technique	Resection Achieved		Total	P-value
	Complete	Incomplete		
Endoscopic	100% (n=21)	0% (n=0)	21	
Microscopic	80% (n=16)	20% (n=04)	20	0.04
Total	90.2% (n=37)	9.8% (n=04)	41	

with the traditional technique of using microscope so that evidence-based advantages of either technique can be established rather than having theoretical knowledge. In our center, 55% of the patients were having macroadenoma while 45% were having microadenomas on presentation, this frequency is different from hospital of Italy where majority of the patients were having macroadenomas[15] There was female predominance with male to female ratio of 0.75:1,this was also observed in study conducted in a hospital in Shanghai, China.[16] Mean age of patients presenting to our center having pituitary adenomas was 35±10 years which was also comparable to the same study conducted in china. Disease control or resectability of the tumour as judged by presence or absence of residual tumour on post-operative MRI , it was observed that 59% i.e. n=83 total population of our patients got complete resection of tumour operated with either endoscopic or microscopic assisted technique. About 70% of our patients undergoing endoscopic transsphenoidal pituitary surgery (group A) got complete resection of tumour while with microscopic surgical technique (Group B) we got 48% patients having complete resection. This was gross difference in outcome what we observed in our study in terms of resectability with p value of 0.003 (highly significant). This is one of an important parameter to compare the efficacy of any procedure with other and most national and international studies compare the outcome of two procedure based on resectability which is easy to measure as radiological evidences are easily available by having postoperative MRI. In an international study of pituitary adenoma,[12] complete tumor excision was achieved in 64.71% patients in endoscopic trans-sphenoidal surgery group, but in only 46.15% patients in microscopic group. In another study of 2272 patients with pituitary adenoma, Aijun Li and colleagues[13] found significantly higher rate of gross tumor removal (P = 0.009) and lower risk of septal perforation (P = 0.014) with Endoscopic transsphenoidal technique in comparison to microscopic approach. A 15 studies literature review[14] concluded more effectiveness, less complication rate & shorter post-operative hospital stay associated with endoscopic trans-sphenoidal approach compared with microscopic surgery. In a similar meta-analysis by Leonie H. A. Broersen,[17] of 97 articles with 6695 pituitry adenaoma patients underoing resection, percentage of patients in remission after endoscopic surgery (76.3 %) was higher as compared to percentage of patients in remission after microscopic surgery (59.9%). Jared D.Ament et all concluded that Endoscopic transsphenoidal surgery is cost-effective compared to microscopic transsphenoidal surgery.[18] Deyan Popov D[19] said that endoscopic group had higher levels of remission in comparison to the microscopic group (81.8% vs. 70.9%). Rodrigo V. S. Bastos and colleagues[20] found the lower rate of postoperative complications in endoscopic transsphenoidal surgery as compared to microscopic transsphenoidal surgery. Hamideh Akbari[21] concluded that endoscopic Transsphenoidal Surgery (ETS) is superior to Microscopic Transsphenoidal Surgery (MTS). Gross total resection (GTR) was observed in the 81.2% of the patient in the ETS group. In the MTS group, GTR was observed in 15.8%. In the present study we analyzed another outcome variable i.e. visual field improvement in patients presenting with visual field defects due to macroadenomas. All patients presented to our centre with macroadenomas were having visual field defects both clinically and confirmed on preoperative ophthalmological assessment as per perimeter. Among n=41 patients having visual field defects due to pituitary adenomas, n=20 were operated using endoscopic surgical technique .100% of the patients got improvement in their visual field defect as compare to 80% n=16 of the patients operated microscopically as shown by clinical and post-operative visual field assessment by perimetery. This is again a reliable parameter to study and analyze and hence establishing the fact that which procedure is better than other based on clinical evidences. Although number of patients in current study is too small to have a reliable comparison b/w surgical technique but still results are very convincing. When we compare with international data, a Canadian study conducted in University of Toronto showed Complete normalization of preoperative visual defects in 50% of the patients treated endoscopically and 39% had gradual improvement[22.] Mortini et al. reported complete recovery in 40% and improvement in 50% of patients underwent treated microscopically[23], while another study conducted in Bellaria Hospital Italy, showed visual improvement in 58.4% of patients underwent endoscopic technique of pituitary surgery[24.] In our data, endoscopic surgical technique seems to superior than microscopic approach with significant difference and p value of 0.04. Our comparison results are very much like a study conducted in china where two surgical technique were compared and statistically significant

the above and other outcome variables.[16]

One limitation to this study is that we didn't compare complication rate among two groups which need to be elaborated further because any technique to be adopted should be studied in detail in terms of its prons and cons. Complications like postoperative pain and CSF rhinorrhea which are most common one and along with that recurrence of tumour. These are very important to study so that we should be confident enough about any of the technique to be adopted but due to short study period we couldn't get the post-operative complication rate in two groups it need long follow up , some complications are immediate but many are long term complications which need long follow up to be elaborated .further studies should be encouraged in our setting so that surgeons should be confident about the efficacy of either procedure i.e microscopic or endoscopic. Traditionally, microscopic technique is widely used in our setting because less expertise are available for endoscopic technique but to be in pace with international recommendations we should opt this technique and should be applied widely.

Conclusion

Our study concluded that endoscopic trans-sphenoidal surgery for pituitary adenoma is much more efficacious than microscopic trans-sphenoidal surgery, as determined by resectability of the tumor and correction or improvement in visual field defects postoperatively. Complete resection will be of value as it will correct other sign and symptoms and hence morbidity and mortality in operated patients as well.

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Original Article

Evaluation of Uterine Structural Abnormalities; Trans-Vaginal Scan Versus Hysteroscopy

Raja Moeed Ullah, Wajid Ali, Bushra Haq, Nighat Haroon Khan, Saira Zafar, Tanzeel-uz-Zaman, Taabeer Malik and Shahid Malik

Objective: To assess diagnostic accuracy of transvaginal ultrasound for uterine structural abnormalities as core part fertility work up taking hysteroscopy as gold standard.

Methods: This cross sectional study was conducted at Radiology Department of Lahore General Hospital in duration of six months. 385 cases were enrolled who reported infertility. TVS was performed in the same cycle. All sonographic examinations were done by an expert radiologist with 10 years of experience. The endometrial cavity was inspected in two perpendicular plane sagittal and transverse views. Irregularities, thickness, echo pattern and any distortion of the endometrium were noted. All patients underwent hysteroscopy. I also recorded the findings in the patients who underwent hysteroscopy after transvaginal scan.

Results: The mean age was 33.2±6.97 years. Mean duration of infertility was 3.15±2.13 years Agreement between trans-vaginal scan and hysteroscopy in evaluating the uterine structural abnormalities causing infertility was assessed as 229(59.48%).

Conclusions: Conclusively, TVS structural abnormalities can be identified and hence we can lessen the investigation burden cost on couples who are to undergo a lot of investigations at the same time to find out structural abnormalities.

Keywords: infertility, sonography, trans-vaginal scan, hysteroscopy, structural abnormalities.

Introduction

Infertility in humans can be labeled if conception does not occur after 12 months of routine regular sexual contact of couple without using good preventive measures for pregnancy. There are many biological and other cause of infertility, including some that medical intervention can treat.[1] Estimates from 1997 suggest that worldwide "between three and seven per cent of all [heterosexual] couples or women have an unresolved problem of infertility. Many more couples, however, experience involuntary childlessness for at least one year: estimates range from 20-35% are due to female infertility, and 25-40% are due to combined problemsin both parts.[2] In 10-20% of cases, no cause is found.[2] The most common cause of female infertility is ovulatory problems which generally manifest themselves by spare or absent menstrual periods.[3] The following causes of infertility may only be found in females. For a woman to conceive, certain things have to happen: vaginal intercourse must take place around the time when an egg is released from her ovary; the system that produces eggs has to be working at optimum levels; and her hormones must be balanced.[4]

For women, problems with fertilization arise mainly from either structural problems in the fallopian tube or uterus or problems releasing eggs. Infertility may be caused by blockage of the Fallopian tube due to malformations, infections such as chlamydia and/or scar tissue. For example, endometriosis can cause infertility with the growth of endometrial tissue in the Fallopian tubes and/or around the ovaries. Endometriosis is usually more common in women in their mid-twenties and older, especially when postponed childbirth has taken place.[5] Approximately 20% of all cases of female infertility is caused by tubal abnormalities.[6]

Another major cause of infertility in women may be the inability to ovulate. Malformation of the eggs themselves may complicate conception. For example, polycystic ovarian syndrome is when the eggs only partially developed within the ovary and there is an excess of male hormones. Some women are infertile because their ovaries do not mature and release eggs. Infertility effects 40% of females with poly cystic ovaries.[7] Uterine leiomyomas are most frequent abnormality seen in females with almost as prevalent as incidence is around 70%.[8] Fibroids can cause infertility in 5-6% of patients in 5-6% of patients and may be only reason for infertility in 1-2.4%.[9] Another major uterine abnormality implicated in infertility are endometrial polyps. According to one prospective study 32% of 1000 patients undergoing IVF were found to have uterine polyps.[10] Other factors that can

overweight or underweight, or her age as female fertility declines after the age of 30. The basic evaluation can be performed by an interested and experienced primary care physician or a gynecologist.

In a study, TVS was carried out in 789 cases before hysteroscopy. TVS and hysteroscopy results showed that there was 50% agreement in case of uterine polyps, 30% in case of uterine fibroids, 42% in case of endometrial hyperplasia, 16% in case of intra uterine adhesions and 27% in case of uterus didelphus.[11] In another comparative study of TVS and hysteroscopy, TVS was successful in explaining infertility in 52.5% of cases while hysteroscopy detected 95% cases. The final agreement between both methods was moderate and significant correlation between the two with the hysteroscopy being a better diagnostic tool. The strength of agreement is considered to be moderate.[12]

The rationale of the study is to find the degree of agreement in detection of different structural abnormalities of females reproductive visceras commonly involved in causing infertility on transvaginal ultrasound which is cost effective, easy to perform, non-invasive and in less time as compared to hysteroscopy which is invasive, expensive and sometimes requires anesthesia. There is hysteroscopy that is commonly applied as gold standard, is invasive procedure but the results are seen similar as diagnosed with the TVS. In a study comparing TVS with hysteroscopy, the degree of agreement was almost comparable, though TVS could be one of the best initial diagnostic modality.[14] This study can facilitate healthcare practitioner to adopt and advise a more accurate initial technique to deal with the female cases presenting with the issue of infertility which can also lessen the investigation burden cost on couples who are to undergo a lot of investigations at the same time to find out structural abnormalities.

Method

A total of 385 cases were enrolled who reported infertility. After approval from hospital ethical committee and informed consent from participants of study, women fulfilling the inclusion criteria (Women of child bearing age between 22-45 years, women with primary infertility as per history, women who had regular unprotected intercourse for more than one year.) were selected from Outpatient Department. Women were asked for their demographics including name, address, and marriage date/year and contact details. TVS was performed in the follicular phase of the cycle (days 5-13) after cessation of bleeding using an Esote Doppler with a transvaginal 6 MHz probe. Structural Abnormalities on trans-vaginal ultrasound, lesions which are commonly implicated in infertility were evaluated on Trans-vaginal ultrasound. endometrial polyps, uterine fibroids, adhesions, endometrial hyperplasia and didelphus uterus. All sonographic examinations were done by an expert radiologist with 10 years of experience. The endometrial cavity was inspected in two perpendicular plane sagittal and transverse views were evaluated. Irregularities, thickness, echo pattern and any distortion of the endometrium were noted. Uterine cavity abnormalities including polyp lesions, uterine fibroids, uterine congenital anomalies such as septum, adhesions and endometrial hyperplasia were investigated. All patients underwent hysteroscopy. All this information was recorded in a pre-designed proforma (attached). The data analysis was carried out using computer based statistical package for social sciences (SPSS) 20 version.

Results

The mean age 33.21±6.97 years. A total of 136(35.32%) cases were <30 years old and 249(64.68%) females were 30-45 years old. The mean duration of infertility was 3.15±2.13 years. The mean BMI in this study was 28.21±4.06. There were 138(35.84%) obese and 247(64.16%) non-obese females. There was positive agreement between TVS a

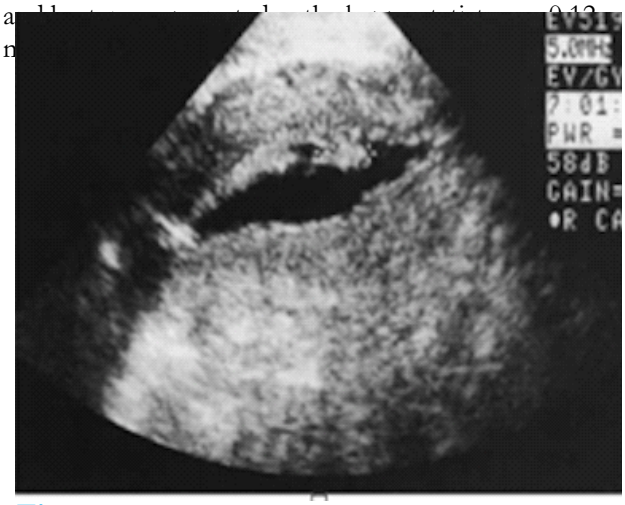

Fig-1: Enodmetrial polyp on ultrasound.

When data was stratified for age, duration of infertility and BMI, The agreement was statistically significant for both age groups (<30 years and >30 years) i.e. Kappa-value =0.267, p-value <0.001, for duration of disease i.e. Kappa-value = 0.121, p-value =0.009 and with respect to BMI i.e. Kappa-value=0.275, p-value <0.001.

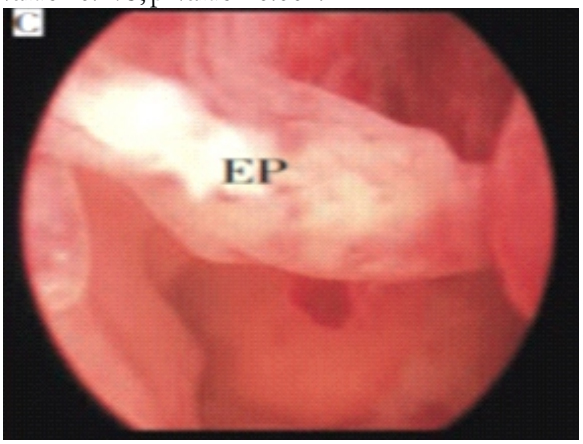

Fig-2: Enodmetrial polyp on hysteroscopy.

Table-1: Percentage of agreement between transvaginal scan and hysteroscopy among the study population.

		Hysteroscopy				
		Yes	No	Total	P-value	K-value
Trans-vaginal scan	Yes	134(64.7%)	73(35.3%)	207(100.0%)	0.00	0.32
	No	26(28.0%)	67(72.0%)	93(100.0%)		

Sensitivity=83%Specificity= 48%PPV= 64%NPV= 72%

Table-2: Impact of Effect Modifiers on the Agreement between TVS and Hysteroscopy among study population.

		Agreement		
		Yes	No	K-value
Age Groups (Years)	<30	108(47.2%)	28(17.0%)	0.32
	30 or more	121(52.8%)	128(82.1%)	
BMI	Obese	110(48.0%)	28(17.0%)	0.27
	Non obese	119(52.0%)	128(82.1%)	
Duration (years)	< 5 years	190(83.0%)	112(71.8%)	0.12
	= 5 years	39(17.0%)	44(28.2%)	

Discussion

Infertility is a widespread phenomenon that affects approximately 10-15% of the couples around the world.[15] There are several congenital or acquired uterine disorders, which cause infertility in the females. The acquired uterine abnormalities that are responsible for female infertility include polyps, some types of fibromas, adenomyosis, and some endometrial disorders such as intrauterine adhesions. On the other hand, the congenital uterine anomalies account for about 3% among the infertile women and is categorized in seven classes.[16] Sonography is known as the first imaging modality in the investigation of the female pelvis to detect the mentioned disorders among the infertile females. It is an "accurate, non-invasive, and cost-effective" modality, which provides useful knowledge for the detection and characterization of the possible female infertility factors.[17] All infertile women undergo an initial ultrasound pelvic exam (baseline sonography) to investigate the probable causes of infertility. A careful pelvic ultrasound, particularly transvaginal sonography (TVS), can detect the uterine abnormalities, ovarian disorders, and other pathologic conditions, which lead to female infertility.[18] Therefore, it can help the midwives, physicians, gynecologists, and infertility experts to examine the infertile women and make better treatment choices for these patients. Hackeloer examined the role of ultrasound in investigation and management of female infertility in a review article in 1984. He precisely described the uterine abnormalities, ovarian disorders, and adnexal masses, which cause infertility using ultrasound images.[19] Recently, Hrehorcak and Nargundhave published a review study on the new perspective of diagnosing female infertility by advanced ultrasound techniques. There are a number of reviews targeting this issue. All of them are written by radiologists and gynecologists and provide advanced and specific knowledge for the specialists.(20) Diagnostic hysteroscopy is not widely performed in the office setting, one of reasons being the discomfort or pain produced by the procedure. Patient compliance and visualization quality were proved in multicentre randomized controlled trial- to be strongly related to: instrument diameter, anatomical difficulties determined by patient's parity and experience of the surgeon.[21] Mini-hysteroscopy compared with conventional hysteroscopy was associated with less pain, less failure rate and better visualization, probably due to the less-traumatic passage through the cervical canal and the internal cervical os. Three-dimensional (3D) sonographic imaging offers some potential advantages over conventional two-dimensional (2D) techniques. The 3D image offers the true coronal view of the uterus, which is not routinely available in 2D imaging. In gynecologic applications, the internal structural details are more important than the surface rendering, except in the diagnosis of müllerian anomalies.[22]

A study reported the final agreement between both methods was moderate and significant correlation between the two with the hysteroscopy being a better

Diagnostic tool. The strength of agreement is considered to be moderate.[12] In another comparative study of TVS and hysteroscopy, TVS was successful in explaining infertility in 52.5% of cases while hysteroscopy detected 95% cases. Agreement of trans vaginal ultrasound and hysteroscopy with respect to polyp is 50%.[11] In current study agreement between trans-vaginal scan and hysteroscopy in evaluating the uterine structural abnormalities causing infertility was assessed as 229(59.48%). These findings are almost similar or better to previous quoted studies.

Similarly another study reported that in 15 cases, endometrial carcinoma was confirmed by hysteroscopy and histopathological examination. Of these, malignancies were suspected based on previous ultrasound scans in 11 patients. In 95 cases, intrauterine polyps were detected. The success rate for predicting polyps by ultrasound examination was 65.1%. The agreement between ultrasound and hysteroscopic/histopathological findings was 72%. The secondary goal of making the description of the uterine cavity easier was not fulfilled. The prediction percentages for the criteria were low. The incidence of pathological findings in ultrasound findings labelled as anechogenic was 4.8%, suggesting a high negative predictive value. Thus, in spite of the better resolution of new ultrasound devices, their predictive value remains limited. Findings that are suspicious in ultrasound should be confirmed by hysteroscopy with biopsy.[23]

The main findings of the study has showed that Hysteroscopy was successfully performed in all subjects. Hysteroscopy diagnosed pathological findings in 22 of 69 cases (31.8%). 3D-TVS demonstrated 84.1% diagnostic accuracy for detecting uterine cavity abnormalities in infertile women. A significant percentage of infertile patients had evidence of uterine cavity pathology. Hysteroscopy is, therefore, recommended for accurate detection and diagnosis of uterine cavity lesion.[24] in this study high negative predictive value was noted the which was due to presence of very small uterine follicle which was not detected on the TVS. Furthermore the segregation of the actual abnormality has resulted in the doubt to the decision to mark weather there lies an abnormality or not. Hence in order to be more specific and accurate any doubt in terms of presence of abnormality was placed in the negative group.

Moreover another Prospective and comparative study, India in a period of 13 months from August 2014 to September 2015 conducted on 60 subjects. The main finding of the study has illustrated that 60 patients were evaluated with diagnosis of primary and secondary infertility. Hysteroscopy showed alterations in 65%, predominantly uterine synechiae, chronic endometritis and endometrial polyp. Hysterosalpingography reported a sensitivity of 90% and a specificity of 100%, with a positive predictive value of 100% and a negative predictive value of 66.6%. The agreement between the two methods was moderate.[25] The result has showed that Hysteroscopy diagnosed endometrial polyps in 197 out of 679 cases (24.5%). TVS confirmed the hysteroscopy findings in 174 of 197 (88.3%) cases. The sensitivity, specificity, and positive and negative predictive values of TVS compared to hysteroscopy in the detection of endometrial polyps were 88.3%, 91.9%, 81.6% and 90.8%, respectively. Hence, TVS is both a cost-effective and non-invasive method for the diagnosis of intrauterine lesions such as polyps. When used in conjunction with a saline infusion, it can be a proper alternative for diagnostic hysteroscopy that saves time and enables the surgeon to perform the operative hystroscopy procedure with greater accuracy.[26,27]

Conclusion

Through this study, we found a moderate agreement (59.48%) between trans-vaginal scan and hysteroscopy in evaluating the uterine structural abnormalities causing infertility. So, by opting TVS structural abnormalities can be identified and hence we can lessen the investigation burden cost on couples who are to undergo a lot of investigations at the same time to find out structural abnormalities.

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Original Article

Measurement of Atmospheric Particulate Matter (PM 2.5 and PM10) Concentrations in Lahore and Their Possible Impact on Mental Illness in Adults and Children.

Shiraz Aslam, Sumira Q. Bokhari and Qambar M. Bokhari

Objective: To measured the particulate matter concentration in the atmosphere around different areas in Lahore and high lights the possible future concerns regarding its impact on the mental health of the people especially children who are directly exposed to it.

Methods: The particulate matter concentrations (PM2.5, PM10, PM1) were measured using a calibrated digital device. The results were tabulated.

Results: The highest concentration of the particles were measured in The Data Darbar area (90 µg/m3) while the lowest was found in the GOR-1 area (61 µg/m3). Even the lowest concentration found was much higher than what the WHO allows in a 24 hour period (24 µg/m3). Health problems including mental health problems start to appear above an annual mean level of PM2.5 of 10 µg/m3. It is foreseeable, the possible immense impact of particulate pollution on mental health in Lahore.Conclusions

Conclusions: The particulate matter concentrations in all areas in Lahore were beyond the acceptable WHO levels. Mental illness is strongly shown to be associated with the high concentrations of these particulate matters. Thus it is imperative that stringent and prompt action is taken to control pollution in all its forms.

Keywords: particulate matter, environmental monitoring, mental disorders.

Introduction

Pollution is a worldwide problem but is much worse health wise particularly in the developing countries like Pakistan. Pollution consists of several chemicals both solids and in the liquid or gaseous forms such as formaldehyde vapours, sulphur dioxide, carbon monoxide and carbon dioxide gases. In addition to these, some particulate matters, of minute sizes, are also present which are the focus of this study and which were measured in various places at Lahore. The particulate matters of interest in this study are the PM 2.5 (0.0025 mm in diameter) and the PM 10 (0.01 mm in diameter) particulates which are called 'fine' and 'coarse' particulates according to their respective sizes. These are usually described in terms of mass per volume of air micrograms per cubic meter (µg/m3). The particulate matters come from various sources such as burning natural coal, organic materials such as wood and some artificially manufactured materials such as rubber and plastics. These can also be produced by emissions from cars and power plants. However, wild fires such as extended bush fires in Mexico, the US and Australia.

According to the Global Burden of Disease Study conducted in 2015, exposure to fine particulate matter (PM) 2·5 was the fifth largest risk factor for deaths throughout the world. Thus, the deaths worldwide due to particulate matter were in the region of 4.2 million and resulted in 103.1 million disabilities in 2015.[1] Cohen and colleagues estimated that pollution resulting from the ambient PM2·5 was the fifth-ranking mortality risk factor in 2015. The 2015 Global Burden of Disease survey estimated that fine particulate matter was responsible for 7.6% of all deaths worldwide.[2] The WHO has issued guidelines regarding the allowable atmospheric levels of PM2.5 and PM10 (Table-1).

Table-1 (Table-1). guidelines, regarding allowable levels of particulate matter (PM) concentrations in the atmosphere. Https://www.who.int/news-room/fact-sheets/detail/ambient-(outdoor)-air-uality-and-health.

	PM 2.5 µg/m3	PM 10 µg/m3
Annual mean measurements	10	20
24 hour man measurements	24	50

Methods

A new specific pollution monitor with multi- item measuring capability was used to measure the particulate matters (PM2.5, PM1,PM10) in the air.

Every locality or area. A route was decided which was logistically convenient and fairly representative of Lahore including affluent and non-affluent areas and busy and not so busy areas. For accurate readings the monitor is kept in the open environment for at least 3 minutes so that the surrounding air has a good chance to penetrate the monitor sensor window. The readings were finally tabulated for analysis and discussion.

Results

The Highest concentration of the particulates called the 'fine' particulates were in the areas where it is most expected such as The Data Darbar (90 µg/m3) due to the large number of people that visit the shrine with accompanying 'Chingxie" rickshaws bellowing out smoke and un-burnt fuel from inefficient and un-tuned engines. The following observation although not statistically substantiated is most important as it conveys the sheer impact on the future health of people of different ages compacted in this busy part of Lahore. In addition to male and female adults the elderly and the children were in large numbers as well. Visitors might inhale their share of the high concentration of pollutants here but there were people who were stationed in the vicinity of the Shrine who were duty bound to stay at that spot for hours. These were the traffic policemen, who were exposed to hours of unfiltered particulate matters. In addition to these the common vendors, rickshaw drivers, children on their way to or back from school and also the small shops on the roadside were noted to be exposed to the heavy particulate laden air. It is conceivable, why and how such people can be affected mentally in an adverse manner by inhaling the particulate matters. Children would be exposed to this pollution for the near future for certain. All this, might possibly result in health problems for adults and children alike, of a physical or a mental form. The lowest concentration was in the Government Officers Residence 1 which is a strictly gated area and is not a thorough fare and thus is free from heavy traffic, especially the motorcycle rickshaws. This only confirms the huge contribution to the pollution by the cars on the busy Lahore road. On average, the concentration of the PM2.5 was 79.43 µg/m3, which is way beyond what the WHO or the Environment Protection Agency has recommended. Similarly, PM1 and PM10 were 187 µg/m3 and 244 µg/m3 on average, respectively, again not in the recommended limit zones.

The average concentration of the PM2.5 in the present study falls into the fourth category (40.0106.9 µg/m3 which is the worst environmental state categorized by the environmental agency of Australia. The WHO recommends 25µg/m3 as the safe environmental levels of PM2.5 worldwide.

Table-2: Measured levels of Particulate Matters (PM) at various sites in Lahore.

	PM 2.5	Pm1	PM 10
Jail Road	73	199	265
Ferozepur Road	81	190	164
Lyttton Road	80	164	196
M.A.O College	77	170	223
Kachehri	77	160	200
G.C.U	77	198	253
Data Darbar	90	259	330
Bhati Gate	80	200	268
Negative predictive value	84	203	247
Bansanwala Bazar	80	185	256
Gawalmandi	85.5	175	232
Lakshmi Chowk	80.3	263	340
Montgomery Road	79	200	256
Shimla Pahari	82	189	245
Davis Road	84	182	223
G.O.R-1	61	155	207

Discussion

It is evident from the measurements at Lahore that in every area measured, the W.H.O. allowable levels were not met and the 'Air Quality Index' obtained is in the 'severe unhealthy range'. Thus, the recommendation in this case is strict and directs especially children to avoid prolong out door exertion. People with preexisting respiratory conditions are especially advised to avoid the outdoors. Unfortunately, during data collection for this study, it was noted that policemen were posted in this polluted spot for hours. School children had to tread along the heavily polluted road side and vendors were no less exposed to the onslaught of these injurious particulate matters. How mental illness is affected by air pollution is described by two hypotheses, called the Neuro-inflammatory hypothesis and the Gene-environment interaction hypothesis. In the neuro-inflammatory hypothesis, the neurovascular unit is damaged by production of autoantibodies against neural and tight-junction proteins.[3-6] The second

Affectaffects how the animals' genes are expressed. These environmental factors can be chemicals in the atmosphere, temperature, oxygen levels, humidity and mutagens. This in turn determines some characteristics of the organism (phenotype).[7]
A multi European study with US contributions concluded that heavy metals such as lead and cadmium, environmental particulate matter and some oxides of sulphur and nitrate can cause psychotic disorders such as schizophrenia. They suggest a mediation role of pollution in the association of urban birth/upbringing and the elevated risk.[8] Thus inflammation is thought to be an important contributor to psychiatric symptoms such as depression and Schizophrenia.[9,10] A Korean study recruited 537 elderly citizens who visited a community centre were examined for depressive symptoms. They concluded that exposure to particulate matters such as PM10 and ozone may increase depressive symptoms amongst the elderly. The symptoms evaluated which were strongly associated with particulate matter and most affected were the emotional symptoms.[11] This study from mainly from Spain also suggests the association between environmental particulate matter and depression.[12] The Canadian study suggests that emergency room admissions and visits were more after ambient air pollution especially in the warm season.[13] This 2015 study, looked at 71, 271 women aged between 57 and 85 years and their anxiety levels associated with ambient pollutant levels of PM2.5 and Pm10 found out that the women had higher
Another urban study recruiting 243 611 people also concluded that pollution is associated with cases of dementia.[15] An unacceptable environmental level of particulate matter is also suspected to be associated with autism spectrum disorders. The quantum of this association depends on the size of the particulate matter the child is exposed to. The most strongly influencing factor is the PM2.5 and the diesel PM.[16] The association between particulate matter especially the PM 2.5 and autism was also suggested by another study where exposure to the pregnant mother was associated with greater odds of a child developing autism.[17] A systemic review and meta-analysis of 23 studies done in China in 2017 strongly suggests that the exposure to the particulate matter of the pregnant mother increases the risk of preterm birth and term low birth weight.[18] Another study in 2017 but from the US suggest that even low exposures to ambient air pollutants (PM2.5) resulted in reduced birth weight but not with risk of preterm birth.[19] A study in Beijing has shown that there is a strong association between psychosis and particulate matter concentrations in the atmosphere. [20] Similarly, it is shown that long-term exposure to fine particulate matter (PM2.5) and nitrogen dioxide was positively associated with dementia.[21] Lancet published a study in 2017,in which the authors used a large population-based cohort which resided near a heavy traffic area, and concluded that the incidence of dementia was greater as the residents were exposed to pollution particulate matters on a long term basis.[22] Thus, both Swiss and German studies have shown that there is ample evidence to safely conclude that environmental factors are associated with mental illness.[24] It was observed that particulate material (PM) was seen in olfactory bulb neurons, and 'fine' PM were observed in the blood from the lung, frontal, and trigeminal ganglia capillaries. These changes result in damage starting in early childhood if the child is exposed to the pollutants.[25] Worryingly, several multi centre international studies have shown a positive association between suicide attempts and exposure to particulate matter.[26-30] When pollutants enter the body they elicit an innate immune response resulting in the release of cytokines such as interleukin 1β and 6. There is also release of the tumour necrosis factor alpha. The consequence of release of these chemicals results are the characteristics of inflammation like swelling and recruitment of more such mediators resulting in a wide spread inflammation resulting in nerve and brain damage. Brockmeyer and colleagues identified such damaged areas in the cortex and the midbrain which caters to cognitive function, especially, a precarious situation if a child is the victim. These researchers also identified reduced blood flow to the brain with resulting demyelination of neurons.[31] A brief and extensive survey of the effects of particulate matter on mental health is found in the Journal of urban design.[32]

Conclusion

Pollution is a worldwide problem but is more so in the developing world due to a poor infrastructure heightened by cultural carelessness. The present study confirmed the presence of high concentrations of particulate matter throughout the areas measured in Lahore. The association between these injurious levels and various mental illnesses is well studied world over. We, as a nation should take prompt and

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Case Series

Pregnancy with Addison Disease; A Case Series

Saima Najam, Syeda Shehla Batool and Ali Raza Haider

Abstracts: Addison disease or primary adrenocortical insufficiency is rare and potentially lethal endocrine disorder, in pregnancy it is even more rarely seen. We report two cases of Patients with known addisons disease were taking treatment before the pregnancy. Both patients fortunately were of same age and conceived spontaneously but had different associated illnesses. Both were very compliant and co operative and they both delivered at around 37 weeks , and were managed in collaboration with the endocrinologist and dietitian. Both patients had uneventful recovery after normal delivery and cessarian section respectively. Therefore we conclude that Patient education, monitoring and titration of her steroids are the only ways to avoid complications associated with the under or over treatment with steroids and should be managed by the multidisciplinary team.

Keywords: addison disease, labor, prednisolone, hydrocortisone.

Introduction

Primary adrenocortical insufficiency is rare because more than 9o% of total gland volume must be destroyed for symptoms to develop. It is a long term potentially severe chronic disease of the adrenal cortex associated with the insufficient production of the glucocorticoids and mineralocorticoids. Auto immune adrenalitis is the most common cause in the developed world while tuberculosis has been recognized as a frequent etiology in the developing world. There is increased incidence of concurrent Hashimoto thyroiditis, premature ovarian failure , type 1 Diabetes and graves disease.[1]

As Addison disease is a very rare chronic condition , with prevalence of 4-11/100,000, So the precise prevalence of the disease in pregnancy is unknown. (2)One of the leading reports, which was done in Norway over 12 years, showed an Estimated incidence of 1/3000 births.[4] Women with Addison disease show reduced parity, the reason being ,firstly they are reluctant to get pregnant because of risk of complications and other concomitant autoimmune diseases, secondly autoimmune thyroid disease can lead to reduce fertility and thirdly the loss of adrenal androgen can play a role in the fertility of this patient, although this is not clear.[2] Addison disease has deleterious effects on pregnancy outcome., it can lead to abortion , intrauterine growth restriction , intrauterine fetal death and postpartum adrenal crisis.[3] Considering this together with the rarity of the condition a pregnant Addison patient is a very infrequent scenario in the clinical practice. We report two cases with Addison disease who got pregnant immediately after marriage and her pregnancy, labor and delivery remained uneventful.

Case Report One

A 31years old house wife , married for two months, known case of Addison disease and Hypothyrodism for last ten years presented to emergency room (ER) eleven months ago with the complaint of fatigue , nausea and frequency of urine before 3 days of her expected period. Her electrolytes (sodium 136mmol/L, reference range 136-145mmol/L, potassium 4.00mmol/L, reference range 3.5-5.1 mmol/L) and thyroid stimulating hormone (TSH 1.52miu/L, reference value 0.27-4.2miu/L) were normal. Her bhcg was done and was found positive and urine culture showed no uropathogen growth after 72 hours. She was booked and managed in collaboration with the endocrinologist with the same dosses of the steroids which she was taking earlier. She was a very compliant patient and visited regularly, she was counselled on every visit about the medication , life style and precautions to be taken in case of stress, infection and surgery. At 7 weeks once she presented with dizziness was found to have hypotension her blood pressure dropped to 80/60 mm of Hg, she was hydrated with normal saline and given Injection Hydrocortisone 50 mg stat. Her blood sugars and electrolytes were normal at that time. Her rest of the pregnancy remained un eventful. She was co managed by the obstetrician and the endocrinologist. She was advised to take increase salt and her serum electrolytes were kept with in the normal range by increasing dose of glucocorticoids

75MCG* OD. By term her predisolone was increased to 10.0 mg at 7.00 AM and 2.5 mg at 3.00PM with the same dose of fludrocortisone and thyoxine. She presented at 37+6 weeks with spontaneous rupture of membranes(ROM) for 5 hours, and labor pains in the emergency room. Her amnisure was positive which confirmed ROM, her bishop score was 6, and cardiotocography (CTG)was reactive so she was admitted for the induction of labor. She was induced with 2.0 mg prostaglandin E2 intravaginal gel after 6 hours of ROM .In active phase of labor she was started with Inj hyrocortisone 100mg intravenous 6 hourly till delivery of the baby and the placenta in collaboration of the endocrinologist.She was kept hydrated with normal saline throughout the labor and delivery.. Her labor progressed smoothly and after 5 hours of active phase she delivered a 2.4 kg , female baby with Apgar score of 6/10 and 8/10 as vertex, the length of her second and third stage of labor was 20 min and one minute respectively. Her post natal recovery was also Uneventful. After delivery her prednisolone was doubled for 48 hours and then tapered to the pre pregnancy dosage before discharge. She was discharged in stable condition on her 5th post natal day. One week follow up showed normal electrolytes and good healing of her episiotomy and successful breast feeding. The progress of the baby was also normal and her electrolytes were normal as well.

Case Report Two

A 31years old house wife , married for 7months , known case of diabetic from last 5 years, and known case of Addison disease from last 2 years , was booked at 7 weeks of pregnancy. She was taking insulin (regular)10 units three times a day and was on hydrocortisone tab 10 mg at 8.00pm and 5.0 mg at 4.00pm. She has been very compliant and did regular visits. She only needed increments in the dosage of insulin which was done in collaboration with the endocrinologist, the insulin was increased to 20 units twice daily of Glargine insulin and 20 units of Aspart three times a day at 29 weeks and was continued in the same dosage till delivery. Her hydrocortisone was continued in the same dosage and no increments were required. she was counselled on every visit about the medications , life style , diet ,exercise and precautions to be taken in case of stress, infection and surgery. She presented at 37+1 weeks with irregular contractions in the emergency room. She was in latent phase of labor at the time of admission, after evaluation cessarian section was planned because of the good size of the baby. Injection hydrocortisone 100mg was given before induction of anesthesia then under spinal anesthesia her cessarian was done . A female baby with Apgar score 8/10 and 9/10 was delivered as cephalic and the weight of the baby was 4.7 kg. Her post op recovery was un eventful. The baby was shifted to NICU for the blood sugar monitoring.Injection hydrocortisone 100 mg intravenous three times a day was continued for 24 hours, then reduced to 50 mg intravenous three times a day for next 24 hours and then was given 50 mg intravenous two times a day for next 24 hours. After that tab hydrocortisone was started, 10.00mg was given at 6.00am and then 5.00 mg was given at 12.00 pm and 5 mg at 6.00pm was continued for 48 hours. The insulin was given acc to sliding scale for first 48 hours and then pre regnancy dosage resumed that is 10mg three times a day. She was discharged on her 6th post op day on hydrocortisone tab 10 mg at 8.00am and then 5.00mg at 4.00pm and the same dose of insulin in stable condition. On follow up visit after a week the patient showed uneventful recovery with the normal healing of her abdominal wound and the baby who was doing well on breast feeding along with bottle feeding. .

Discussion

Managing a patient with Addison disease in pregnancy and labor is a challenging clinical scenario. The replacement of the glucocorticoids and the mineralocorticoids should be continued throughout the pregnancy, delivery and lactation. The dose depends on clinical scenario and serum electrolytes. Two third of the total daily dose is given when the patient awakens and one third is given in the after noon as in the normal circadian rhythm of cortisol.[4] The increment is usually needed in third trimester. Mineralocorticoid treatment is a concern as well. Ambrosi et al in their review has suggested that reduction in the dose of the Fudrocortisone is required if the patient has hypertension and hypokalemia.[5] how ever as our patient did not develop the hypertension so we continued with the same dose 0.1 mgm of Fludrocortisone as she was using before pregnancy. Our patient delivered normally, During labor adequate hydration with continuous infusion of normal saline and glucocorticoids was required. As the second patient required cessarian section so she received 100mgm of hydrocortisone IV before surgery begins , which was then continued every

Both babies came out to be healthy and no teratogenic effect was noticed because of the Glucocorticoid and mineralocorticoid treatment through out the pregnancy ,as observed by Lindsay et al.[7]

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Original Article

Reliability of Diagnostic Performance of Alvarado Score and Ultrasound in Patients Suspected of Having Acute Appendicitis

Junaid Khan Lodhi, Tayyiba Akhter, Saba Tahir Bokhari, Asim Malik.Luqman Ahmad Bajwa and Muhammad Asjad

Objective: To evaluate diagnostic reliability of Alvarado score and ultrasound in patients who have suspicion of having acute appendicitis to get to a safe diagnosis without radiation exposure.
Methods: This is a retrospective study conducted on 100 patients who presented in emergency with presumed acute appendicitis at Fatima Memorial Hospital from 2016 to 2018. Study design is retrospective cross sectional.
Results: Using a cutoff value of ≥5.5 Alvarado score resulted in sensitivity of 76%, specificity of 93%, accuracy of 84%, PPV 94%, and NPV 73%. US showed a sensitivity of 66%, specificity of 97.6%, accuracy of 79%, PPV 97% and NPV 67%. There was no difference of accuracy between the two modalities. Using both of these modalities can eliminate the use of CT scan.
Conclusions: Using Alvarado score as tool of exclusion and US as 1st investigation of choice, a case of acute appendicitis is not only diagnosed correctly but also radiation hazards of CT scan can be eliminated.
Keywords: acute appendicitis, ultrasound, alvarado score

Introduction

Acute appendicitis is acute inflammation of appendix.1 It is a common acute surgical condition for which mainstay standard treatment is appendectomy.2 While delay in diagnosis and intervention may lead to serious complications like perforation and abscess or mass formation, rushing to surgery without considering other pathologic conditions can lead to unindicated appendectomy up to 15-30%.3 Computed abdominal tomography (CAT) is now gold standard tool for diagnosis. It is highly sensitive and specific. While helping surgeons reach a definitive diagnosis of acute appendicitis, radiation exposure remains an Achilles heel for this effective diagnostic modality which can lead to increased incidence of cancer.4,5 Hence, other diagnostic modalities have also been suggested.

Ultrasound scan is not only cost effective but also has lesser radiation exposure. Its efficacy is marred by operator dependability leading to its low sensitivity. Alvarado score is a clinical scoring system of for diagnosis of acute appendicitis developed by Alvarado6. To our knowledge no evaluation has been done or published study yet to compare diagnostic performance of Alvarado score and ultrasound in our set up.

Methods

It was a retrospective cross sectional study conducted in Surgical Unit-1 Fatima Memorial Hospital Lahore. This study was conducted for 2 years from January 2016 to December 2018. Sample size calculated was 100 with 95% confidence interval. All patients, both males and females aged above 18 years coming to hospital with acute abdomen suspected of having acute appendicitis were included in the study. Patients aged less than 18 years of age or who had previous appendectomy were the exclusion criteria of the study.

Demographic data was collected from medical records. Alvarado score was calculated for each patient in accordance with original Alvarado score. Alvarado score comprised of the following components:

M= migration of pain to RIF	1
A=anorexia	1
N=nausea and vomiting	1
T=tenderness RIF	2
R=rebound tenderness	1
E=elevated temperature	1
L=leucocytosis	2
S= shift to the left	1
Total	10

All patients in the study had ultrasound scan of the abdomen for diagnosis of appendicitis. All ultrasounds were performed by a single radiologist on Toshiba Xario 100 ultrasound machine using a 3.5-5MHz Curvilinear and 7.5-15 MHz Linear probe. Both transverse and longitudinal images were taken. Following parameters were used for confirmation of

cross sectional diameter of the appendix> 6mm, appendicolith, infiltration of peri-appendiceal fat and free fluid in RIF **(Fig.1).**

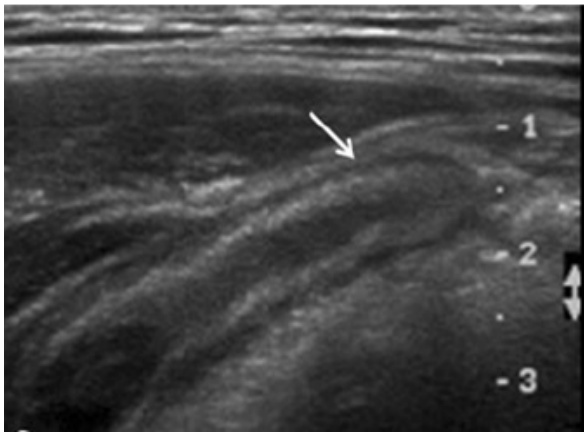

Fig-1: showing an inflamed appendix measuring about 8 mm in cross sectional diameter with increased peri appendiceal echogenicity.

All surgeries were done by level 5 expert surgeon. Following operations, all samples were sent to histopathology for confirmed diagnosis. We used SPSS version 21 for data analysis in our study. Regarding continuous variables, descriptive statistics were computed and described as mean ± SD. Categorical variables were stated using frequency distributions. Paired samples were subjected to t-test to report differences in the means of numerical variables and Chi-square test was applied for qualitative variables. P value of <0.05 was taken as significant.

Results

Our study included 100 patients out of which 68 were males and 22 were females. Age of the patients range from 20-54 years with a mean age of 33.6±11.2 years. Surgery was performed in 59 patients and samples sent confirmed acute appendicitis on histopathology. A total of 41 patients did not had appendicitis but some other diseases confirmed on ultrasound scan. These patients were treated accordingly without doing an appendectomy. The abdominal ultrasound examination was the first imaging in all patients. True positive patients reported were 39 cases (39%), true negative in 40 cases (40%), False positive 1 case (1%) and false negative 20 cases (20%). Statistically checked, these findings found to be significant (p=0.001)) showing great difference of ultrasound findings between appendicitis positive and appendicitis negative groups **(Table-1).** The various ultrasound parameters included in our study were also analysed and all of them were found to be statistically significant as shown in**(Table-2).** Alvarado score in both groups; i.e. appendicitis positive and appendicitis negative group also showed significant difference. True positive patients were found in 45 cases (45%), true negative in 38 cases (38%), false positive in 3 cases (3%) and false negative in 14 cases (14%). When analysed statistically, these findings found to be significant (p=0.001)) showing great difference of Alvarado score between appendicitis positive and appendicitis negative groups **(Table- 3).** In our study, the best cut-off point found was ≥5.5 that was predictive of appendicitis. It resulted in sensitivity of 76%, specificity of 93%, accuracy of 83%, positive predictive value of 94% and negative predictive value of 73% **(Fig-4).** When analysed further, Alvarado score was also found to be tool of exclusion; a score ≤ 4.5 has highest sensitivity of 98% while a higher score ≥6.5 resulted in highest specificity of 97.8% **(Table-5).** On comparing the two diagnostic modalities, there is almost no difference in accuracy and specificity of the two modalities (p> 0.001) indicating efficacy of both modalities in diagnosis of acute appendicitis **(Table-4).**

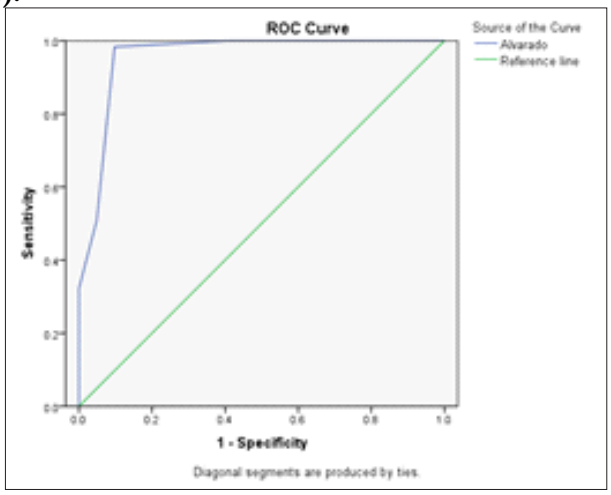

Fig-2: Receiver operating characteristic curve for the performance of Alvarado score.

Table-1: Comparison between ultrasound report and biopsy proven cases of acute appendicitis

Alvarado Score	Actual Condition Appendicitis	No Appendicitis	Total
Ye s(Appendicitis)	39	1	40
No (Appendicitis)	20	40	60
Total	59	41	100

In the end, we suggest initial diagnostic tool should be Alvarado score followed by ultrasound examination. This scheme can eliminate use CT scan in patients with Alvarado score ≥5.5 and positive ultrasound findings.

Table-2: Analysis of ultrasound parameters for statistical significance

Ultrasound Parameters		Appendicitis	No Appendicitis	P-Value
Cross sectional diameter of appendix		6.53±1.150	3.46±1.22	0.0001
Transducer induced tenderness RIF	Yes	15	0	0.0001
	No	44	41	
Appendix non compressible	Yes	19	0	0.0001
	No	40	41	
Appendicolith	Yes	12	0	0.0001
	No	47	41	
Peri-appendicular Fat	Yes	21	0	0.0001
	No	38	41	
Fluid RIF	Yes	28	0	0.0001
	No	31	41	

Table-3: Comparison between Alvarado score and bio-psy proven cases of acute appendicitis.

Alvarado Score	Actual Condition Appendicitis	No Appendicitis	Total
Ye s(Appendicitis)	45	3	48
No (Appendicitis)	14	38	52
Total	59	41	100

Table-4: Comparison of diagnostic performance of ultrasound and Alvarado score.

	Ultrasound (n=100)	Alvarado score=5.5 (n=100)
Sensitivity	66%	76%
Specificity	97%	93%
Accuracy	79%	83%
Positive predictive value	98%	94%
Negative predictive value	67%	73%

Discussion

Although CT scan is the investigation of choice for diagnosis of acute appendicitis but radiation exposure and long term risk of cancer remains the pitfall of this scan[4]. These hazards can be dealt with utilization of a clinical score and an US scan if diagnosis is in doubt. In the current study graded compression US was done in all cases and we found a sensitivity of 66%, specificity of 97.6%, accuracy of 79%, PPV 97% and NPV 67%. These findings suggest that acute appendicitis can be diagnosed on basis of a positive ultrasound. Moreover, if an ultrasound is negative, it does not mean that appendicitis is ruled out and patient can be discharged. Blitman et al also concurred with our these findings[7]. However Pinto et al reported variations in diagnostic accuracy ranging from 44% to 100%[8]. He attributed these variations to lack of operator skills, obesity and increased bowel gas content. We included an expert sonologist in our study to overcome these issues. We found out that there is an increasing trend of doing US scan as 1st imaging scan and decrease in CT scan concomitantly[9]. This is due to fact that we trust expertise of our sonologists and US results, although these results are operator dependent. Other reason is that US is cheap and cost effective. We also observed that convincing patient for getting an US scan is easy because of affordability issue. This fact is opposite to some authors as Kotagal et al noted 8 times higher use of CT scan in non-paediatric hospitals.[10] Various scoring systems have been formulated to be used as diagnostic tool in cases of suspected acute appendicitis[11]. Alvarado in his original article reported a cut-off value of 7 for diagnosis[6]. Sun et al reported that use of 6 as cut-off value has higher sensitivity and is more compatible with diagnosis of acute appendicitis[12]. In this study, a cut-off point of ≥ 5.5 was found to be best for compatibility with acute appendicitis. This resulted in sensitivity of 76%, specificity of 93%, accuracy of 84%, PPV 94%, and NPV 73%. These findings show that a cut-off value of ≥5.5 can be confidently labelled as an appendicitis case. By using these two modalities, we found out that we can safely predict possibility of suspected acute appendicitis. Stephen et al stated that neither of the two modalities are significantly advantageous to predict acute appendicitis possibility[13]. This is in contrast to our findings as we not only got satisfactory results for predicting but also nullified the rate of negative appendectomy. Addis et al with Flum & Koepsell cited annual negative appendectomy rate of 15%[14,15]. Our study showed declining trends to nil in negative appendectomy rate using these two diagnostic modalities comprising of ultrasound and Alvarado scoring system.

Conclusion

Using Alvarado score as tool of exclusion and US as 1st investigation of choice, a case of acute appendicitis is not only diagnosed correctly but also radiation hazards of CT scan can be eliminated.

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Original Article

Range of Ankle Movements After Fixation with Precontoured Anatomical Locking Plate for Comminuted Distal Tibia Fracture

Shoaib Anwar, M Amir Sohail, Sohail Razzaq, Tauqeer Ahmad, Arif Mahmood and Kamran Butt

Objective: To assess the frequency of patients achieving the full range of ankle movements after fixation with pre-contoured locking plate of distal tibia fracture.

Methods: Seventy five patients fulfilling inclusion criteria were included in the study.patients underwent surgery by a single surgical team. Patients were followed in OPD for 24 week after every 2 weeks and frequency of patients achieving full range of ankle movements was assessed.

Results: The mean age was 37.49±11.062 years, 33(44%) were male and 42 (56%) female, 33 (44%) patients had left side tibia fracture whereas 42(56%) patients right side tibia fracture. Minimally invasive fixation was done with pre contoured anatomical distal tibia locking plates. All patients were followed for 24 weeks and range of motion was assessed. Mean ROM was 31.52±10.06 the minimum ROM was 15 and maximum was 50.62(82.7%) patients had full range of motion. Conclusion: Patients presenting with comminuted distal tibia fracture can be effectively managed in terms of full range of ankle movement with precontoured locking plate.

Conclusions: Results of this study demonstrate that patients presenting with distal tibia fracture can be effectively managed in terms of full range of ankle movement with precontoured locking plate. However further long-term studies are needed to compare other relevant outcomes with this treatment modality.

Keywords: distal tibia fracture, precontoured anatomical plate, range of motion.

Introduction

Distal tibia fractures are complex injuries with a high complication rate.[1] The presence of significant osteoporosis increases the risk for more complex fractures associated with higher morbidity and mortality.[2] More severe tibia fractures stem from high-energy trauma, most often motor vehicle collisions.[3,4] Fractures of the distal tibia can be challenging to treat because of the limited soft tissue, the subcutaneous location, and poor vascularity. The best treatment remains controversial.[5,6] The goal of Orthopaedic surgeons is to restore the tibial anatomy, to fix the epi-metaphyseal block with the diaphysis and to avoid complications.[1] The literature suggests that minimally invasive plating is appropriate management option for these fractures, but further studies are required.[6, 7]The management of distal tibial fracture involves open reduction and internal fixation (ORIF) of the associated fibular fracture when present, followed by minimally plate osteosynthesis of the tibia utilizing precontoured tubular plates and percutaneously placed cortical screws. This minimally invasive technique for treatment of distal tibial fractures proves to be a feasible and worthwhile method of stabilization while avoiding the severe complications associated with the more standard methods of internal or external fixation of those fractures.[8] In a study it has been noticed that full range of ankle movements was achieved in all 100% cases after 6 months (n=38).[9] But another study has showed that full range of ankle movements was achieved in all 26% cases after 6 months (n=19).[5] One more study supported the evidence and also showed that full range of ankle movements was achieved in all 27% cases after 6 months (n=26).[10]Rationale of this study was to assess the frequency of patients achieving the full range of ankle movements after reduction with precontoured

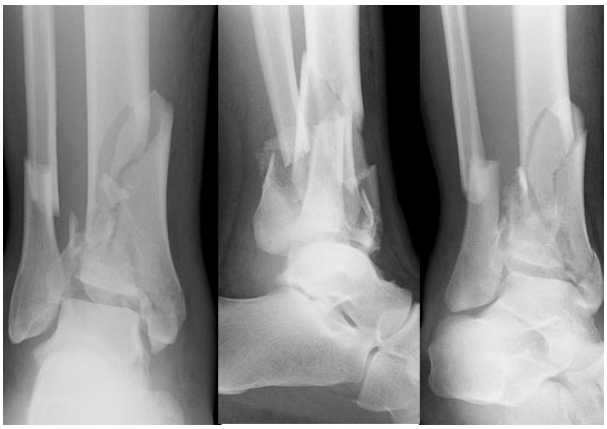

Fig-1: X-ray of a fracture involving the articular surface of the Tibia[15]

locking plate for distal tibial fracture. It has been observed in literature that locking plate can be more successful in achieving full range of ankle movements. But controversy exits in literature which showed that it is only 26-27% patients, full range of ankle movements can be achieved. So, we are unable to implement the use of precontoured locking plate for management of distal tibial fracture in adults. But previous studies were conducted on small sample size. So a larger sample size study will help us to determine the efficacy of distal tibia locking plate in achieving full range of motionat local settings.

Methods

This was a Descriptive case series study, performed at Department of Orthopedic Surgery, Jinnah Hospital, from July 2017 to July 2018. Sample size of 75 cases was calculated with 95% confidence level, 10% margin of error and taking expected percentage of full range of ankle movements i.e. 26% in patients underwent reduction with precontoured locking plate for distal tibial fracture. Non probability, consecutive sampling technique was used. Patients of age 20-70 years of either gender presenting withdistal tibia fracture AO type 43C1, 43C2, 43C3 were included in the study. Patients with osteoporosis, osteoarthritis, osteomalacia or positive RA factor (on medical record), multiple fractures or open fracture with infection and debris (on clinical examination), INR>2, Bilateral fracture, Diabetics BSR> 180mg/dl were excluded from study.

Total 75 patients fulfilling the selection criteria were included in this study from emergency of Department of Orthopedic Surgery, Jinnah Hospital, Lahore. An informed consent was obtained. Demographic profile (name, age, gender, anatomical side and contact) was also be obtained. Then patients underwent surgery by a single surgical team under general anesthesia. Then patients were shifted in post-surgical ward and then discharged from their ward on very next day. Then patients were followed-up in OPD for 24 week after surgery on every 2 weeks. After 24 weeks, frequency of patients achieving full range of ankle movements was assessed by researcher himself. Range of motion comparable to contralateral ankle was considered as full range of motion. All the information was collected through a specially designed proforma. All the data was entered and analyzed through SPSS version 21. The quantitative variables like age and range of movement were presented as mean & standard deviation. The qualitative variable like gender, anatomical side and full ROM were presented as frequency and percentage. Data was stratified for age, gender and side of fracture. Chi-square was used to compare stratified groups. P-value<0.05 was considered as significant.

Results

The mean age of the patients in our study was 37.49±11.062 the minimum age was 20 years and maximum was 55 years. **(Table-1)** There were 33 (44%) males and 42 (56%) females in our study. There were 33 (44%) patients in which left anatomical side was involved where as in 42 (56%) patients right side was involved. The mean ROM was 31.52±10.06 the minimum ROM was 15 and maximum was 50. **(Table1)** There were 62(82.7%) patients who had full range of motion whereas there were 13(17.3%) patients without full range of motion.**(Fig-1)** No statistically significant association was seen between age group of patients and full range of ankle movement. i.e. p-value= 0.83. No statistically significant association was seen between gender and full range of ankle movement. i.e. P-value=0.291. No statistically significant association was seen between side of fracture and full range of ankle movement. i.e. p-value= 0.658

Table-1: Descriptive statistics for full Range of ankle movement.

N(%)	75
Mean	(31.52%)
SD	(10.06%)
Minimum	(15%)
Maximum	(50%)

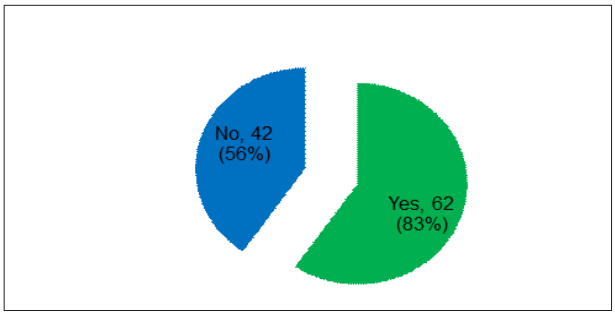

Fig-2: Full range of ankle movement in patients.

Discussion

Treatment for distal tibial fractures ranges from

demerits and hence there is no consensus for superiority of one method over the other for these types of fractures. Soft tissue healing is of paramount importance along with bone healing in distal tibial fractures for a successful outcome.[13,14] Minimally invasive plating techniques reduce surgical soft tissue injury and maintain a more biologically favorable environment for fracture healing.[12] Most of the studies showed good results with open reduction and internal fixation. Few studies with this type of fixation have shown poor results. However the results depend on severity of injury, soft tissue trauma, surgical timing, surgical technique and co-morbidities of the patient.[20]

In this study full range of ankle movement was seen in 62(83%) of patients. However no statistically significant association was seen for full range of ankle movement with age of patients (p-value=0.831), gender (p-value=0.291), side involved (p-value=0.658) and BMI of patients (p-value=0.825). Lakhotia D from Indian in his study reported that full range of ankle movements was achieved in all 100% cases after 6 months (n=38).[9] Results of this study is consistent with the findings reported by Lakhotia D.[9] However Ronga M in his study showed that full range of ankle movements was achieved in all 26% cases after 6 months (n=19).[5] However Mohammad MM supported the evidence and also showed that full range of ankle movements was achieved in all 27% cases after 6 months (n=26).[10] However Ronga M and Mohammad MM study did not support the results of this study as in both study full range of ankle movement was quite low as compared to this study. Ronga M: 26% vs. This study: 83% & Mohammad MM: 27% vs. This study: 83%. It has been proposed that the reduced plate-to-bone compression afforded by locking plates serves to protect the viability of the bone by maintaining microvascular circulation within the cortex and its investing tissues. Screw locking minimizes the compressive forces exerted by the plate on the bone because the plate does not need to be tightly pressed against the bone to stabilize the fracture.[15,19] Gupta et al., found that open reduction and internal fixation in distal tibial fractures jeopardises fracture fragment vascularity and often results in soft tissue complications. Minimally invasive osteosynthesis, if possible, offers the best possible option as it permits adequate fixation in a biological manner. Seventy-nine consecutive adult patients with distal tibial fractures, treated with locking plates, were retrospectively reviewed. The 4.5-mm limited-contact locking compression plate was used in 33 fractures, the metaphyseal locking plate in 27 fractures and the distal medial tibial locking plate in the remaining 20 fractures. Fibula fixation was performed in the majority of comminuted fractures ($n = 41$) to maintain the second column of the ankle so as to achieve indirect reduction and to prevent collapse of the fracture. There were two cases of delayed wound breakdown in fractures fixed with the 4.5-mm locking plate. Five patients required primary bone grafting and three patients required secondary bone grafting. All cases of delayed union ($n = 7$) and nonunion ($n = 3$) were observed in cases where plates were used in bridge mode. Minimally invasive plate osteosynthesis with locking plate was observed to be a reliable method of stabilization for these fractures.

Peri-operative docking of fracture ends may be a good option in severely impacted fractures with gap. The precontoured distal medial tibial locking plate was observed to be a better tolerated implant in comparison to the 4.5-mm locking plate or metaphyseal locking plate with respect to complications of soft tissues, bone healing and functional outcome, though its contour needs to be modified.[18] The distal end of the precontoured locking compression plate is anatomically contoured to the distal medial tibia, thus preventing primary displacement of the fracture caused by inexact contouring of a normal plate; it allows a better distribution of the angular and axial loading around the plate, and also, the distal end allows placement of up to nine locking screws that provide stability where satisfactory bone purchase is difficult.[19]

The clinical importance of these advantages, however, is still debatable. Several studies had investigated the differences between fractures fixed by locking plates and those fixed by nonlocking plates and found that there were no statistically significant differences between locking plates and nonlocking plates for patient-oriented outcomes, adverse events, or complications.[103, 104] With careful attention to surgical timing, respect for soft tissue handling and using a minimally invasive technique, incisions may be placed less than 7 cm apart depending on the needs of the fracture pattern. Revision surgery for implant removal due to implant prominence can be avoided with anterolateral plating.

Conclusion

Results of this study demonstrate that patients presenting with distal tibia fracture can be effectively

managed in terms of full range of ankle movement with precontoured locking plate. However further long-term studies are needed to compare other relevant outcomes with this treatment modality.

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Original Article

Frozen Shoulder Management with Hydro Dilatation Versus Steroid Injection

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Objective: To evaluate and compare the results of treatment of frozen shoulder by hydraulic distension and intra articular steroid injection with alone intra-articular steroid injection.

Methods: Clinical study comprising of two groups was carried out in the orthopedic department of services hospital, Lahore from Sept. 2013 to Dec. 2017. Patients were divided in 2 groups. Group-I was treated by hydraulic distention of gleno-humeral joint with 50 ml normal saline under local anesthesia with steroid followed by oral analgesics and muscle relaxants accompanied by exercises. Patients in group II were treated by intra-articular steroid injection followed by oral analgesics and muscle relaxants accompanied by exercises. Follow-up for both the groups was for 45 days, during the follow-up period both the groups reported pain relief, but patients in group II were unable to return to their normal activities due to less improvement in ROM.

Results: In Group 1 at the end of 45 days 25(86%) patients got complete resolution of pain while 4(14%) patients complained of occasional mild pain (VAS 3 or 4), In group-II 18(60%) patients got a complete resolution of pain while 12(40%), patients complained of occasional pain. The pain relief was statistically insignificant when compared between the two groups (p-values >0.05). The improvement in the standard of living observed in group I patients was statistically significant as compared to group I, p-value<0.001. An immediate and remarkable improvement in range of movement (ROM) 46%-95% was observed in patients of group I as compared to group II. At the end of the 45 day there was marked difference in improvement in ROM 84% in group-I and 63% in Group-II. This difference was much significant (P-Value<0.001). Twenty six (90%) patients in group-I were satisfied with the treatment and 3(10%) were unsatisfactory, while in group-II only 10(33%) were satisfied and 20(67%) were not satisfied.

Conclusions: The study concluded that outcome of treatment of patients in group I was better and statistically significant than group II patients. It is further suggested that for quick, safe and earlier results

Keywords: frozen shoulder, hydraulic distention, intra-articular steroid injection.

Introduction

The term FS was first used by Codman 1932, who described the common features as a gradual onset of pain, inability to sleep on the affected side, painful restriction movements and a normal radiological appearance.[1] More recently, ZuCkerman and Cuomo defined FS, as a condition characterized by substantial restriction of both active and passive shoulder motion that occurs in the absence of any known intrinsic shoulder disorder.[2] FS has been divided into three stages depending on its symptoms. Freezing phase (painful phase), lasting for 2-9 months. Frozen phase (stiffening phase), lasting for 4-12 months. Thawing phase (recovery phase), may last for 6-9 months.[3] Adhesive capsulitis usually occurs during the fourth to sixth decades, a gender predisposition is seen affecting women more often.[4] A close relationship also exists between FS and diabetes mellitus, the incidence in general population is 2-5% while among diabetics is 10-20%.[1] A wide range of varying lines of treatment with some success rate have been adapted to date, these include benign neglect, chiropractice manipulation oral corticosteroids, injection of corticosteroids, Physical therapy exercises and modalities, manipulation under anesthesia and arthroscopic and open release of the contracture.[2] Fareed and Gallivan (1989) treated 20 cases of FS syndrome and concluded that the distension technique of the joint brought immediate resolution of previous pain and resumption of normal sleeps with no side effects.[5] The current study is conducted to evaluate and compare the results of treatment of frozen Shoulder by hydraulic distension under local anaesthesia with steroid and with intra-articular steroid therapy.

Methods

59 patients with 60 shoulders, clinically diagnosed as FS syndrome were selected and treated as out-

Lahore and PSRD hospital Lahore, from September 2013 to December 2017. All patients were selected according to an inclusion and exclusion criteria. All patients in this study were between the ages of 30-70 years. Pain stiffness and functional restriction of affected shoulder was for more than one month. Restriction of passive shoulder motion was 100 degree of abduction or less and less than 50% of external rotation as compared with the motion of the contralateral shoulder. All patients with fracture of proximal humerus. Patients having age below 30 years and above 70 years. Patients who refused. Patients having evidence of severe osteoporotic bones on X-rays and shoulder stiffness due to other causes. The selected patients were randomly divided into two groups by lottery method; In Group-I, 30 cases were treated with hydraulic distention of GH joint under local anesthesia with steroid followed by exercises and oral medicine (NSAIDS analgesics and muscles relaxant). In Group-II, 30 cases were studied with intra-articular steroid followed by exercises and oral medicines (NSAIDs, analgesics and muscles relaxants). Patients were managed initially by preparing skin with povidone iodine solution. 03 ml of 1% plain lidocaine was injected into the skin and soft tissues overlying the joint. Thereafter, 3 ml of 1% lidocaine was injected intra articularly by anterior approach followed by steroid (40 mg triamcinolone acetonide mixed with 2 ml of 1% lidocaine. Distension of the capsule was then performed with 50 ml sterile saline solution. The patient then had active and assisted ROM exercises under supervision. These consisted of pendulum exercises, resisted flexion, extension, internal and external rotation and abduction exercise. Patients were followed with oral medicine (NSAIDs, analgesics and muscles relaxants). The patients continued with regular home physical therapy exercises performed four time daily, assisted by the family. after preparing skin with povidone-iodine solution, intra-articular steroid injection (40 mg triamcinolone acetonide mixed with 3 ml 1% plain lidocaine). The injection was carried out through anterior approach as in group-I, followed with exercises and medicine as in group-I. Follow up examination was done in each group on day 0, 7,15,30,45. When ROM exercises, pain grading, patients satisfaction, complications and activity level was taken note of by the same observer on each visit to decrease interobserver bias. Functional assessment of the shoulder was done by scoring system modified from constant score by constant CR and Murley AHG[6,7] which is based on the subjective and objective assessment.

Results

Results were evaluated according to the subjective and objective findings. Pain and daily activities level was grouped as subjective findings while ROM was grouped as objective findings by scoring system modified from constant score by constant CR ad Murley AHG.[6,7] Pain was assessed with visual analogue score (VAS). All patients in group-I and group-II noted immediate pain relief (VAS<3), at the end of 45 days 25(86%) patients got complete resolution of pain while 4(14%) patients complained of occasional mild pain (VAS 3or4)In group-II 18(60%) patients got a complete resolution of pain while 12 (40%), patients complained of occasional pain **(Table-2).** There was no significant difference in pain relief as a whole 97% improvement in group-I and 92% improvement in group-II, the pain relief was statistically insignificant when compared between the two groups (P-values >0.05). Most of the patients in our study complained of extreme difficulty in toileting, personal hygiene problems, combing hair, change of dress. The patients in group-I after hydraulic distension technique got immediate freedom from the aforementioned problems and this technique was much appreciated. 23(79%) patients resumed their full daily activities, however, 06(23%) patients were not fully satisfied. In contrast to group I, most of the patients in group II were not as happy, only 03(10%) patients returned to near full daily activities. 22(73%) patients could achieve half of their daily activities **(Table-3).** The improvement in the standard of living observed in group-I patients was statistically significant as compared to group-II, P-value < 0.001. An immediate and remarkable improvement in range of movement (ROM) 46%-95% was observed in patients of group-I as compared to group-II. This marked difference continued till 45th day. At the end of the 45 day there was marked difference in improvement in ROM 84% in group-I and 63% in Group-II. This difference was much significant (P-Value<0.001). There was maximum improvement in forward elevation and lateral elevation (abduction). 93% and 87% in group-I, 78% and 59% in group-II, respectively, and least improvement in external rotation and internal rotation, 83.5% and 73% in group-I, 63.5% and 53% in group-II respectively. 26(90%) patients in group-I were satisfied with the treatment and 3(10%) were unsatisfactory, while in group-II only 10(33%) were

Table-1: Subjective grading of pain in 29 patients with 30 shoulder in GROUP -I.

Pain	Score	No. of Patients Before Treatment	7 DAY	15 Day	30 Day	45 Day
None	0-2	0	03	15	21	25
Mild	3-4	0	26	14	8	4
Moderate	5-6	25	0	0	0	0
Severe	7-10	04	0	0	0	0

Table-2: Subjective grading of pain in 30 patients with 30 shoulders in Group -II.

Improvment	No. of Patients Group-I	No. of Patients Group-II	Results Assessment
85% - 100%	23	03	Excellent
75% - 84%	14	22	Good
65% - 74%	02	03	Fair
65% or Less	-	02	Poor

Table-3: Improvement in activities of daily living in both groups after 45 days

Pain	Score	No. of Patients Before Treatment	7 DAY	15 Day	30 Day	45 Day
None	0-2	0	03	11	16	18
Mild	3-4	0	27	19	14	12
Moderate	5-6	28	0	0	0	0
Severe	7-10	02	0	0	0	0

Table-4: Improvement in ROM after 45 days.

	No. of Patients Group-I	No. of Patients Group-II
ROM	84%	63%
Forward Evaluation	93% (167°)	78% (140°)
Lateral Evaluation	87% (157°)	59% (160°)
External Evaluation	83.5%	63%
Internal Evaluation	73%	53%

Discussion

FS is a very protracted condition, which only resolves after years rather than months.[8] Distension treatment has been advocated as giving immediate pain reduction but without any support in the literature.[9] Review of the previous literature on frozen shoulder demonstrates controversy about which of the many available treatment is best.[2] A number of different treatments, such as rest and analgesics, NSAID, local or oral steroids physiotherapy, distension of the joint capsule, manipulation or a combination of these have been advocated. No standard treatment regime is universally accepted.[17] Recently arthroscopic treatment and surgical release has been recommended for this condition.[5]

Some studies have found that local steroid injection have some pain relief, but without restoring movements and with no superior effect on the duration of symptoms compared with other treatments e.g. Heat physiotherapy, ice, local analgesic injections manipulation or no treatment. Other studies have reported that local steroid was without advantage compared to physiotherapy or oral non-steroidal anti-inflammatory therapy.[9] Corticosteroid therapy was suggested in 155 by Crisp and Kendall and since has been advocated in FS with the belief that inflammation has played an important role in the pathogenesis. Naviaser found mild subsynovial inflammation in some cases, with edema, vascular dilatation, and mononuclear cell infiltration. However, Lundberg did not find significant inflammation; excellent response to steroid therapy was also noted in one patient in group-II. Manipulation of the shoulder under general anesthesia with an intra-articular steroid and local anesthetic injection has been recommended for FS. This requires a more costly inpatient stay with general anesthesia and immediate post-operative physio-therapy. There are also risks of fracture of the humeral neck and rupture of the rotator cuff during manipulation. MUA may accelerate recovery but literature has failed to support MUA as a treatment in diabetic patients. A similar study has demonstrated similar short- and long-term outcomes in non-diabetics and diabetic patients.[10-12]

Sharma RK, treated 32 patients, who had FS which had not improved with physiotherapy were treated by manipulation under general anesthesia or by steroid injection and hydraulic distension under local anesthesia and recommended dissension technique as it was easy to carry out and gave better results than manipulation.[13] In a prospective study Van Royen said that hydraulic distension technique and manipulation under local anaesthesia is safe, reliable and effective treatment for frozen shoulder.[14] Fareed and Gallivan treated 20 cases of FS syndrome by hydraulic distension under local anaesthesia. All these patients noted immediate resolution of previous pain and resumption of normal sleep.[5] The patients in group I of the current study also noted immediate relief of pain and resumption of normal sleep pattern. It was noted by Fareed and Gallivan that the local anaesthetic, lyses adhesions and allows progressive motion.

In a study Loyd JA and Loyd HM, noted that the steroid injections have not been shown to improve the rate of return of shoulder motion. This is in concurrence with our results that did not show

45 days in group II No side effects, other than mild pain during hydraulic dissension technique were observed in group-I. One female patient with a previous history of fear of injections, however, went into transient shock (vasovagal) during hydraulic distension technique but recovered immediately by conservation measures.

Conclusion

We conclude by saying that because this technique is safe, and cost effective and provides immediate relief of symptoms and early return to nearly full function should be considered first in the management of frozen shoulder. Further studies are required to know more about etiology pathology and treatment of FS. These could lead to better understanding of this common, protracted and painful condition.

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Original Article

Prevalence of Depression in Patients With Migraine A Study from Central Lahore

Muhammad Adnan Aslam, Niamat Ali, Zaheer Ahmad, Moazzam Javid, Gauhar Mahmood Azeem and Faisal Maqbool Zahid

Objective: To determine the prevalence of depression in migraine patients and its association with characteristics of migraine and pharmacotherapy.

Methods: This cross-sectional-observational study was conducted at outpatient clinic, Neurology Department, Services Hospital, Lahore from January 2019 to June, 2019. Three hundred patients of migraine were included in the study. Information collected was comprising of age, address, gender, contact number, HAM-D score. Depression was defined as patients scoring 8 or more on Hamilton Depression rating scale (HAM-D). Severity of migraine was assessed on a Visual Analogue Scale from 0 (no pain) to 10 (most severe pain).

Results: Prevalence of depression was much higher than general population (6-30%) up to 52.7%. Severity of depression was evenly distributed among mild 36(12%), moderate 74(24.7%) and severe 48(16%) depression. An association of the attributes pharmacotherapy & severity of pain in migraine with different levels of depression was observed with p-value <0.001.

Conclusions: It is concluded that depression is strongly correlated with migraine and severity of migraine headache, average duration of migraine episode, no pharmacotherapy are independent risk factors correlated with migraine.

Keywords: migraine, depression, hamilton depression rating scale.

Introduction

Migraine is chronic condition with several neuropsychiatric aspects encompassing a multitude of factors each playing a different role. These include environmental, genetic, dietary, psychological and sleep aspects.[1] Among neuropsychiatric manifestations, migraine has been found associated with depression significantly. Several studies estimated prevalence of migraine ranging from 0.9 to 5.1% using different criteria for diagnosis of migraine most commonly SilbersteinLipton criteria (or equivalent).[2] Migraine is considered to be a neuropsychiatric illness.[3] At the core of migraine syndrome lies the element of depression. Many epidemiological surveys have been done and reported the association between depression and migraine.[4,5,6] Depression is a complex illness of chaotic feelings which may include hopelessness, suicidal thoughts, worthlessness, despair, decreased energy and libido, interest loss in one's life. It may also include somatic symptoms like insomnia anorexia or hyperphagia, headache and vague or sometimes regional pain syndromes.[7] Depression in itself is a very common illness worldwide with more than 300 million people affected,[8] causing significant disability among the victims.[9] Mood Disorders like anxiety and depression along with headache syndromes are viewed as major brain disorders each having a place among top causes of disability in the world.[10] Comorbidities increase the risk of chronic migraine, impairment of quality of life, cause additional disability, worsen likely outcome, increase the healthcare-costs of migraine and has the possibility of mutually causal relationships which needs to be established in future studies.[11-15]

Migraineurs had been found to have a 33.9% depression in one study in US resulting in major contribution towards health-care expenditure in migraineurs with depression amounting to mean-annual-total health-expenses per person (10,012 dollars versus 4,740 dollars).[16]

Most data on this subject come from the western world. As there is scarcity of data in our part of the world, therefore, current study was conducted to explore the extent to which migraine and depression are associated.

Method

This cross-sectional-observational study was conducted at outpatient clinic, Neurology Department, Services Hospital, Lahore from January 2019 to June, 2019. Three hundred (300) patients of Migraine (diagnosed using criteria given below) were included in the study using non-probability consecutive sampling technique. Male and female

patients with age between 18 and 50 years suffering from migraine were included in the study while Pregnant females, lactating mothers, substance abuse/dependence, patients with other chronic medical comorbidities like diabetes, hypertension, decompensated chronic liver disease, renal insufficiency (creatinine >3.0mg/dl), stroke, dementia and bed bound patients were excluded. Depression was defined as patients scoring 8 or more on Hamilton Depression rating scale (HAM-D) Annexure II.[17] HAM-D score is a 17-item scale, administered by a health professional, with minimum value 0 and maximum value of 52. The severity of depression was divided into four mutually exclusive groups based on HAM-D scores as: Normal (0-7), mild (8-16), moderate (17-23), and severe (≥24). Severity of migraine was assessed on a Visual Analogue Scale from 0 (no pain) to 10 (most severe pain). Migraine Without Aura was defined as patients having at least five attacks lasting 472 hours (unless successfully treated) in addition to at least two of the following pain characteristics: pulsating quality, unilateral location, moderate-severe intensity, aggravated by or causes disruption of physical activity. One of the following should be present during headache: vomiting or nausea, phonophobia or photophobia.[18]

Migraine With Aura was defined as headache having same features as migraine without aura plus any of the following: Visual phenomenon including positive features like flickering spots, lights or lines or negative phenomenon like blind spots or loss of vision, or both, sensory phenomenon including positive features like pins, needles sensations or negative phenomenon like numbness or both, speech disturbance like dysphasia, symptoms of aura that develop over at least 5 minutes and last less than 1 hour; headache, if present, that follows within the hour.[18] The overall data and the gender-based data were analyzed using the statistical software SPSS version 20. The descriptive statistics like mean and standard deviation for the variables of quantitative nature, and frequencies with percentage of occurrences for categorical variables were considered. To study the linear relationship between HAM-D score and each of the observed variables, significance of Pearson correlation coefficient was tested using t-test. However, for multi-category variables like pharmacotherapy, Mann-Whitney test was used to test the significance of correlation. The association between severity of depression, based on HAM-D scores, with each observed attributed was also tested using chi-squared test statistic.

Results

The overall sample of n = 300 patients comprised of nM = 84 males (28%) and nF =216 (72%) females (Table 1). Furthermore, the p-values for testing the significance of correlation coefficient between each variable with HAM-D score are also presented in these tables. The number of females (nF = 216) in the study was more than double the number of males (nM = 84). The mean age of males (36.76 + 9.01) was observed to be higher than females (32.02 + 9.44) but with smaller variation in it. In contrast to females, some males (nM = 4) were observed with HAM-D scores equal to zero. The migraine was more frequent in females (3.84 ± 2.06 episodes per month) than in males (3.77 ± 1.52 episodes per month), but with approximately same average duration in both genders. The literacy rate in the females (nF = 153 (70.8%) was observed to be double than males (nM = 30 (35.7%). The males were taking more antidepressant (nM = 22 (26.2) as compared to female (nF = 43 (19.9). The percentage of females facing photophobia (males =72.6% vs females = 76.4), nausea (males = 58.3% vs females = 68.5%), vomiting (males = 61.9% vs females = 72.2%), pulsatility (males = 61.9% vs females = 72.2%) and functional disability (males = 61.9% vs females = 72.2%) was higher than males. In contrast, the problem of phonophobia (males = 83.3% vs females = 80.6%) and aura (males = 32.1% vs females = 17.1%) was more common in males. The results of significance of pair wise correlation between HAM-D score and each other variable were similar for both genders. The correlation coefficients for age, visual analogue pain score, duration of migraine, education, pharmacotherapy were significantly different from zero at 5% level of significance. The p-values for testing significance of correlation coefficients for different variables are given in Table 1. The frequencies of patients falling under different severity levels of depression (normal, mild, moderate and severe) are presented in the form of a pie chart in figure 1. Furthermore, association between each attribute and severity of pain (with four categories) is examined using chi-square statistic. The corresponding cross tabulation with p-values associated with each test of independence is given in table 2. The results exhibited an association of attributes pharmacotherapy and severity of pain in

(Normal, mild, moderate, and severe) are presented in the form of a pie chart in Figure 1. Furthermore, association between each attribute and severity of pain (with four categories) is examined using chi-squared statistic. The corresponding cross-tabulation with p-values associated with each test of independence is given in **(Table-2).** The results exhibited an association of attributes pharmacotherapy and severity of pain in migraine with different levels of depression. The other attributes were found independent with severity of depression at 5% level of significance.

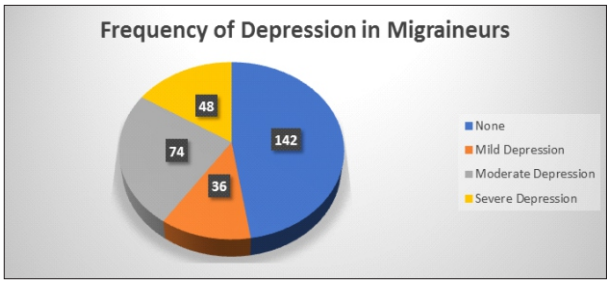

Fig-1: Frequency of depression in migraineurs

Table-1: Descriptive statistics of migraineurs for all patients, for male and female groups.

	Variable		Total 300	Male 84(28)	Female 216 (72)
Continuous Variables	Age		33.34±9.55(17-57)	36.76±9.01(21-55)	32.02±9.44(17-57)
	HAM-D		16.23±9.83(0-35)	15.65±9.45(0-34)	16.46±9.98 (2-35)
	Frequency of migraine per month		3.82±1.92(1-18)	3.77 ± 1.52 (2-13)	3.84 ± 2.06 (1-18)
	Visual analogue pain score		6.17 ± 1.31 (4-9)	6.08 ± 1.39 (4-9)	6.21 ± 1.28 (5-9)
	Average duration of migraine in hours		2.21 ± 1.96 (1-7)	2.20 ± 2.06 (1-7)	2.21 ± 1.93 (1-7)
Categorical variables: n (percentage)	**Education**	Literate	183(61)	30(35.7)	153(70.8)
		Illterate	117(39)	54(64.3)	63(29.2)
	Employment	Employed	208(69.3)	69(82.1)	139(64.4)
		Unemployed	92(30.7)	15(17.9)	77(35.6)
	Pharmacotherapy	Antide Pressant	65(21.7)	22(26.2)	43(19.9)
		No therapy	201(67)	55(65.5)	146(67.6)
		No Antipressant	208(69.3)	7(8.3)	27(12.5)
	Photophobia	No	74(24.7)	23(27.4)	51(23.6)
		Yes	226(75.3)	61(72.6)	165(76.4)
	Phonophobia	No	56(18.7)	14(16.7)	42(19.4)
		Yes	244(81.3)	70(83.3)	174(80.6)
	Nausea	No	103(34.3)	35(41.7)	68(31.5)
		Yes	197(64.7)	49(58.3)	148(68.5)
	Vomiting	No	92(30.7)	32(38.1)	60(27.8)
		Yes	208(69.3)	52(61.9)	156(72.2)
	Pulsatility	No	92(30.7)	32(38.1)	60(27.8)
		Yes	208(69.3)	52(61.9)	156(72.2)
	Side Involved	No	92(30.7)	32(38.1)	60(27.8)
		Yes	208(69.3)	52(61.9)	156(72.2)

Aura	No	236(78.7)	57(67.9)		179(82.9)
	Yes	64(21.3)	27(32.1)		37(17.1)
Diability	No	92(30.7)	32(38.1)		60(27.8)
	Yes	208(69.3)	52(61.9)		156(72.2)

Table-2: Stratification of severity of depression with respect to gender, education, employment status, pharmacotherapy, photophobia, phonophobia, nausea, vomiting, aura and functional disability

		Severity of Depression					
		Non	**Mild**	**Moderate**	**Severe**	**Total**	**P-value**
Gender	Male	41	9	21	13	84	63(29.2)
	Female	101	27	53	35	216	
Education	Literate	93	18	42	30	183	77(35.6)
	Illterate	49	18	32	18	117	
Employment	Employed	98	22	49	39	208	153(70.8)
	Unemployed	44	14	25	9	92	
Pharmacotherapy	Antide Pressant	24	3	24	21	72	
	No therapy	105	28	42	22	197	0.303
	No Antipressant	13	5	8	5	31	
Photophobia	No	33	5	26	10	74	0.196
	Yes	109	31	48	38	226	
Phonophobia	No	26	7	16	7	56	10.806
	Yes	116	29	58	41	244)	
Nausea	No	50	9	31		103	0.218
	Yes	92	27	43	35	197	
Vomiting	No	39	9	31		92	0.116
	Yes	103	27	43	35	208	
Aura	No	68	54	72	48	236	0.279
	Yes	15	19	13	11	64	
Functional Diability	No	113	25	59	39	236	0.117
	Yes	29	11	15	9	64	
Severity of pain in Migraine	Mild	0	0	5	0	5	<0.001*
	Moderate	70	68	59	30	227	
	Severe	13	5	21	29	68	

Discussion

Many studies over the years have shown that migraine patients are more predisposed to have depression. This is a part of the disease or a separate entity just happened to be associated with migraine still remains elusive. However, the evidence is arising with each passing day supporting strong association between these two illnesses. Scarcity of data on the subject makes it imperative to look further into this matter and establish firm grounds on which solid recommendations can be given for evaluation and management of depression in migraineurs. This was a small study including only 300 patients. A large number of these migraineurs were female (72%) which might be due to sampling bias as patients were enrolled from a tertiary care outdoor patient clinic and

A large number of female migraineurs attend clinic as compared to males. It can also represent the increased prevalence of migraine in females. It has been found in previous studies that migraine has been prevalent in females 3 times more as compared to males.[19] and this supports the finding in our study.

In our study, prevalence of depression was much higher than general population up to 52.3%. In a multicultural study evaluating depression in general population, it was found that lifetime depression prevalence ranges from 6.6 to 23% across different cultures.[20] In Pakistan, overall prevalence of depression has been reported up to 6-30%[21,22] In a study of migraineurs, prevalence of depression was found to be 20%.[23] In another study, prevalence of depression has been reported to be around 18.8% in migraineurs.[24] it can be seen from the results of our study that depression is much more prevalent in migraineurs in our country as compared to the developed countries. Many factors can contribute towards this including increased prevalence of depression in our population, lack of pharmacotherapy and deteriorating socioeconomic conditions. Other factors can be inadequate pharmacotherapy and poor socioeconomic status of masses. In our study, Severity of depression was mild 36 (12%), moderate 74 (24.7%) and severe 48 (16%) depression. In our study, it was found that depression was found strongly associated with lack of Pharmacotherapy (more common among migraineurs taking no therapy) and severity of pain in migraine (more common in migraineurs experiencing severe pain during migraine episode). Mitsikostas et al., [25] determined that migraine intensity has got nothing to do with depression however duration and frequency are related to increased depression prevalence among migraineurs. These results are in disagreement with this study which needs to be further explored. Photophobia has been found increasingly associated with depression in some studies and it has been hypothesized that depression contributes towards photophobia between migraine episodes.[26,27] However, this is not the case with our study population which needs further evaluation on a larger scale study. Several limitations can be pointed out for this study including a small sample population, convenient sampling, study setting. It can be recommended that a larger scale study with a control group preferably in a general population survey setting can answer a few questions in more appropriate manner.

Conclusion

It is concluded that depression is strongly correlated with migraine and severity of migraine headache, average duration of migraine episode, no pharmacotherapy.

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Original Article

Role of Memantine in Treatment of Migraine

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Objective: To look for the response of the Memantine for migraine in our society.
Methods: This was a prospective observational trial conducted at Neurology department, Services Hospital Lahore over a period of 1 year, from January 2019 to December 2019. A total of 55 patients were included in the study and they were observed for 1) Headache frequency per month; 2) Headache severity as per pain rating scale (1-10 as mild to most severe); 3) Level of distress as per distress rating scale (1-10, as mild to most sever distress); and hindrance of activity of daily living as per Migraine Disability Assessment Scale (MIDAS). These study variables were noted before the start of treatment. Memantine was started to all of the patients and after 3 months of treatment all patients were re-evaluated for same variable. Also side effects of the drug were noted in the study.
Results: The mean age of the patients in our study was calculated as 43±11.42 years. The headache frequency of the patients per month significantly reduced after 2 months treatment. Also in 76.3% of patients, more than 50% reduction in the frequency of headache was noted after the treatment. The mean MIDAS score before start of the treatment was 81.8±14.76. After 3 months of treatment with Memantine, the MIDAS score found was 15.52±2.84 (P value = <0.05). It was also found that minimal side effects of the drug were encountered by the patients in our study.
Conclusions: On the basis of this study, we conclude that Memantine is a safe drug and can be used for migraine management. However still further randomized trials with larger sample size are being recommended.
Keywords: migraine, memantine, midas score.

Introduction

Following anxiety, migraine is the second most common brain disorder. According to a report by World Health Organization, migraine is ranked as 19th disease among all diseases causing disability.[1] Migraine is generally considered as severely disabling disease which reduces significantly the quality of life of the patients. However, inspite of its high prevalence, only 48% of the people know about their diagnosis of migraine and even smaller percentages of patients seek medical advice for it.[2] According to Bukhari FA , majority of patients of migraine in Pakistan do not seek medical advice, rather they get help from local healers and herbal medicine.[3] A neurologist is usually consulted by most of the doctors only when it is of highest severity and is most disabling to their daily routine life. Migraine typically starts at puberty but the peak age is considered to be 35 to 45 years. Migraine patients suffer from severe headache along with nausea, vomiting, aura symptoms and photophobia.[4] Pain is the most bothersome and common symptom of migraine. There is much research available for the main causative factor for migraine but still its phenomenon is not fully understood. Previously most commonly used treatments for migraine include triptans, pain killers like NSAIDS, ergot derivatives and antiemetics.[5] Recently it has been proposed that glutamate may also play a role in pathophysiology of pain. That's why glutamate blocking agents like Memantine had been proposed for the management of migraine. Actually memantine neither reduces the levels of glutamate nor decreases its release, rather it reduces the action of glutamate by blocking N-methyl-D-aspartate (NMDA) receptor, so preventing the calcium influx and blocking pathway of pain transmission.[6] Only few studies are available in the literature regarding the role of Memantine for migraine management. Recently published studies have emphasized the role of Memantine for migraine with promising results. Therefore, we planned this study to see the effects of Memantine for migraine management in our population.

Method

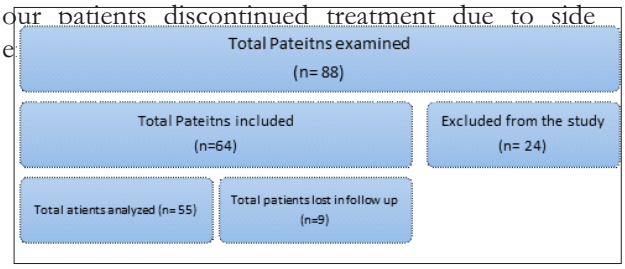
This was a prospective observational study conducted at Neurology Department, Services

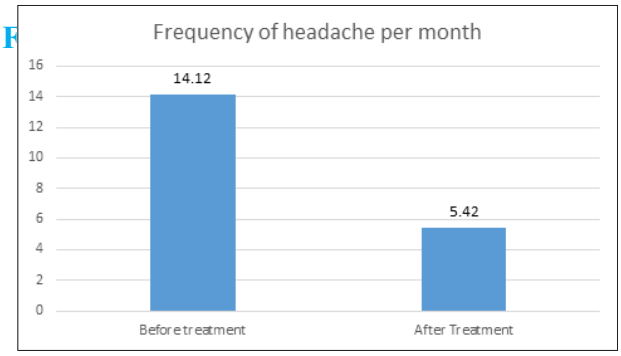
All the male and female patients, with 18-65 years of age, presenting with migraine were included in the study. The diagnosis of migraine was made according to ICHD-II criteria. Patients already taking memantine or those with other types of headache were excluded from the study. Also pregnant women and migraine patients with any neurological or cardiovascular diseases were excluded. All the included patients were supposed to provide consent for inclusion in the study. All of them were started with memantine as 5mg for 1st week, 10mg for 2nd week, 15mg for 3rd week and 20mg from 4th week. They were maintained at a dose of 20mg till the end of 3 months. All these patients were supposed to maintain a headache diary. They were asked for four questions at the start of the study and at the end of 3 months: 1) Headache frequency per month; 2) Headache severity as per pain rating scale (1-10 as mild to most sever); 3) Level of distress as per distress rating scale (1-10, as mild to most sever distress); and hindrance of activity of daily living as per Migraine Disability Assessment Scale (MIDAS). MIDAS is a self-rated short questionnaire which is used to quantify headache related disability over 3-month period. Also side effects of the Memantine use among study participants were noted. All the data were entered on the proforma. Data were analyzed by descriptive statistics programme of SPSS version 21. Mean and standard deviation (SD) were calculated for qualitative variables while frequency was calculated for quantitative variables. Mean MIDAS score was calculated both before and end of the treatments and student t test was applied for calculating the significance by taking P value as <0.05 significant

Results

A total of 88 patients presenting with headache were evaluated in the OPD. Of all these, 24 were excluded from the study as not fulfilling the inclusion criteria. Treatment was started to 64 patients as per protocol of the study. However 9 patients were lost in the follow up and didn't appear in the OPD. So they were excluded from the study and we were left with 55 patients who completed the study (figure 1). Of these 55 patients, 43 patients (78.2%) were female, while 12 were male (21.8%). The age of the patients ranged from 18 to 63 years. The mean age calculated was 43 ± 11.42 years.

Of all the patients included in the study, 21 patients (38.2%) had migraine with aura, while 34 patients (61.8%) had migraine without aura. The headache frequency of the patients per month significantly reduced after 2 months treatment (figure 2). Also in 76.3% of patients, more than 50% reduction in the frequency of headache was noted after the treatment. The headache severity and level of distress of the patients along the scale before and after the treatments is summarized in figure 3 and 4. The mean MIDAS score before start of the treatment was 81.8±14.76. After 3 months of treatment with Memantine, the MIDAS score found was 15.52±2.84 (P value = <0.05) (Table 1). In our study 21 patients had history of migraine along with aura. After treatment, the aura state was not being experienced by 14 of 21 (66.66%) patients. During whole of the treatment, minimal side effects were encountered by our patients, which included rash, agitation, confusion, dizziness and fatigue. However none of our patients discontinued treatment due to side e





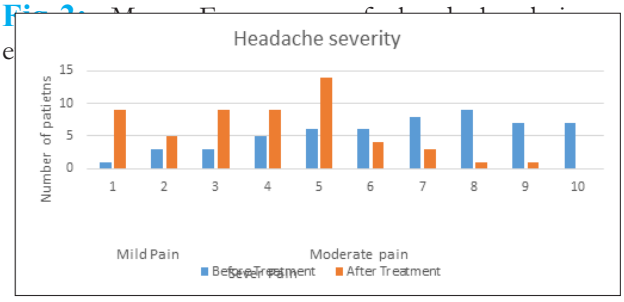


Table-1: Means ± SD of MIDAS score of the patients before and after the treatment.

	Before Treatment MIDAS Score (Mean ± SD)	After Treatment MIDAS Score (Mean ± SD)
Q1: On how many days in the last 3 months did you miss work or school because your headaches?	8.945± 3.365	3.436±1.648
Q2: How many days in the last 3 months was your productivity at work or school reduced by half or more because of your headaches?	26.8±3.73	4.163±2.078
Q3: On how many days in the last 3 months did you not do household work because of your headaches?	11.19±6.543	2.472±1.319
Q4: How many days in the last three months was your productivity in household work reduced by half of more because of your headaches?	214±6.543	4.072±1.766
Q5: On how many days in the last 3 months did you miss family, social or leisure activities because of your headaches?	13.2±5.813	1.381±1.327

P Value = <0.005

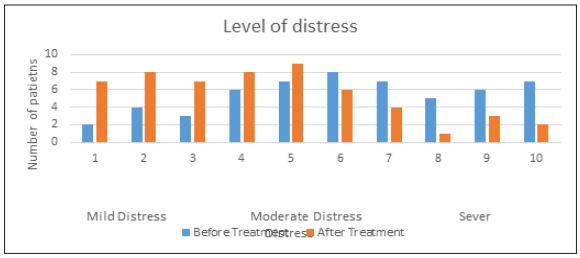


Fig-4: Level of distress as experienced by patients in the study.

Discussion

Memantine has been approved by FDA and is being used for many diseases including headaches, migraine, Alzheimer's disease, alcohol dependence, post-traumatic stress disorder, dementia and obesity.[7-8] Memantine has been proposed for the management of migraine as well as for prevention of migraine. It is because all of these neurologic disorders are thought to be using glutamate for their conduction pathway and Memantine is an NMDA antagonist.[9] During last 5 years, some studies have been conducted on this topic, but still it is a newer drug for neurologists and is not being widely used. Migraine is mainly considered as a disease of females as in our study, 78.2% of patients were females. Similarly Samaan Z et Al conducted a large cohort over 646 patients and they found that there were 82% female patients in the study.[10] In our study, the mean age of the patients was 43 ± 11.424 years. This is also in concordance to the previous large series.[11,12] In our study, patients had high baseline headache frequency which reduced after the memantine therapy. Also in 76.3% of patients, more than 50% reduction in the frequency of headache was noted. Lindelof K et Al. in their placebo-controlled randomized trial found that headache intensity was significantly lower with memantine (3.8) than with placebo (4.1; P = 0.03) on VAS scale.[13] Krusz also reported a 52% and 58% decrease in the frequency of tension-type headache and frequency of migraine respectively from the baseline levels after usage of Memantine.[14] Noruzzadeh R & cooleagues conducted placebo controlled randomized trial on patients with migraine and they found significant decrease in monthly attack frequency in Memantine group than the placebo group. They also found that patients taking memantine had greater reduction in the severity of pain, number of work absence days and disability score than the patients in the placebo group.[15] In our study, memantine was used successfully in all patients with minimal side effects. Jones RW also found in his trial that memantine was well tolerable and fewer side effects were noted. Most commonly noted side effect in that study was dizziness and recurrent headache. Huang L et Al.[16] also found in their systematic review that it was a well tolerated drug in most of the trials with minimal side effects.[17] None of the patient in our study abandoned the protocol because of the side effects. However, Charles A and colleagues mentioned in their study that 6 patients left the treatment because of the side effects which was not the case in our study.[18] As memantine is a relatively newer drug, therefore understanding its pharmacokinetics is important. It has been approved by FDA for usage in USA and is also available in Pakistan. It is usually administered as immediate release formulation and is given twice daily. The maximum recommended dose is 20 mg/day. At the same time, titration of the drug is important.[19] Therefore in our trial, we started the administration of drug as 5 mg, then increasing to 10 mg and 15mg/day. In most of the previous trial same

For analysis of pain score, we used VAS scoring system. It is the most commonly used scale for pain scoring in most of trials. Boonstra AM and colleagues have analyzed VAS and they determined the cut-off level for mild, moderate and sever pain. In their trial, they used 8 different combinations and found that most of the patients labelled VAS ≤3.4 as mild, 3.5-7.4 as moderate and ≥7.5 as severe pain.[20]

Also in our study MIDAS score was calculated for each patient at the start and end of the trial. We found that MIDAS score was significantly low after the treatment of 3 months. Similar findings were noted in another trial which had been conducted in Pakistan. Khalid S et al also found that MIDAS score significantly decreased after 3 months treatment (P= 0.000 (<0.05)).[21] Our trial had many strengths as it was a prospective trial which has shown evidence based medicine in our own population regarding a newer treatment of migraine. At the same time, it had some limitation. It was not a randomized trial and was conducted at a single center. Therefore we recommend more multi-center randomized trial to unreveal the effects of memantine.

Conclusion

On the basis of this study, we conclude that Memantine is a safe drug and can be used for migraine management. However still further randomized trials with larger sample size are being recommended.

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Original Article

Primary Hip Spica Versus External Fixator for Management of Femoral Diaphysealfractures in Children

Sohail Razzaq , Zulfiqar Zahoor Ahmad Cheema, Arif Mahmood, M. Amir Sohail and Mehran Khan

Objective: To compare the results of primary hip spica (HS) to external fixation (EF) for treatment of femoral shaft fractures in children aged 5-10 years in terms of Hospital stay, time to union and Radiological assessment.

Methods: Forty children of age 5-10 years with fracture shaft of femur were divided into two groups; Hip Spica (HS) and External Fixator (EF) which were treated with hip spica & external fixator respectively. Both groups were compared for duration of hospital stay, time for radiological union, radiological assessment, functional outcome, complications and parent/children satisfaction.

Results: Mean duration of hospital stay in Group HS was 1.5 days and in Group EF was 2.0 days ($p < 0.03$). Time for radiological union was lower in Group HS compared to Group EF (8-weeks vs 10-weeks; $p<0.05$) regarding angular deformity at fracture site, in group HS 80% children got sagittal plane angular deformity at fracture site with mean of 16.5° and in group EF 65% children had 11.3° of sagittal plane angular deformity ($p>0.05$). In group HS 70% and in group EF 60% of children had coronal plane angular deformity with the mean of 11° &10° respectively($p>0.05$). There was no rotational deformity in any case of both groups. Patient satisfaction was higher in group EF.

Conclusions: External fixation is better than primary hip spica for treatment of close femoral shaft fracture in children 5-10 years of age because it is associated with lesser complications and it is better tolerated.

Keywords: femoral shaft fracture, external fixator, primary hip spica.

Introduction

Femoral diaphyseal (shaft) fracture is a common pediatric injury with reported incidence of 28 per 100,000 children per year.[1] They usually result from violent injuries especially road traffic accidents and falls from height.[2] Treatment is aimed to allow healing in an acceptable position with minimal disruption to the muscles and joints there by restore the child to normal functions as quickly and effectively as possible.

Non-operative methods of treatment include immediate spica cast application, traction and delayed spica cast immobilization. Operative methods include external fixation, flexible intramedullary nailing and plating.[3] Choice of treatment depends upon age of patient, fracture type (open vs closed), parent's acceptance and surgeon preference.[4] In recent times, surgical intervention has been gaining popularity over nonsurgical treatment as it shortens hospital stay, allows early mobility and has better patient and parent satisfaction.[5] The main disadvantages of external fixation are over growth, pin tract infections and increased risk of refracture.[6] Contrary to this, non-surgical treatment in the form of spica casting is still preferred treatment option because it is cost effective in school going children.[7] The purpose of present study is to compare the results of non-operative (primary hip spica) to operative (external fixation) treatment of femoral shaft fractures in children aged 5-10 years.

Method

This prospective, descriptive, randomized study carried out in the Department of Orthopaedic Surgery, Services Hospital, Lahore from October 2012 to December 2013.Informed consent was obtained from the parents of all participants. Forty patients of age 5-10 years with closed femoral shaft fractures were randomly assigned numbers. Patient with odd numbers were placed in HS group those with even number were placed in EF group. Group HS, children were treated with hip spica, and in Group EF they were treated with external fixator. Children with open femoral fractures, metaphyseal or epiphyseal extension of femoral shaft fractures, segmental femoral shaft fracture and multiple fractures and children with head, chest and abdominal injuries were excluded from study. The deomgraphic profile of the patient is shown in (**Table-1)**.

Table-1: Demographic profile.

		Group- HS	Group-EF
	Age (Years)	7.6±1.6	7.1±1.2
	Gender (M/F)	15/7	13/5
Mode of injury n(%)	Fall from height	14 (35.0%)	17 (42.5%)
	Road traffic accident	4 (10.0%)	5 (12.5%)
Fractures level distribution n(%)	Middle third	11 (27.5%)	13 (32.5%)
	Proximal third	4 (10.0%)	3 (7.55%)
	Distal third	4 (10.0%)	5 (12.5%)
Type of fractured n(%)	Transverse fracture	14 (35.0%)	17 (42.5%)
	Oblique	2 (5.0%)	3 4.5%)
	Spriral fracture	1 (2.5%)	3 (7.5%)
Side of fractured n (%)	Right	14 (35.0%)	9 (22.5%)
	Left	9 (22.5%)	8 (20.0%)

History and examination was done once patients were stabilized as per ATLS protocols. Pediatric size Thomas Splint was applied in emergency settings before specific management. AP and lateral X rays of injured limb with joint above and below the injury were obtained. In Group HS, half hip spica was applied under sedation and analgesia with injured limb in 45°flexion at hip and 70° flexion at knee. The hip was abducted at 30°. However for more proximal fracture the abduction was increased up to 45°. EF group was fixed in AO external fixator with Shanz screw size 4mm. Two proximal and two distal Shanz screws were inserted under Image Intensifier after General Anesthesia. In two cases the fracture side had to be opened due to soft tissue inter position. In both groups, post-operative radiographs were done and children were discharged from the hospital with instructions of either plaster care or external fixator care 24-48 hours after the procedure. All children were followed at three weekly intervals with fresh radiographs of affected femur. The first follow up visit however was after 02 weeks. At each follow up children/ parents problems were discussed, any complication detected, radiograph assessed and further instruction were given. In Group HS, spica cast was removed when on radiographs fracture callus achieved the density of normal cortical bone. In Group EF, full weight bearing was started with the help of stick when there was sufficient callus at fracture site. When radio density of callus approached that of normal cortical bone the fixator was removed and regular dressing was done for pin tracts. Hospital stay, time for radiological union, radiological assessment, functional outcome, complications and parent/children acceptance for these methods of treatment was noted. Data was analyzed using SPSS V20.0, Inc, USA. Frequency and percentage were calculated for categorical data while mean and standard deviation was calculated for numerical data. Student t test and chi square/fisher exact tests were used to test the difference between groups.

Pit Falls of the Treatment:

Both method of treatment had some pitfalls e.g patients in HS group had to face problem of mobility in the bed and nursing care. There was difficulty in changing clothes in this group. Parent had to face soaking of spica with urine and foul smell which was mainly because of wetting by urine and excreta. Another pitfall of this statement was the breakage of spica at hip level. Four patients developed loss of reduction at fracture side in HS group and were re manipulated at two weeks follow up.

In EF group mobility and nursing care was relatively a minor issue then HS group. These patients had more issues regarding pain and fever which was mainly because of pin tract infection. Which was superficial and didn't progress to osteomyelitis. **(Table -2)**

Table-2: Pitfall of the two treatment.

Problem n(%)	Group- HS	Group-EF
Restricted mobility in bed	20 (100%)	6 (30%)
Inability to walk	20 (100%)	12 (60%)
Fever	2 (10%)	4 (20%)
Difficulty in cloth changing.	20 (100%)	0 (0%)
Plaster soakage with excreta	4 (20%)	0 (0%)
Problem in taking bath / cleaning	20 (100%)	20 (100%)
Inability to attend school	20 100%)	20 (100%)
Sinability to carry out indoor playing activities.	20 (100%)	10 (50%)
Plaster problem (sores, impingement)	6 (30%)	0 (0%)
Pin tract infection / discharge	0 (0%)	2 (10%)
Loss of reduction	4 (20%)	0 (0%)
Pain due to stiffness (Hip, Knee) or pin tract	5 (25%)	10 (50%)

Results

Mean duration of hospital stay in Group HS was 1.5 days and in Group EF was 2.0 days ($P < 0.03$). Time for radiological union was lower in Group HS, with mean 8 weeks (Range 7-9 Weeks) as compared to mean 10 weeks (Range 9-11 weeks) in Group EF ($P <$

In Group HS 80% children got sagittal plane angular deformity at fracture site with mean of 16.5° and in Group EF 65% children had 11.3° of sagittal plane angular deformity (P > 0.05). In Group HS 70% and in Group EF 60% of children had coronal plane angular deformity with the mean of 11° and 10° respectively (P > 0.05). In EF group 02 cases out of 20 cases developed pin tract infection but none of them reach to the state of osteomyelitis.

Fortunately, they responded very well to the one week course of antibiotics. In HS group 04 patients developed loss of reduction that was mainly because of loosening of hip spica at hip joint level. Among these 04 cases 03 cases had fracture at the proximal third of shaft of femur and 01 at the mid shaft level. All these patients were remanipulated at 02 weeks follow up. There was no case of refracture. Functionally, children in both groups regained full range of hip and knee movements within three weeks of removal of fixation. Clinically there was no rotational deformity in any case in both groups.

Discussion

Ideal treatment of femoral shaft fractures in children as defined by Staheli and Sheridan[8] is the method that controls length and alignment, prevents excessive elevation or compression of extremity, comfortable to handle for children as well as for parents and results in minimal psychological effects. Spica casting is associated with psychosocial impacts for children and their parents as has been reported by Hughes et al.[9] External fixation is a good alternative for the operative management of femoral shaft fractures in children. It provides good stability, is less invasive and allows early mobilization.

Time of radiological union was more in external fixator (70 days) than spica cast (56 days). Feld et al managed femoral shaft fracture with external fixator with average time of 67 days.[10] In Group HS 80% children got sagittal plane angular deformity at fracture site with mean of 16.5° and in Group EF 65% children had 11.3° of sagittal plane angular deformity (P > 0.05). In Group HS 70% and in Group EF 60% of children had coronal plane angular deformity with the mean of 11° and 10° respectively (P > 0.05). Wallace ME et al in their series concluded that in children under 13 years of age mal union of as much as 25° in any plane will be remolded enough to give normal alignment of the joint surfaces.[5] They received 28 children with unilateral middle third fracture of femoral shaft who had an angular deformity after union of 10°-26°. At average follow up of 45 months. The average correction was 85% of the initial deformity. They found that 74% correction occurred at physis and only 26% at fracture site.[11]

Commonest complications reported in previous studies include delayed union, refracture, pin tract infection and malunion.[12] With recent advances in material and design of external fixator pin along with use of sharp drill bits, hydroxyapatite-coated pins, early use of antibiotics for pin sit infection has resulted decrease incidence of complications.[13] In our study, there was no case of refracture. Rate of refracture cited in literature is 1%-22%.[14]

It was because we progressively destabilized the fixator from 2 weeks postoperative time onwards which resulted in gradual load transfer to the bone from the fixator. Conversely, pin tract infection was major complication involving 10% of cases and cause of pain at pin site and fever in some patients in external fixator group. However, it was superficial infection in all cases and healed with proper pin care and oral antibiotics (amoxicillin). Kirschenbaum et al in a series of 10 femoral fractures reported, a 30% incidence of pin tract sepsis.[15] Tolo mentioned a 50% incidence of pin tract sepsis using Hafman fixator.[16] Gregory et al reported a 34 tibial and femoral shaft fracture in children treated with external fixator. They reported pin site infection rate of 10.3%.[17]

Main complication in spica group were plaster sores in 30%, loss of fixation. Remanipulation and change of cast was done in 4(20%) cases. Plaster sores usually occur due to improperly molded plaster edges or soakage and wetting of cast with excreta. Plaster soakage and softening causes loss of fixation that require remanipulation and change of cast. It was noted in our study that out of 04 patients which resulted in loss of reduction 03 had fracture in the proximal third of femoral shaft and one in the middle showing that maintaining the reduction with spica is much difficult in proximal femoral shaft fractures. After remanipulation the spica cast was applied in more flexion and abduction at hip that is 45°.

Regarding parent satisfaction in Group HS, majority of the parents were not satisfied with the method of treatment because it was difficult for them to properly take care of the children, especially cleaning the child, cleaning clothes and turning the child in bed. They were also annoyed with the smell coming out of plaster cast soaked with urine. Plaster sore were also

patients regain nearly normal range of motion at hip and knee during the follow up period of 06 months and there was no residual limp in any case.

Conclusion

We conclude that for children of 5-10 years age, external fixation is better treatment option for close femoral shaft fracture as it is associated with lesser complications and it is better tolerated.

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Original Article

Is Pre-operative Ultrasound Scoring Helpful in Predicting Conversion to Open in Laparoscopic Surgery?

Said Umer, Wasim Hayat Khan, Usman Ismat Butt, Muhammad Umar and Mahmood Ayyaz

Objective: To determine the positive predictive value of preoperative ultrasound score of ≥3 in predicting conversion from laparoscopic to open cholecystectomy.

Methods: Consenting adult patients of both genders who had been evaluated by ultrasound performed by a consultant radiologist 48 hours before the surgery and were undergoing laparoscopic cholecystectomy were included in the study. Patients with American Society of Anesthesia score (ASA) III-IV were excluded from the study.180 patients were included in the study.

Results: There were 66 males (36.7%) and 114 females (63.3%). The mean age was 47.33± years and the range was from 19 to 77. Conversion to an open procedure was required in only six cases. There was no association between gender, age group, diabetes, obesity No association between preop ultrasound score and conversion was found (Positive predictive value 3.3%).

Conclusions: Preoperative ultrasound scoring doesn't predict conversion from laparoscopic to open cholecystectomy.

Keywords: laparoscopic cholecystectomy, conversion, predictive factors.

Introduction

Management of gallbladder disease has undergone major shift over the past 25 years. The introduction of laparoscopic surgery has dramatically altered the way in which cholecystectomy is done. Laparoscopic surgery has now become the gold standard.[1] The major advantage laparoscopy holds over open surgery are the minimally invasive approach which results in smaller incisions, less patient pain, notable decrease in post-operative pain, decreased hospital stay, shorter post-operative fasting period, early mobilization m earlier return to routine activities, an overall decreased patient morbidity and cosmetic scars.[2,3] There has been evaluation and progression in laparoscopic surgery. Single port laparoscopic surgery and Natural Orifice Endoscopic Surgery (NOTES) are now moving towards mainstream surgery.[4] Despite the advances in laparoscopic technology and technique there is at times a need to convert to open operation.[5] Although necessary this conversion is associated with increased morbidity in terms of wound infections, respiratory comp-lications and prolonged hospital stay.[6,7] Evaluation and understanding of pre-operative predictors for conversion is helpful to the surgical team and patient to prepare for the outcome. The gold standard investigation for the pre-operative investigation of gallbladder disease is abdominal ultrasound.[8, 9] Although operator dependent, it provides crucial information on the characteristics of the gallbladder and its contents pre-operatively.[10, 11] Long standing inflammation of the gall bladder causes contraction and thickening of the wall of gall bladder. Increased adhesion formation, severe pericholecystic fibrosis and distorted anatomy in Calot's triangle are associated with these. All these can result in increased difficulty for the surgeon performing the surgery and are associated with increased risk of conversion of open surgery.[12]

A scoring system was proposed by O' Leary et al in 2013.[13] They proposed a 4 point scoring system for preoperative ultrasound. They are recorded presence of a gallstone impacted in Hartmann's pouch, diameter of the common bile duct, gallbladder wall thickness (>4 mm) and contraction of the gallbladder. These were noted by means of ultra-sound. They found that patient who had a preoperative score of 2 or more had a 19.2% chance of conversion from laparoscopic to open cholecystectomy. [13,14]

The objective of our study was to determine the positive predictive value of preoperative ultrasound score of ≥3 in predicting conversion from laparoscopic to open cholecystectomy.

Methods

This was an cross sectional study of 180 patients who underwent laparoscopic cholecystectomy at the Department of Surgery, National Hospital & Medical Center, Lahore between January 2016 to December , 2018. We included patients undergoing laparoscopic

history of upper abdominal surgery and coagulopathy were excluded. All patients provided informed written consent for the procedure and study protocol. All the patients after clinical history and examination, underwent ultrasound examination before the procedure. Ultrasonic variables that were recorded included presence of a gallstone impacted in Hartmann's pouch, diameter of the common bile duct (CBD), gallbladder wall thickness (> 4 mm) and contraction of the gallbladder. All patients were operated by a single consultant laparoscopic surgeon with more than fifteen year experience after post graduation.

Demographic variables collected from hospital record. Demographic and USG findings documented. A score based on the ultrasound calculated with a score of 1 given for each ultrasound feature present. A minimum score of 0 and a maximum score of 4 recorded. Operation notes used to determine whether there was any conversion or not. All data recorded from patient file, ultrasound report, and operation notes and recorded on a questionnaire .

Data was analyzed on SPSS statistical software version 21. Qualitative data i.e gender, comorbid condition, ultrasound features and score based on ultrasound were represented with frequency and percentage. Chi square was used for association between demographic, comorbid condition and conversion to open.

Results

A total of 180 were included in our study.

There were 66 males (36.7%) and 114 females (63.3%). Female to male ratio was 1.72:1. The mean age was 48.15 years ±14.40 SD and the range was from 19 to 77. The mean ASA grade was 2. 78 (43.3%) patients had DM. 54(30.0%) had HTN. Obesity was prevalent in only 36 (20.0%) patients.

Ultrasound scores of all the patients were recorded. Mean score for male patients was 1.14 ± 0.89 and mean score for female patients was 1.34 ± 0.99. There was conversion from laparoscopic to open surgery in six cases. The reason for conversion in all patients was inability to proceed due to dense adhesions and thick walled gallbladder. The overall rate of conversion was 3.34%. A total of 4 ultrasonic features were noted and used for analysis. The overall mean gallbladder wall thickness was 2.6±2.4 mm and ranged from 1.4 mm to 6.7 mm. The gallbladder wall thickness in the converted group was 4.6 mm. Of the 180 cases studied 138 patients had gall bladder wall thickness more than 4 mm and two were converted. 6 cases had a stone impaction at the neck. None were converted to open procedure. In our study there were 144 contracted gallbladders out of which 6 were converted to open cholecystectomy. 24 patients had dilated CBD on ultrasound. None were converted. However none of these were statistically significant. After univariate analysis of the pre-operative variables, 1 patient variable and no ultrasonic variable was found to be significantly associated with conversion to an open procedure. The positive predictive value for an ultrasound score of ≥3 came out to be only 3.3%. Age (p= 0.09) and gender (p=0.6) had no effect on conversion. The most common age group affected was 41 to 60 years old patients. Diabetes and obesity also had no significant effect on conversion (p-value 0.85 and 0.31 respectively). Hypertension , surprisingly , being the only patient variable that showed significant correlation with conversion to open. (P=0.0006) When we stratified the results according to the ultra-sound score , we had 42 cases with ultra-sound score 0 out of which there were no conversions , 66 cases had ultra-sound score 1 of which 2 were converted , 57 had score of 2 with there being 2 conversions while 12 had score of 3 out of which one was converted. There were 4 cases

Table-1: Clinical features and their distribution.

Clinical Features		n(%)
Gender	Male	66 (36.7%)
	Female	114 (63.3%)
Comorbid	Hypertension	54 (30.0%)
	Diabetes	78 (43.3%)
	Obesity	36 (20.0%)
Ultrasound features	Thick wall	138 (76.60%)
	Contacted gallbladder	6 (3.33%)
	Hartman pouch stone	144 (80.0%)
	Common bile duct dilation	24 (13.3%)
Score	0	42 (23.3%)
	1	66 (36.7%)
	2	57 (31.7%)
	3	12(6.7%)
	4	3 (1.7%)
Age Groups	40 years or less	54 (30.0%)
	41 60 years	90(50.0)
	61 and above	36 (20.0%)
Conversion		6 (3.3%)

Having score of 4 and 1 had to be converted. Results are summarized in (**table-2)**. Even though patients having score of 3 or more were more likely to undergo conversion(3 % converted for ultra-sound score of 1 vs 33% converted for ultrasound score of 4) this difference was not found to be significant. (p = 0.08) . None of the ultrasound features had a positive correlation with conversion.

Table-2: Ultra-sound and conversion to open.

USG Score	Number of Cases	Conversion to Open
0	42	0
1	66	2 (3%)
2	57	2 (3.5%)
3	12	1 (8.3%)
4	3	1 (33.3%)

Table-3: Association of gender, age group and comorbid condition w.r.t conversion to open.

		Conversion to Open Yes	No	P-value
Gender	Male	3 (4.5%)	63 (95.5%)	0.60
	Female	3 (2.6%)	111 (97.92%)	
Age Groups	40 & less	3 (2.08%)	141 (100.0%)	0.09
	More than 40	3 (8.3%)	33 (91.7%)	
Diabetes	Yes	3 (3.8%)	75 (96.2%)	1.00
	No	3 (2.9%)	99 (97.1%)	
Hypertension	Yes	6 (11.1%)	48 (88.9%)	0.0006
	No	0 (0.0%)	126 (100.0%)	
Obesity	Yes	3 (8.3%)	33 (91.7%)	0.09
	No	3 (2.1%)	141 (97.9%)	
USG Score Variables	No	4	132	0.6
	Wall thickness	0	42	
	>4mm	0	24	1.00
	Dilated CBD	0	156	
	Stone	0	6	1.00
	Impaction	0	174	
	Contracted Gb	138	6	1.60
		36	0	
USG Score of 3 or more than 3	No	4 (2.2%)	161 (89.44%)	0.08
	Yes	2 (1.11%)	13 (3.33%)	

Discussion

We studied the ultra-sound features of 180 patients . Out of these , almost one third were male(36.7%) while two third were female(63.3%). This is inline with findings of other researchers who have shown an increased tendency of formation of gallbladder stones in female gender.[15,16] Only 30 % of the patients were under the age of 40 , while majority (70%) were older. The same has been noted in other studies which showed a dramatic increase in the incidence of gall bladder disease after age of 40.[15,16] In our study only six patients had conversion. (3.34%). This figure is comparable to international literature. The conversion rates documented in different studies range from 5% to 10%.[17] In our study we have included 180 patients in which four ultrasonic parameters for predicting difficult laparoscopic cholecystectomy were analyzed. The parameters in literature for predicting difficult laparoscopic cholecystectomy are: Gall stone size, Gall bladder wall thickness, Gall bladder volume, Number of stones, Common bile duct size, and stone impaction in the neck of gall bladder.[18,19,20] Out of these gall bladder wall thickness, common bile duct diameter, contraction of gall bladder and stone impaction shows the maximum correlation with the difficulty during laparoscopic cholecystectomy and/or risk of conversion to open procedure.[21,22] In our study however, we found no statistical correlation between preoperative ultrasound score and conversion in the laparoscopic cholecystectomy. This is different from what has been reported in international literature which suggest a role of ultrasound in the preoperative prediction of conversion to open.[10,23,24] We failed to reach this conclusion and our results suggest otherwise. There appears to be no role of ultrasound in predicting conversion to open in laparoscopic cholecystectomy. Such conclusion were also reached in other studies which showed that shows that there is no correlation between the ultrasonographic findings and difficult laparoscopic cholecystectomy.[25]

Our study shows that preoperative ultrasound does not predict conversion to open for laparoscopic cholecystectomy to a good extent.However our study has a small sample size and larger more powered studies are needed to confirm the findings of our study.

Conclusion

On the basis of our study we conclude that the use of preoperative ultrasonography to predict the conversion from laparoscopic cholecystectomy to open is not a very reliable tool. It can however be used tp predict the difficult anatomy and serve as a warning to the surgeon.The role of hypertension in prediction of conversion need to be further investigated.

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Original Article

FREQUENCY OF PREVENTION OF OMPHALITIS BY TOPICAL APPLICATION OF CHLORHEXIDINE TO NEONATAL UMBILICAL CORD STUMPS

Fatima Tahira, Muhammad Khalid Masood, Riffat Omer and Humayun Iqbal Khan

Objective: To determine the frequency of prevention of omphalitis by topical application of chlorhexidine to neonatal umbilical cord stumps.

Methods: This quasi experimental study was conducted at departments of Pediatrics and Obstetrics & Gynecology, Lahore General Hospital Lahore, from 01-05-2019 to 01-08-2019. A total of 200 neonates were included in this study. 4% chlorhexidine was applied to neonatal umbilical cord on first, third and fifth day of life and were then observed for prevention of omphalitis in first seven days of life.

Results: Mean age of the neonates was 1.45±0.98 days. There were 90 (45.0%) males and 110 (55.0%) females. Prevention of omphalitis was observed in 188 cases (94.0%) (Table-3). Stratification with regard to age and gender was also carried out.

Conclusions: We concluded that topical application of chlorhexidine to neonatal umbilical cord stumps resulted into significant reduction in omphalitis.

Keywords: neonates, chlorhexidine, umbilical stump, omphalitis

Introduction

Every year, almost 4 million neonatal deaths occur in under developed countries.[1] Infections contribute to be the major cause of neonatal mortality estimating about 1·44 million (36%) deaths. Fifty percent neonatal deaths in developing world are due to infections.[2] Omphalitis is the common cause of sepsis in the first few days of life.[3] Infection of the umbilical cord can lead to omphalitis, resulting into pus, abdominal wall erythema, or swelling. However, if we look around there is not enough data available on the incidence of omphalitis and most centers in developing world don't focus much on cord care and there is also limited evidence exists for appropriate cord-care, so there is a need to address on this issue.

There are various topical antimicrobials available in the market for cord care (eg, ethanol, silver sulfadiazine, triple dye, gentian violet, chlorhexidine, povidone iodine), however 4% chlorhexidine seems to be better choice among all. It has potent bactericidal activity, safe to use, strong binding potential that results in residual effectiveness, and easily affordable due to low cost 4. It decreases bacterial colonization of the cord stump and reduces superficial skin infections .[5]

Omphalitis is a main cause of sepsis.[6] Different studies were conducted in Nepal, Pakistan and Bangladesh to see the effect of chlorhexidine application to the newborn umbilical cord for prevention of omphalitis . A total of 54624 neonates were taken and prevention of omphalitis is noted in a range from 27% to 56%.[7] Another study conducted in Nepal showed prevention of omphalitis in 95% by use of topical chlorhexidine.[2] As there is only one local study conducted in Pakistan on the role of chlorhexidine in prevention of omphalitis and there is disparity among the results of different studies, also no such study has been conducted in tertiary care hospital set up so this study is planned to see the role of chlorhexidine in prevention of omphalitis in neonates born at tertiary care hospital so that if there is significant reduction in the incidence of omphalitis then we can recommend application of chlorhexidine to umbilical cord stump to neonate in tertiary care hospital.

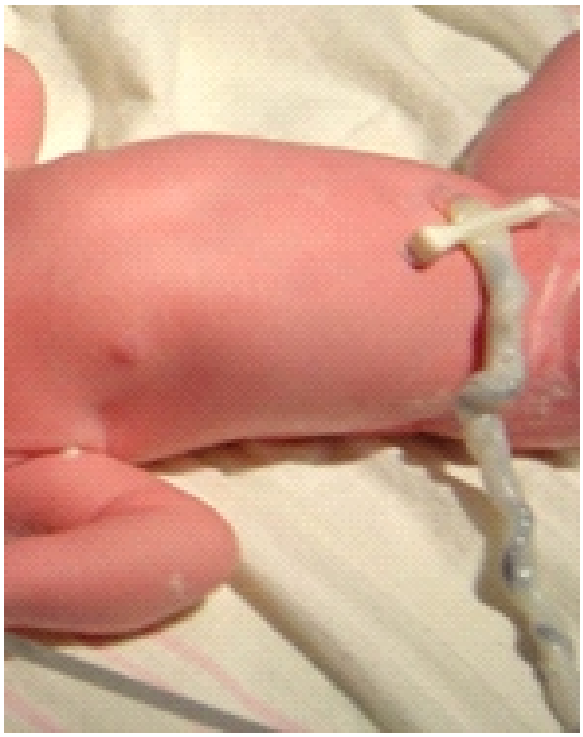
Methods

The quasi experimental study was conducted in the Department of Pediatrics and Obstetrics &Gynecology, Lahore General Hospital Lahorefrom 01-05-2019 to 01-08-2019. A sample of 200 cases was taken using 95% confidence level, 7% margin of error taking an expected percentage of prevention of omphalitis in 42% of cases. 8 Non-probability consecutive sampling was used. Neonates both male and female born at term (38 weeks of gestation determined by ultrasonography) in Lahore General Hospital were included in the study however those neonates born to mothers with history of any infection assessed on the basis of increased total leucocyte count , neonates with congenital anomalies

and ultrasonography and neonates requiring umbilical vein catheterization with serum total bilirubin level > 16mg/dl within first 24 hour of life were excluded.

After ethical clearance, neonates fulfilling the inclusion criteria were recruited for study from neonatal or postnatal ward in Lahore General Hospital. After taking informed consent from parents, neonate was examined by researcher herself and 4% chlorhexidine was applied to neonatal umbilical cord on first, third and fifth day of life and were then observed for prevention of omphalitis in first seven days of life as described in operational definition. All the information was collected and noted in structured proforma.

Data analysis was done with SPSS version 20.0. Quantitative data like age was presented in the form of mean and Standard deviation. Qualitative data like gender, prevention of omphalitis presented in the form of frequency and percentages. Prevention of omphalitis stratified between age and gender to see effect modification. Post stratification done through Chi square test and p value > 0.05 was considered significant.



Umbilical cord of a three-minute-old child. A medical clamp has been applied.

Results

Total 200 neonates were included in this study during the study period of six months from 01-05-2019 to 31-08-2019. Mean age of the neonates was 1.45±0.98 days. **(Table-1)** There were 90 (45.0%) males and 110 (55.0%) females **(Table-2).** Prevention of omphalitis was observed in 188 cases (94.0%) **(Table-3).** Stratification with regard to age and gender was carried out and presented in **Tables 4 and 5.**

Table-1: Distribution of cases by age.

Age (Days)	Number	Percentage
1 Day	111	55.5%
2 Days	89	44.5%
Total	200	100.0%
Mean±SD	1.45±0.98	

Table-2: Distribution of cases by gender

Gender	Number	Percentage
Yes	188	94.0%
No	12	06.0%
Total	200	100.0%

Table-3: Distribution of cases by age.

Prevention	Prevention of Omphalitis Yes	No	Total
0-1 Day	106	05	111
2 Days	82	07	89
Total	200	12	200

Table-4: Stratification with regard to age.

Age	Prevention of Omphalitis Yes	No	Total	P-value
0-1 Day	106	05	111	
2 Days	82	07	89	0.320
Total	200	12	200	

Table-5: Stratification with regard to age.

Gender	Prevention of Omphalitis Yes	No	Total	P-value
Male	106	07	90	
Female	82	05	110	0.338
Total	200	12	200	

Discussion

Every year, 3.1 million neonatal deaths occur worldwide. Out of which infections account for about 30% .[1] In areas with high-mortality rates, infections are the major cause .[9] In such a situation, it is essential to take such measures that can prevent infection-related death. These measures should be simpleand cost-effective so that can be implemented in different regions across the world .[10] Topical application of antiseptics is one such measure that can decrease the rate of infections by reducing the

Among different antiseptics available, chlorhexidine is the most studied agent in newborn infants. Different researches have shown that topical application of chlorhexidine has resulted into significant reduction in the rates of bacterial colonization of the umbilical cord. [11,12]

In our study, out of 200 cases, 90 (45%) were male and 110 (55%) were female. While 111 (55.5%) were on day 1 of life and 89 (44.5%) were on 2nd day of life with mean+SD 1.45±0.49. Frequency of prevention of omphalitis by topical application of chlorhexidine to neonatal umbilical cord stumps in tertiary care hospital was done that showed 12 (6%) developed omphalitis and 188 (94%) remained healthy. A 2-year hospital-based study of neonatal omphalitis in eastern Turkey reported an even increased incidence of omphalitis , 7.7% inpatient newborns per year .[13] Gram-positive bacteria (mainly S. aureus) 68% were more commonly isolated from the cord than Gram-negative bacteria (mainly E. coli) 60%. Mortality rate was 15%.

A study conducted at Royal Women Hospital Elsevier that was of 6 years duration. In that study bacteria isolated from swabs taken from clinically apparent infections of the stump of the umbilical cord showed an overall infection rate of 0.7% (200/27,107), in which Gram-negative organisms were more isolated as compared with Gram-positive organisms (171/118). [14] In the last few years, new evidence from different studies conducted in Bangladesh, Nepal and Pakistan has been published regarding prevention of omphalitis and is noted in a range from 27% to 56%.[2,3,13] Another study conducted in Karachi, showed prevention of omphalitis in 42% after application of topical chlorhexidine on neonatal umbilical cord.[7] Another study conducted by Mullany et al (2006) demonstrated prevention of omphalitis in 95% by use of topical chlorhexidine. [2]

Based on CHERG (child health epidemiology reference group) rules,they concluded that application of chlorhexidine to newborn umbilical cord can significantly reduce incidence of umbilical cord infection and all-cause mortality among home births in community settings. This cost effective and simple measures can save a major number of newborns in developing countries. Chlorhexidine has now been used for cord care in hospitals and is included in WHO's essential drug list. There has been no side effect noted by its use in hospital and community setting and also no side effects have been noted in any of the included subject in our study.

Conclusion

We concluded that there is significant prevention of omphalitis by topical application of chlorhexidine to neonatal umbilical cord stumps in our tertiary care hospital.

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Original Article

Diagnostic Outcomes of Patients Presenting with Per Rectal Bleed in Surgical Departments of Services Hospital Lahore

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Objective: To determine the diagnostic outcome of patients presenting in Out-Patient Department with per rectal bleeding.

Methods: Patients presenting in the SOPD falling under inclusion criteria were recruited for the study. Detailed history along with clinical examination and laboratory tests were carried out for every patient. Data of each participant was recorded on a structured questionnaire, and the data was entered in SPSS version 22. Descriptive statistics were used to calculate frequency and percentages, represented using pie charts and cross tables.

Results: In the study, male to female ratio was 1:1.9. Hemorrhoidal disease was the most common cause of rectal bleed at 39% among the participants followed by anal fissure (30.5%). Colorectal carcinoma (21%) was the third most common cause.

Conclusions: It was concluded that hemorrhoid disease was the most common cause of rectal bleeding in surgical OPD followed by anal fissure. Colorectal carcinoma was the third most common cause in this study.

Keywords: rectal bleeding, out-door patient department, diagnostic outcome.

Introduction

Rectal bleeding, referred to as rectal hemorrhage, is a common symptom in general population that occurs due to an underlying pathology.[1] It may be a serious underlying cause or a self-limiting one. The incidence of rectal bleeding has been reported to be between 16% and 33% during life of an adult.[2] The causes of rectal bleeding include hemorrhoids, colorectal carcinoma, anal fissure, rectal polyp, ileocecal TB, mesenteric ischemia, solitary rectal ulcer, ulcerative colitis, rectal prolapse and gastro intestinal stromal tumors (GIST),[3] there are many other pathologies that can lead to rectal bleed but this study will limit to the causes mentioned. Colorectal carcinoma has been found in high prevalence among adults of age more than 50 years[4] along with cases of hemorrhoids and anal polyps. In young population, mostly hemorrhoids and anal fissure are related to rectal hemorrhage.[5]

In developed countries colonoscopy is done after the age of 40 years as a screening tool for anorectal malignancies. However, in the developing countries, due to lack of resources, colonoscopy is not usually done as a screening tool. In these countries patient usually present with per rectal bleed which is then diagnosed through clinical examination and proctoscopy and the doctor advises colonoscopy or sigmoidoscopy if the etiology is not understood.[6]

Bleeding per rectum is a common presentation in the surgical out-patient department (OPD). This study focuses on the diagnostic outcome of patients presenting with this symptom in the Surgical Outdoor of Services Hospital Lahore, which is a tertiary care hospital present in the heart of Lahore city, Pakistan. It is an 1192 bedded hospital containing all the major specialized departments. The outcome will provides facts about prevalence of different surgical pathologies that lead to per rectal bleed ii surgical department of our setup.

Methods

This was a cross sectional study carried out in the Surgical Out-Patient Department (SOPD) of Services Hospital Lahore from 1st September 2017 to 31 August 2018, including 367 patients. Non-probability purposive sampling technique was performed for participant recruitment. Patients of both sexes and age greater than 16 years and presenting with chief complaint of rectal bleeding were included in the study. Patient with upper gastrointestinal source of bleeding, rectal bleeding as an outcome of infectious bloody diarrhea and patients with previously known bleeding disorders, chronic liver disease, taking any anti coagulants and medical causes of bleeding (IBS etc) were excluded from study.

Patients presenting in the SOPD falling under inclusion criteria were recruited for the study.

Tests were carried out for every patient. Consent was taken from every participant and permission from the ethical board of the hospital was also granted. Participants who were not diagnosed through clinical examination of rectum were advised to undergo sigmoidoscopy or colonoscopy Age, gender and diagnostic outcome of each participant was recorded on a structured questionnaire, and the data was entered in SPSS version 22. Descriptive statistics were used to calculate frequency and percentages, represented using pie charts and cross tables. All the work performed in this study was in line with the STROCSS criteria.[8]

Results

In the study the most common age group was 26-35 years followed by 36-45 years at 21%. Male participants were more in number than females at 65.4%. In the present study, hemorrhoidal disease remained the most common cause of rectal bleed in total at 39% and it was found to have occurred most frequently in age group 36-45 years. The second most observed disease was anal fissure at 30.5% and it was seen in age group of 26-35 years most commonly. Diseases such as GIST, ulcerative colitis, rectal prolapse and solitary rectal ulcer were the most rare with frequency less than 1%. Rectal polyp, ileocecal TB and mesenteric ischemia were also not very common among the participants with an average percentage of 2.5 each. Colorectal carcinoma was found out to be the third most commonly occurring cause of rectal bleed at 21%. Furthermore, it was illustrated that hemorrhoidal disease was most common disease in both genders with percentages of 12.8% and 26.2% in males and females respectively, followed by anal fissure. In addition, it was also deduced from the study that anal fissure and hemorrhoidal disease were more common among females with rectal bleed, but colorectal carcinoma was more common among male patients presenting with rectal bleeding.

Table-2: Diagnostic outcome according to gender.

Diagnosis	Gender		Total (%)
	Female	Male	
Anal Fissure	20 (100%)	20 (100%)	6 (30%)
Hemorrhoids	20 (100%)	20 (100%)	12 (60%)
Colorectal Carcinoma	2 (10%)	2 (10%)	4 (20%)
Rectal Polyp	20 (100%)	20 (100%)	0 (0%)
Ileocecal TB	4 (20%)	4 (20%)	0 (0%)
Mesenteric Ischemic	20 (100%)	20 (100%)	20 (100%)
G IST	20 100%)	20 100%)	20 (100%)
Solitary Rectal Ulcer	20 (100%)	20 (100%)	10 (50%)
Ulcerative Colitis	6 (30%)	6 (30%)	0 (0%)
Rectal Prolapse	0 (0%)	0 (0%)	2 (10%)
Total	4 (20%)	4 (20%)	0 (0%)

Table-1: Diagnostic outcome according to age of the study participants.

Diagnosis	Age Group (%)						Total (%)
	16-25	26-35	36-45	46-55	56-65	>65	
Anal Fissure	23 (6.3)	41 (11.2)	23 (6.3)	22 (6)	2 (0.5)	1 (0.3)	112 (30.5)
Hemorrhoids	19 (5.2)	35 (9.5)	35 (9.5)	26 (7.1)	16 (4.4)	12 (3.3)	143 (39)
Colorectal Carcinoma	10 (2.8)	13 (3.5)	13 (13.5)	12 (3.3)	22 (6)	7 (1.9)	77 (21)
Rectal Polyp	5 (1.3)	2 (0.5)	0 (0)	1 (0.3)	2 (0.5)	0 (0)	10 (2.7)
Ileocecal TB	2 (0.5)	2 (0.5)	4 (1.1)	1 (0.3)	0 (0)	0 (0)	9 (2.5)
Mesenteric Ischemic	1 (0.3)	1 (0.3)	2 (0.5)	2 (0.5)	2 (0.5)	1 (0.3)	9 (2.5)
G IST	0 (0)	1 (0.3)	0 (0)	0 (0)	0 (0)	0 (0)	1 (0.3)
Solitary Rectal Ulcer	1 (0.3)	0 (0)	0 (0)	1 (0.3)	0 (0)	0 (0)	2 (0.5)
Ulcerative Colitis	1 (0.3)	0 (0)	0 (0)	0 (0)	1 (0.3)	0 (0)	2 (0.5)
Rectal Prolapse	0 (0)	1 (0.3)	(0)	0 (0)	0 (0)	1 (0.3)	2 (0.5)
Total	62(16.9)	96 (26.2)	77 (21)	65 (17.7)	45 (12.3)	22 (6)	367 (100)

Discussion

This study shows that rectal bleeding was more frequent in males as compared to the females with a ratio of 1:1.9. This pattern was also seen in other similar studies carried out in Pakistan by Mehanna et al.[9] showed a male to female ratio as 1:1.8, a study by Shennak and Tarawneh[10] had a ratio of 1:1.34. Hemorrhoidal disease was the most common cause of rectal bleed in this study attributing to 39% of the total cases that presented in the OPD followed by Anal fissure at 30.5%, collectively these two benign causes summed up to about 70% of the total cases.

Was also observed in a study by Manzoor, A., S. Shah, and A. Inam.[11] A study by Rhee and Lee[12] also reported hemorrhoids to be the most common cause with 65.5% cases, Goulston et al.[13] showed that hemorrhoidal disease was responsible in 72% of the patients. A research conducted by Mehanna et al.[9] had 96% of participants with hemorrhoids. In this study anal fissure was the second most common pathology of rectal bleeding attributing to 30.5% cases, this proportion was not in line with other studies, Shennak and Tarawneh[10] had 3% cases of anal fissure, Tade et al.[14] reported only 3.7% cases.

Colorectal carcinoma is one of the most common type of malignancy worldwide and also in Pakistan. In this study, the frequency of bleeding per rectum due to this pathology attributed to 21% of the total participants with a male to female ratio of 2:1,this result was supported by other studies also, Manzoor, A., S. Shah, and A. Inam [11] in a study reported this ratio as 4.3:1. Same pattern was seen in a research by Makela et al.[15] with 10% cases of colorectal carcinoma, Metcalf, J., et al.[3] reported 8%, Schmulewitz et al.[16] 7%, Farner et al.[17] reported a frequency of 17% cases of colorectal carcinoma.

Rectal polyp was the fourth most common cause of rectal bleeding in this study at 2.7%, Zia et al.[7] reported 2.5% cases, Longstreth et al.[2] 4%. Only 0.5% patients of rectal prolapse were recorded in this research, Tade et al.[14] observed 2.4% frequency, Manzoor, A., S. Shah, and A. Inam[11] reported 2.5% of rectal bleeding due to rectal prolapse. Ulcerative colitis attributed to 0.5% patients as an underlying pathology of rectal hemorrhage, Rhee and Lee[12] reported 3.3%, Farner et al.[17] observed 3%, Longstreth et al.[2] reported 2% frequency.

Solitary rectal ulcer caused 0.5% cases of rectal bleed, Zia et al.[7] reported 4% cases of this syndrome, Manzoor, A., S. Shah, and A. Inam[11] observed a frequency of 1%. However, solitary rectal ulcer syndrome(SURS) can be a representation of an underlying malignancy, so a histological examination is important.[18] As the incidence of rectal bleeding is increasing in our society, more studies should be done regarding the frequency of different causes. Investigations such as sigmoidoscopy and colonoscopy should be introduced in primary and secondary health units for timely diagnosis of serious pathologies that can prove to be fatal if left untreated. There is a need to provide awareness to people about peri anal region hygiene as diseases such as anal fissure can be prevented through proper hygienic measures.

Conclusion

Hemorrhoidal disease was the most common cause of rectal bleeding in surgical OPD followed by anal fissure. Colorectal carcinoma was the third most common cause in this study. There is a need to upgrade the investigation procedure giving preference to colonoscopy and sigmoidoscopy for a proper diagnosis of an underlying malignancy.

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Original Article

Protective Effects of Flaxseeds (Linum Usitatissimum L.) on Hepatotoxicity Induced by Triazophos on Male Wistar Rats

Arooj Nawaz, Rabia Ejaz, Shagufta Nasreen, Fozia Farzana, Mariam Ashraf and Sharjeel Ilyas

Objective: To determine the effects of flaxseeds on triazophos-induced-hepatotoxicity.
Methods: In the current study 24 Wistar albino rats (age: 6-8 weeks, weight 150-200gms) were segregated into four groups comprising six rats each. Group A was kept as control group. Groups B, C and D were labelled as experimentalgroups. Group B was given powdered flaxseeds (800mg/kg b.w.), Group C was administeredtriazophos (8.2mg/kg b.w.) and Group D was giventriazophos (8.2mg/kg b.w.) and flaxseeds (800mg/kg b.w.), each dose was administered twice in a day for 21 consecutive days.On day 22, 24 hours after administration of last dose, all the rats were sacrificed under deep anesthesia. Liver slides were made for H & Estaining. Number of degenerated hepatocytes and nuclear pyknosis were observed in each group.
Results: Number of degenerated hepatocytes and pyknotic nuclei were alleviated in group D with the simultaneous use of flaxseeds. (P value ≤ 0.005).
Conclusions: Flaxseeds in powdered form decreases hepatotoxicity induced by triazophos.
Keywords: pyknosis,degenerated, triazophos, flaxseeds

Introduction

Approximately 2500 years ago, Hippocrates (father of modern medicines) correctly described "Let food be your medicine and medicine be your food".[1] The need for pesticide products and the produced concentration for agricultural efficiency are clear, but the volume of production indicates that the potential for mishandling and accidental exposure is great.[2] Triazophos is a broad spectrum organo- phosphorus pesticide which is abundantly used throughout the world for plant protection, veterinary medicine and public health against different insects, flies and pests that damage variety of crops.[3]Triazophos induces oxidative stress which guides to subsequent histological as well as pathological reorganizations in liver in terms of scattered fatty changes extending from mid-zonal area to the complete liver lobule.[4]Triazophos has also been reported to induce oxidative stress into liver, kidney, brain and fetus of the pregnant rats.[5]

Functional foods are becoming popular alternatives to pharmacological treatments by providing health benefits and decreasing the risk of chronic diseases.[6] Flaxseeds are a dietary botanical supplement with high fiber, minerals, lignans and omega-3 fatty acids having anti-inflammatory and antioxidant properties.[7]Flaxseeds were first grown in the ancient Egypt and China and are full of healthy fat, fiber and antioxidants.[8] Flax plants also contain micronutrients, manganese, vitamin B6 and vitamin B1.[9]

Experimental and clinical research findings showed that due to flaxseed components (omega 3 fatty acids, phytoestrogens, fiber and proteins) powdered flaxseed is a useful strategy to limit several life threatening diseases.[6]

Methods

An experimental animal study was carried out at Animal house and Histology laboratory of Postgraduate Medical Institute (PGMI) Lahore. The study protocol was accepted by Advanced Studies and Research Board of University of Health Sciences, Lahore, and Ethical Committee of PGMI. Healthy adult male Wistar rats of same age group and weighing (170-200mg) were selected for the study. Rats were acclimatized in properly ventilated room at ambient temperature of 25.0 ±2.0ºC under 12 hour light/dark cycles and well administered with standard rat diet and water ad libitum. 24 adult albino Wistar male rats were divided. Four equal groups were made in which rats were divided randomly as group A, group B, group C and group D, so that each group had 6 rats. Details of all the groups are in the following **Table**.

n = Number of rats in each group.

Triazophos is a pesticide. It was weighed on electronic weighing scale and dissolved in distilled water. Flaxseeds were bought from Punjab University Lahore. These are easily available in raw form and then were freshly grinded in grinder machine. The livers of all the groups were dissected out, washed with cold normal saline and fixed in10% neutral

Table-1: Showing detail of the Animal Groups and Experimental Intervention.

Groups	Day of Sacrifice	Specifications for 21 consecutive days	Pintervention and Dosage (orally)
A Control	On day 22	Standard rat feed and distilled water by oral gavage/day	4 ml distilled water (divided in 2 doses)
B Experimental	On day 22	Powdered flaxseeds (800mg/kg b.w. in 0.5ml distilled water)/day	Flaxseeds 800mg/kg b.w in 0.5ml distilled water
C Experimental	On day 22	Triazophos by oral gavage (8.2mg/kg b.w.)/day	Triazophos 8.2mg/kg b.w
D Experimental	On day 22	Triazophos (8.2mg/kg b.w.) and powdered flaxseeds (800mg/kg b.w. in 0.5ml distilled water)/day	Triazophos 8.2mg/kg and high dose of powdered flaxseeds 800 mg/kg b.w. in 0.5ml distilled water

 # Fisher's Exact Test. p-value#< 0.001

Table-2: Comparison of number of degenerated hepatocytes (/mm2) among groups.

	Mumber of degenrated hepatocytes (/mm^2)				
Groups	Absent	Mild	Moderate	Severe	Total
Group A	6 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	6 (100.0%)
Group B	6 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	6 (100.0%)
Group C	0 (0.0%)	0 (0.0%)	1 (16.7%)	5 (83.3%)	6 (100.0%)
Group D	0 (0.0%)	2 (33.3%)	4 (66.7%)	0 (0.0%)	6 (100.0%)

 # Fisher's Exact Test. p-value#< 0.001

Formalin solution. Slides were stained with standard procedures of Hematoxylin and Eosin. Nuclear pyknosis was evaluated for any structural change under bright field microscope, while number of degenerated hepatocytes were seen under 20/20 grid microscope.

Degenerated hepatocytes on 4 corners of slide and in the center (counted the 5 different places in 1 slide) were counted and then took the mean of all the readings. During counting, margins of lower and left side are left. Area of central vein was avoided as it occupied most of the space and can affect the number of degenerated hepatocytes.

Results

Two parameters were studied under this experiment, number of degenerated hepatocytes and nuclear pyknosis. Out of 24, 12 (50.0%) animal had degenerated hepatocytes. No degenerated hapatocytes were seen in group A and B. In group C, 1 (16.7%) animal had moderate degenerated hepatocytes while 5 (83.3%) animal had severe degenerated hepatocytes. In group D, 2 (33.3%) animal had mild degenerated hepatocytes while 4 (66.7%) animal had moderate degenerated hepatocytes **(Table 2, Fig-1).** Nuclear pyknosis in hepatocytes was noticed and it was found that out of 24, 7 (29.2%) animal had nuclear pyknosis in hepatocytes. No nuclear pyknosis in hepatocytes were seen in both the groups (A and B). In group C all animal had nuclear pyknosis in hepatocytes. In group D, only 1 (16.7%) animal had nuclear pyknosis in hepatocytes **(Table 3, Fig-2)**.

Table-3: Comparison of nuclear pyknosis in hepatocytes among groups.

Groups	Nuclear Pyknosis in Hepatocytes Absent	Present	Total
Group A	6 (100.0%)	0 (0.0%)	6 (100%
Group B	6 (100.0%)	0 (0.0%)	6 (100%)
Group C	0 (0.0%)	6 (100.0%)	6 (100%)
Group D	5 (83.3%)	1 (16.7%)	6 (100%)

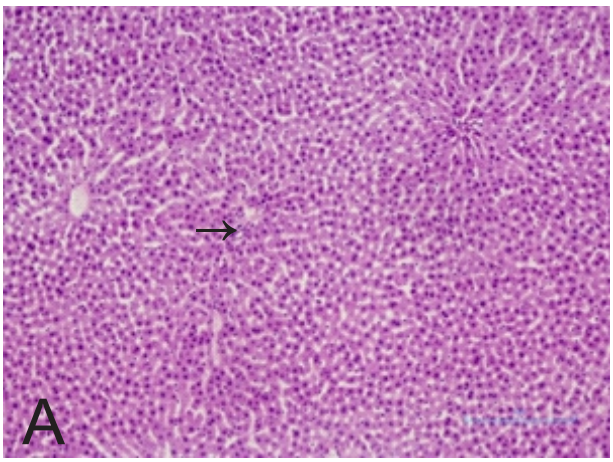

Fig-1: Photomicrograph of the liver from the Group A showing normal hepatocytes (black arrow) and no pyknosis. H & E stain. X 10.

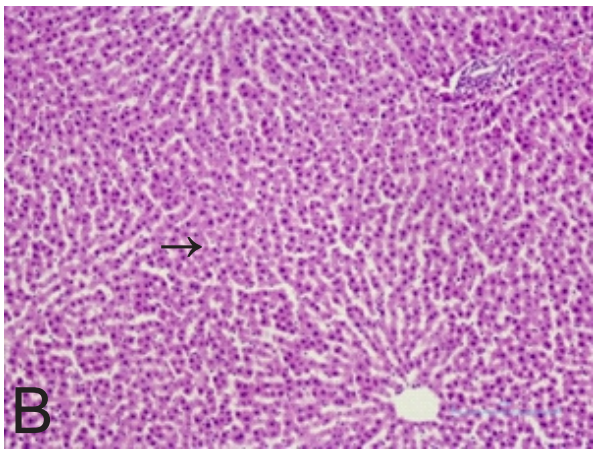

Fig-2: Photomicrograph of myocardium of ventricular wall of group A; showing mature myocardial cells with central oval nuclei (black arrow) and striated cytoplasm (yellow arrow) (Stain H&E. X400).

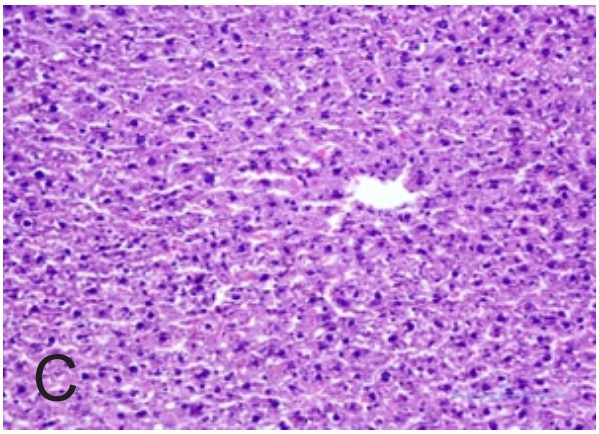

Fig-3: Photom icrograph of the liver from the group C treated with triazophos showing degenerated hepatocytes (black arrow), pyknosis (yellow arrow). H & E stain X 10.

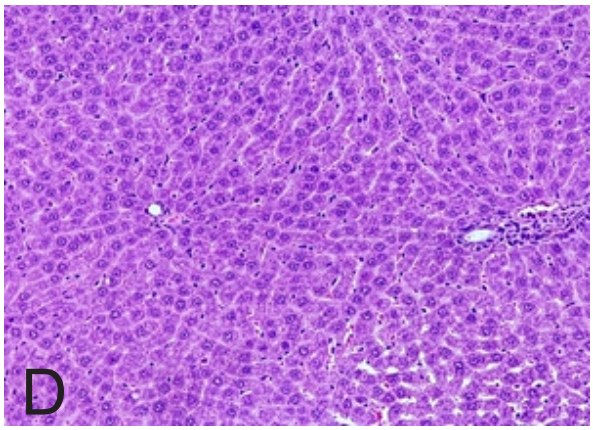

Fig-4: Photomicrogr ph of the liver from group D treated with flaxseeds and triazophos simultaneously showing no pyknosis and decreased degenerated hepatocytes. H & E stain X 10.

Discussion

In present investigation, hepatoprotective potential of flaxseed powder was assessed against pesticide/triazo- phos induced hepatotoxicity in rats. Administration of flaxseed powder had protected hepatic architecture damage with marked improvement in hepatic function and normalization of hepatic enzyme profiles (Hendawiet al10 used 500mg/kg flaxseeds). This study demonstrated that the architecture of hepatocytes remains the same in group A (controlled) and group B (given only flaxseeds 800mg/kg orally for 21 days). While massive destruction of hepatocytes in group C (rats treated with 8.2mg/kg triazophos only) occurred due to oxidative stress. Hepatic degeneration was evaluated under 40X magnification. Findings of Raj et al11 also supported the present study. They used pesticides with the dose of 208mg/kg orally in male Wistar albino rats and showed that malathion and other pesticides induced architectural disarray in hepatocytes in liver of the experimental animals. Jain et al4 also agreed with the results. The group D in which triazophos and flaxseeds both were given, observed the minimized architectural disarray in hepatocytes due to antioxidative property of flaxseeds. The presence or absence of nuclear pyknosis was also found in the cells of hepatocytes of all the animals in this study. The animals of control group had no cells with pyknotic nuclei. It was observed that the hepatocytes in group B showed normal architecture of hepatic cells with no pyknosis. The conclusion of this study was in concordance with those of Hendawiet al10, in this study 500mg/kg b.w flaxseed powder was given to group of rats. In the group C of current study various pyknotic nuclei were observed. Pyknotic nuclei formation in hepatocytes of triazophos treated rats is due to the reactive oxygen species produced as a result of necrosis mostly characterized by pyknosis. Sherma and Sanga12 have also indicated that oxidative stress through reactive oxygen species causes necrosis. Group D demonstrated that the flaxseed powder co-treatment alleviated the lesions caused by triazophos toxicity in rats.

Conclusion

The current study proved that the flaxseeds reduce hepatotoxicity induced by triazophos. It is hoped that this study will produce an awareness of the advantages of supplementation with flaxseed powder in daily life and restriction of unlimited use of triazophos pesticide especially at living places.

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Original Article

Karydakis Procedure vs Limberg Flap in the Treatment of Saccrococcygeal Pilonidal Sinus

Shumaila Rafique, Zainab Hassan, Rohaba Shahid, Shabbar Hussain Changazi, Zeeshan Talib and Mustansar Iqbal

Objective: To compare differences in the outcomes between these two techniques.
Methods: This was a randomized controlled trial conducted in the Services Institute of Medical Sciences, Lahore from August 2017 to August 2018. A total of 60 patients were enrolled in the study. Patients were randomly allocated in the two groups. In group A, pilonidal sinus was treated with karydakis procedure. In the group B, pilonidal sinus as excised with limberg flap. Patients were then followed on 7th day, 14th day, 1 month, 6 month and 18 months after the surgery to evaluate the postoperative results.
Results: The mean age of the patients was 28.65±10.58 years. 58 patients were males and 2 patients were females. The mean BMI of the patients was 23.83±3.26 kg/m2. The mean duration of surgery was 40±8 mins in karydakis procedure and 55±10 min in limberg flap (p=0.02). The mean pain score (VAS) in karydakis group was 4.83±1.34 while it was 4.10±2.30 in limberg group (p=0.141). The mean hospital stay in karydakis group was 2.72±0.80 days whereas the mean hospital stay in limberg group was 4.45±0.92 days (p=0.000). Wound infection developed in 2 (6.67%) patients following karydakis procedure and in 1(3.33%) patient after limberg flap with p-value of 0.346. The mean time for wound healing in case of karydakis group was 14.93±2.79 days while it was 12.42±2.36 days. In the study, 4/30(13.33%) patients in karydakis group presented with recurrence and 2/30 (6.67%) patients in limberg group developed recurrence with p-value of 0.344.
Conclusions: It was concluded that there was shorter hospital stay in karydakis procedure and shorter healing time in limberg flap however there was no statistically significant difference in postoperative pain, wound complications and recurrence in these two procedures.
Keywords: karydakis procedure, limberg flap, comparison, postoperative outcomes.

Introduction

Pilonidal sinus is a common disease of skin affecting mostly the saccrococcygeal region (natal cleft). It results from the penetration of shed hair shafts through the skin and forming blind tract into the superficial fascia to reach the sacral fascia. This tract can be secondarily infected to form abscess.[1,2] However, it mostly presents as a cyst or sinus tracts with or without discharge.[3] The incidence of pilonidal sinus is approximately 26/100,000. It commonly affects young males with high body hair density.[4,5] The etiology of the pilonidal sinus is a matter of debate. Initially, congenital origin was suggested that it was secondary to a remnant of an epithelial lined tract from postcoccygeal epidermal cell rests or vestigial scent cells. Now the view has widely shifted towards the acquired theory and is based on the observations that congenital tracts do not contain hair and are lined by cuboidal epithelium. Furthermore, the tip of hair is pointing towards the sinus tract.[6] In acquired theory, three factors play a pivotal role in genesis of pilonidal sinus, namely high quantity of hair, extreme force, and vulnerability to infections. Natal cleft is a favorable site for these factors and these are further reinforced by sweating, maceration, bacterial contamination and penetration of hair. As a result, the hair start getting buried into the deep skin to form a blind tract which is lined by granulation tissue. Other risk factors include obesity, local trauma or irritation, sedentary life style, family history and poor hygiene.[7,8]

Although pilonidal sinus can be treated using several defined conservative and surgical methods, recurrence rates remain high.[9] Complete removal of the pilonidal sinus or sinuses and appropriate reconstruction can lead to successful recovery.[10] Various techniques for management of saccrococcygeal pilonidal sinus have been described that range from, clipping of hair with good hygiene of the area, wide excision of the area and packing, excision and primary closure like karydakis procedure, marsupialization and flap techniques like Limberg flap, modified Limberg transposition flap,

This study was conducted to evaluate Karydakis procedure and Limberg flap in treatment of saccrococcygeal pilonidal sinus with reference to postoperative pain, hospital stay, wound healing and recurrence.

Methods

This was a randomized controlled trial conducted in the department of surgery, Services Institute of Medical Sciences, Lahore from August 2017 to August 2018. A total of 60 patients were enrolled in the study. Approval was sorted out from ethical committee of the institute (IRB). Written consent was taken from all the patients. Patients with both sexes and age above 15 years with a diagnosis of pilonidal sinus assessed in the outdoor department were included in the study. Patients with infected pilonidal sinus, pilonidal abscess, recurrent pilonidal sinus and immunocompromised patients like uncontrolled diabetes and using steroids were excluded from the study. After initial evaluation, patients were randomly allocated in the two groups. In group A, pilonidal sinus was treated with karydakis procedure. In this technique, asymmetric elliptical or semi lunar incision with the poles of ellipse was placed about 2 cm to the side of the midline. The tissue was then excised down to the sacral fascia. After excision full-thickness mobilization of the contralateral surgical margin was carried out and fixation of the base of the flap to the sacral fascia was done and finally, the skin edges were sutured off the midline. In the group B, pilonidal sinus was excised with limberg flap. In this technique, a rhomboid-shaped incision was given with cephalic and caudal apex of the rhombus placed about 2 cm to the side of the midline. After incision dissection was done down to the sacral fascia and the tissue was excised. A fasciocutaneous rhomboid flap was then created and transposed over the defect without tension. All the operations were done by a consultant, at least at the level of senior registrar. Patients were then followed on 7 th day, 14th day, 1 month, 6 month and 18 months after the surgery to evaluate the postoperative results. Appearance of discharging sinus/sinuses on scare line was considered as recurrence after surgery.

Frequency and percentages were calculated for quantitative data.. T test (mean postoperative pain score, mean hospital stay, mean healing time) and chi-square tests (recurrence) were applied in order to compare the data of both groups. A p value of 0.05 or less was taken as significant. This trial as registered to clinicaltrial.gov with reference number NCT03765086.

Results

Total of 60 patients were enrolled in the study with 30 patients in each group. The mean age of the patients was 28.65±10.58 years. The man age in karydakis group was 27.66±11.53 years while mean age in limberg group was 29.58±9.7 years. Out of total 60 patients, 58 patients were males and 2 patients were females. The mean BMI of patients was 23.83±3.26 kg/m2 **(Table 1)**. The mean duration of surgery was 40±8 mins in karydakis procedure and 55 ± 10 min in limberg flap with significant p-value (0.02). The mean pain score (VAS) in karydakis groups was 4.83 ±1.34, while it was 4.10±2.30 in limberg group however the value was statistically significant (p=0.141). The mean hospital stay in karydakis group was 2.72 ± 0.80 days whereas the mean hospital stay in limberg group was 4.45±0.92 days with p-value of 0.00. In this study, wound infection developed in 2 (6.67%) patients following karydakis procedure and in 1(3.33%) patient after limberg flap with p-value of 0.346. The mean time for wound healing in case of karydakis group was 14.93±2.79 days while it was 12.42±2.36 days in limberg group with statistically significant p-value. In the study, 4/30 (13.33%) patients in karydakis group presented with recurrence and 2/30 (6.67%) patients in limberg group developed recurrence with p-value of 0.344 **(Table - 2)**.

Table-1: Comparison of preoperative parameters of both group.

Variables		Karydakis Group	Limberg Group	Total	p-value
Age (mean)		27.66±11.53	29.58±9.7	28.65±10.58	0.486
BMI (Mean)		23.65±3.68	24±2.87	23.83±3.26	0.868
Gender	Male	29	29	58	0.987
	Female	1	1	2	

Table-2: Comparison of postoperative parameters in both surgical procedures.

Variables	Karydakis Group	Limberg Group	p-value
Postoperative Pain	4.83±1.34	4.10±2.30	0.141
Hospital Stay (Days)	2.72±0.80	4.45±0.92	0.00
Healing time (Days)	14.93±2.79	12.41±2.36	0.00
Recurrence	4 (cases)	2 (cases)	0.344

Discussion

There is still no consensus about the treatment of choice for pilonidal sinus disease. Ideally, therapy should be associated with short hospital stay, less painful postoperative time, rapid healing and return to work, less painful dressing of wound, short duration of wound care and a low recurrence rate. No technique fulfills all of these criteria. Since the source of the disease is thought to be natal cleft and deep intergluteal sulcus, the aims of the flap techniques are natal cleft flattening, lateralization and fulfilling of the defect without tension. This study was conducted to compare the postoperative outcomes in primary closure by karydakis method and flap coverage by limberg flap.

Pilonidal disease usually affects male and young people.In this study most of the patients affected with pilonidal sinus were males and mostly presented in their second decade of life. These results were in close agreement with the results reported by Akca et al.[16] and Mahdy et al.[17] in their studies. In this study, the mean operative time in limberg flap was longer as compared to karydakis procedure with statistically significant p-value. Similar results were also elaborated by other researchers.[18,19] However, some studies showed that there was no statistically significant difference between the two procedures.[20] Longer duration of surgery in limberg procedure in this study can be attributed to the flap dissection and then flap rotation and closure as compared to primary closure after excision in the karydakis procedure.

In the present study, there was no significant difference in the mean pain scores between the two groups. However, hospital stay was shorter in karydakis procedure and healing time was shorter in limberg flap with statistically significant difference. Karaca et al.[21] and Ersoy et al.[22] reported that the limberg flap group had lesser postoperative pain, shorter hospital stay and early wound healing as compared to karydakis procedure. However, Can et al.[24] in their study demonstrated comparable postoperative pain and hospital stay in both groups but early healing in karydakis procedure.

In the current study, there was no significant difference in wound infection and recurrence between the two methods (P>0.05). These results were in concordance with studies conducted by Campbell et al.[24] and Bali et al.[25] however, Mentes et al.[15] and Ersoy et al.[22] reported that limberg flaps presented lower complication rates and recurrence than karydakis procedure in their respective series. Conversely, Ates et al.[18] reported lower recurrence and complication rates for the karydakis technique than for the limberg flap technique.

Conclusion

It was concluded that there was shorter hospital stay in karydakis procedure and shorter healing time in limberg flap however there was no statistically significant difference in postoperative pain, wound complications and recurrence in these two procedures.

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Original Article

Awareness About Gestational Diabetes Among Antenatal Patients of Services Hospital Lahore

Madeeha Rashid, Kiren Khurshid Malik, Asma Mushtaq and Rubina Sohail

Objective: To determine awareness about gestational diabetes mellitus among pregnant women attending antenatal outpatient department of Services Hospital Lahore.

Methods: This was a cross sectional study in which 200 pregnant patients were enrolled from antenatal outpatient department of Services Hospital Lahore. A comprehensive questionnaire was given to the participants after taking informed consent. Apart from demographic data it comprised of questions regarding awareness and knowledge about gestational diabetes. The areas in which knowledge of women was explored were risk factors, screening, long-term concerns, prevention and follow-up of post-partum period.

Results: Total number of study participants were 200 pregnant females with mean age of 27 years. 38% had primary education.62.5% of women were aware of fact that gestational diabetescould occur for the first time in pregnancy. Only 20% had information about the glucose levels which considered to be abnormal and 24% were aware of fact that gestational diabetes could persist after delivery.33% had no knowledge regarding risk factors and 42% were unaware of complications of gestational diabetes mellitus. Major source of information was family and friends (49%).

Conclusions: Awareness of antenatal women on different aspects of gestational diabetes is not up to the mark and as incidence of disease is growing, adequate knowledge on risk factors, course of disease and effect of GDM on fetomaternal outcome will help in improving pregnancy outcomes.

Keywords: gestational diabetes mellitus, knowledge, awareness.

Introduction

Pakistan has population of 207 million and reported to be 6th most populous country of the world.[1] Diabetic Association of Pakistan and WHO showed an overall prevalence of diabetes as 17%. In males the prevalence is 11.20% and in females 9.19%. One in every six persons is a diabetic in Pakistan.[2] Among the adult population 35.3 million people are found to be diabetic.[3] International diabetic federation estimated that until 2035, Pakistan will be ranked 8th among the world's top 10 countries having a rise in prevalence of Diabetes.[4] Among non-communicable diseases, Diabetes is at fourth place causing 1.5 million deaths each year globally.[5] Frightening scenario is that about 175 million people with diabetes are still undetected. Hence this high rate of diabetes in a country with huge population requires raising awareness about the disease on urgent and emergency basis.

Gestational diabetes mellitus is defined as increased blood sugar levels that happens or recognized for the first time during pregnancy.[6] It is one of the major cause of maternal and neonatal mortality and morbidity. Mothers can develop number of complications like gestational hypertension, preeclampsia, increase rate of recurrent infections and caesarean section.[7]

If woman previously had gestational diabetes, she carried a lifetime risk of progression to type 2 diabetes of up to 60%.[8] Newborns are at greater risk for macrosomia, hypoglycemia, jaundice, respiratory distress syndrome, polycythemia, and hypocalcaemia and in later life are at risk of metabolic syndrome.[9] The main risk factors for GDM are advanced maternal age, family history of type 2 diabetes, preperganacy obesity and excessive weight gain in pregnancy.[10] If a woman does not have the awareness about a disease which is going to affect her pregnancy and baby adversely the better control and prevention at mass level can prove to be very difficult. Hence the information gathering about knowledge of our population about this alarming disease in pregnancy is an essential step towards preventive and curative medicine.

Globally, incidence and occurrence of gestational diabetes mellitus is on rise. In 2017, approximately 1in 3 women of reproductive age had diabetes. About 21.3 million or 16.2% of live births had some form of hyperglycemia in pregnancy and 85% were due to gestational diabetes. Majority of these cases were in

health is already poor.[11] In Pakistan exact prevalence of GDM is still undetermined but many local studies shows data is similar to global incidences but complication rates are higher, perhaps due to poorer glycemic control.[12] Poor knowledge and awareness is the underlying factor for poor glycemic control.

It is of vital importance to categorize at risk women, making an early diagnosis, introduce lifestyle modification, dietary measures and where needed start oral hypoglycemic/Insulin to prevent complications of GDM. Educating and giving awareness about GDM and its risk factors to reproductive age females will results in adopting health life style, better self-care which ultimately leads to its prevention.[13] Despite of fact that Pakistan has high prevalence of diabetes mellitus our general public still lacks awareness about management and basic treatment of disease. Due to lack of preconception planning and poor antenatal care utilization maternal health care constantly remained a challenge in Pakistan. It is the need of the day to start structured educational and informative programs regarding diabetes and its types, which will help individuals to follow and adopt a healthy lifestyle.[14] So far, little has been done to assess the level of awareness and knowledge among pregnant women about diabetes. This study tries to determine general awareness about GDM in pregnant ladies, so that based on facts further planning for guidance policy formation can be formulated.

Methods

The study was carried out in Services hospital antenatal outpatient department. Antenatal clinic of Gynae unit I is on every Tuesday and Friday. Women were selected by non-probability convenience sampling. After informed consent, questionnaire was used for collection of data. Apart from demographic data it consists of questions determining patient awareness level about gestational diabetes, risk factors, diagnosis, treatment, complications and prevention strategies. Patients were asked to tick the options given i.e. yes, no, and don't know.

Questionnaire consist of 20 questions like whether they know about gestational diabetes. Do they have any idea about blood sugar level at which person is labeled to have GDM? Their awareness level regarding diet and lifestyle whether healthy eating and regular exercise can prevent GDM or not. Awareness of the risk factors of GDM was assessed by asking them regarding effect of pre-pregnancy obesity, rapid weight-gain during pregnancy, family history, and a past history on GDM. Their awareness regarding diagnosis assessed by whether they have heard about test for diabetes after glucose load. Knowledge on treatment options was assessed by giving options of life style modification and diet, oral medication or Insulin.

Results

Two hundred pregnant ladies were enrolled in study .They have age bracket of 18-40 years with mean age of 27 years.Majority of the women (43%) were in the 25-32 years age group and 25.5% were above 32 years of age. With respect to education, 19% of the women were illiterates, 45.5% had primary & secondary education, 28.5% had intermediate education, and 7% graduates. 64.5% of the women were multigravida.

Overall, 57.5% women had awareness about gestational diabetes, while 62.5% had knowledge that gestational diabetes occurs first time in pregnancy. The awareness of the women on the various aspects of GDM is given in **tables (1-3)** below.

Table-1: Demographic Indices.

		Number of women (n=200)	Percentage
Age	18-25 years	63	31.5%
	26-32 years	86	43%
	33-40 years	51	25.5%
Parity	Primiparous	71	35.5%
	Multiparous	129	64.5%
Education	Illiterate	38	19%
	Primary & Secondary	91	45.5%
	Intermediates	57	28.5%
	Graduates	14	07%

Table-2: Awareness of the course and consequences of GDM

	Known (n=200)	Don't Know
Awareness about Gestational Diabetes	115 (57.5%)	85 (42.5%)
Awareness that gestational diabetes occurred first time in pregnancy	125 (62.5%)	75 (37.5%)
Blood sugar level considered to be abnormal	40 (20%)	160 (80%)
Blood test after oral glucose load	67 (33.5%)	133 (66.5%)
Diabetes persist after delivery	48 (24%)	152 (76%)

Table-3: Awareness about treatment of GDM.

	Known (n=200)	Don't Know
Food & exercise	76 (38%)	124 (62%)
Oral medications	22 (11%)	178 (89%)
Insulin	40 (20%)	160 (80%)
No idea about treatment	62 (31%)	138 (68%)
Healthy diet and exercise as preventive measures	59 (29.5%)	141 (70.5%)

Fig-1: Awareness about risk factors.

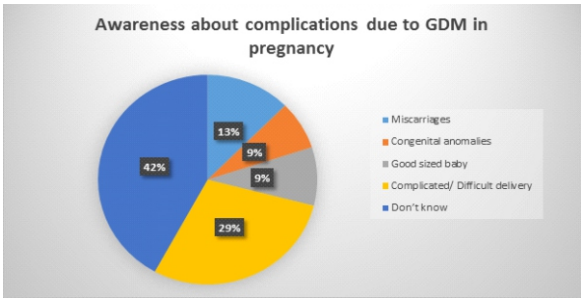

Fig-2: Awareness about complication due to GDK in pregnancy.

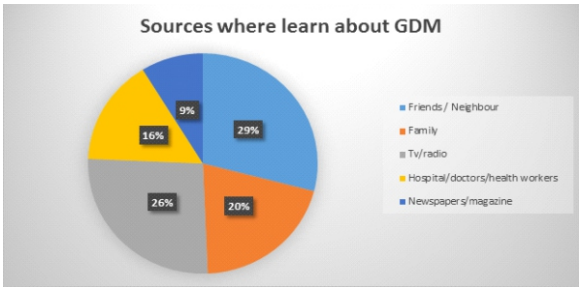

Fig-3: Sources where learn about GDM.

Discussion

In The commonness of diabetes in Pakistan is creating substantial health and economic problems for patients. We as South Asians are prone to the development of diabetes due to biologic and lifestyle issues and also due to increased visceral adiposity, insulin resistance, and a genetic predisposition to diabetes, chances of having diabetes markedly increased in our population.[15] Furthermore, now a day's people do lessened physical activity, eating more dietary fats and processed foods with increasing mental stress, all these leading to insulin resistance and ultimately abdominal obesity.[16] Frequency of gestational diabetes is increasing globally. Those suffering from GDM has 60% incidence of developing type-2 diabetes in later life. In pregnancy if left untreated GDM can cause serious neonatal and maternal consequences. If general public has awareness about disease, its risk factors and consequences, they will have better self-care. Therefore to control disease government should also play role by launching specific national disease control plans, using television and printed media and setting awareness days to promote awareness among local population.

The data collected by my study shows that 57.5% of study population was aware of term gestational diabetes and 62% from fact that it occurs first time in pregnancy. But even those who were aware of disease know it by name sugar rather than gestational diabetes. Lakshmi D et al in there study found that, 35.2% had adequate knowledge about GDM and 21.5% had adequate knowledge about risk factors of GDM.[17] Shreeram et al, in their study in south India found that only 17.5% of women had good knowledge about GDM which was lower when compared to our study.[13] Similarly, in a Bangladesh study showed that 26.3% hadgood knowledge about GDM.[18] Study by Price LA in Samoa, knowledge about GDM among women was varied. 58% of patients were aware that diabetes can occur for the first time during pregnancy, 23% were unsure, and 19% did not think that it could.[19]

Study by Khalid at holy family hospital showed that 87.2% had awareness regarding diabetes but only 30% could tell the normal blood sugar level.60.4% knew that it develops during pregnancy and 67% considered it as a high risk conditions.[20] Difference in knowledge and awareness level with different studies is due to fact that services hospital catchment area is mostly from urban localities with good educational status. 81% of the study participants were educated. Hospital has separate diabetic management center which helps in rising awareness about diabetes. Hence 57% of population at SIMS antenatal outdoor were at least aware of diabetes in pregnancy. Awareness regarding risk factor, diagnosis, screening test and long term consequences of disease is low. A three year survey was conducted in Chennai[21] concluded that people having more awareness about disease can manage themselves better with decreased number of diabetic cases and associated complications. In our study despite of knowledge about occurrence of DM in pregnancy was better but awareness about risk factors and management was poor so they have difficulties in following management plans leading to harmful consequences in pregnancy.

In my study 33% people were unaware of risk factors that can lead to gestational diabetes. 21% people think that obesity before pregnancy is an important risk factor for developing diabetes followed 19% thinking

60%of antenatal population had no idea about risk factors and contributory factors towards GDM which is an alarming situation. In similar study in Samoa 49% identified a family history of GDM as a risk factor followed by 23% considering pre pregnancy diabetes as risk factor. [19]As we all know awareness and recognition of risk factors of any disease is first step towards prevention and help patient to seek early advice from doctor which will be helpful in reducing morbidity and mortality associated with gestational diabetes and it reduces the risk of developing type 2 diabetes in later life.[22]
38% ladies think that eating healthy and regular physical activity have preventive role in gestational diabetes similar results shown in study carried out in Samoa in which according to 78% of women exercising regularly with healthy eating were preventing steps in GDM.[19]
49% gets information from family and friends followed by 35% from electronic and print media while only 16% gets information from health care providers and hospitals. One of the important fact is that most family people do not have precise knowledge about pathology of disease, preventive measures to reduce the risk of Diabetes, and the possible outcomes of the disease. This shows that existing health care system in Pakistan needs involvement of healthcare specialist, healthcare worker and strategy makers. As by promoting awareness and knowledge among general population regarding disease help in early diagnosis and reduces incidence of severe complications and overall prevalence of disease will be decreased as people will intend to have healthy life style.[23]

Conclusion

As incidence of diabetes and especially in pregnant population is on rise, there is an enormous need to get population aware of the fact that it is a tip of an ice berg .In upcoming years the diabetes will emerge as an epidemic especially in Pakistan. In next fifteen years Pakistan will be in top ten countries of the world regarding prevalence of diabetes. A structured Approach is compulsory to create and raise awareness regarding GDM among people for which recommendations are given below.

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Case Report

Fat Fracture; Anterior And Medial Knee Pain Rare Cause

M. Amir Sohail, Kamran Butt and Sohail Razzaq

Abstracts: Blunt injury to the anterior aspect of knee results in a fracture of the patella or contusion. And, injury to the extensor mechanism can result in partial or full thickness tear of the patellar or quadriceps tendon. A young girl suffered an injury to her knee after she hit her leg with a hard object.[1] Acute swelling in the suprapatellar and medial soft tissues concealed a palpable defect, which initially was suspected a case of patellar dislocation. Magnetic resonance imaging of the knee revealed an intact extensor mechanism; moreover, a partial tear of medial retinaculum was foundalong with signal changes in the infrapatellar fat pad and diagnosed as a fat fracture.[2]
Fat fracture is a rare diagnosis. As Conservative management failed, Arthroscopy of the knee was done to debride the fat fracture that effectively treated the injury.[3]
Blunt injury to the anterior part of knee can cause fracture of the patella or contusion,instability of the patella, and tear of the quadriceps or ligamentum patellae.A blunt injury or undisplaced fracture of the patella cancause point tenderness and anterior knee effusion. A communited fracture of patella or tendon disruption typically has difficulty in extension of the leg. In literature one case of Fat fracture of knee has been reported by blunt injury. Here we present a case of a 17-year-old girl who face a blunt injury to her left knee after hitting her leg with the hard object and got pain on the medial and anterior aspect of knee.

Case

A 17-year-old female hit the wheat sack, and present with increasing pain and was unable to walk and she felt as her patella slip out. She complained of pain, with patellar instability sign but no signs of meniscal injury. On Physical assessment patient have mild swelling on the medial and anterior side of the patellar tendon region, as well as on the medial femoral condyle. However, joint effusion was not there. There was tenderness on the superior and medial aspect of the patella, but joint line was not tender. Percussion testing to the patella was negative. The extensor mechanism has no defect in it, she has been able to do SLR Test against resistance but was painful. The patellar laxity was comparable to that of opposite knee. Her Hip range of motion (ROM) was ok, but knee ROM was limited to 90° of flexion, with the complaint of anterior tightness at this position. She can extend knee without pain. There was no varus and valgus instability at 0° and 30° of flexion. anterior and posterior drawer tests and Lachman test were negative. The McMurray test for meniscus was negative. X-rays of the left knee has no positive finding.

Outcome:

Patellar dislocation and sprain of the medial retinaculum were initial diagnosis, and she was treated by traditional bone settler. Activity modifications and physiotherapy forquadriceps muscle strength done. treatment was given for 12 weeks and symptoms were settled but pain on walking and knee flexion was continued. Follow up showed decreased swelling, but there was tenderness and patellar apprehension test was positive. Patient can perform a SLR, an incomplete injury to the quadriceps became plausible. Magnetic resonance imaging shows An acutely marginated, longitudinal and transverse fluid defect "crevasse" in the infrapatellar fat adjacent to the patellar tendon that correlate the clinical abnormality.**(Fig-1)** This shows localized "fat fracture, the patellar and quadriceps tendons were intact. Last, there were evidence of medial retinaculum injury. We done arthroscopic debridement of fat fracture that was brownish discolored, this management led to the resolution of symptoms. At a 1-month follow-up, she was pain free with full range of motion of the knee joint.

Discussion

A fat fracture was initially described in the buttock by blunt trauma.[3] geometry of the fat lobulesarranged in layers and enhanced by horizontal and vertical fibrous septa. Heavy loading flatten the lobules and forces disperse throughout the layer. Whenever there is injurye to a local area this will lead to disruption the fat lobules and septa. Buttocks have more fat tissue in comparison to extremity, and the anterior part of

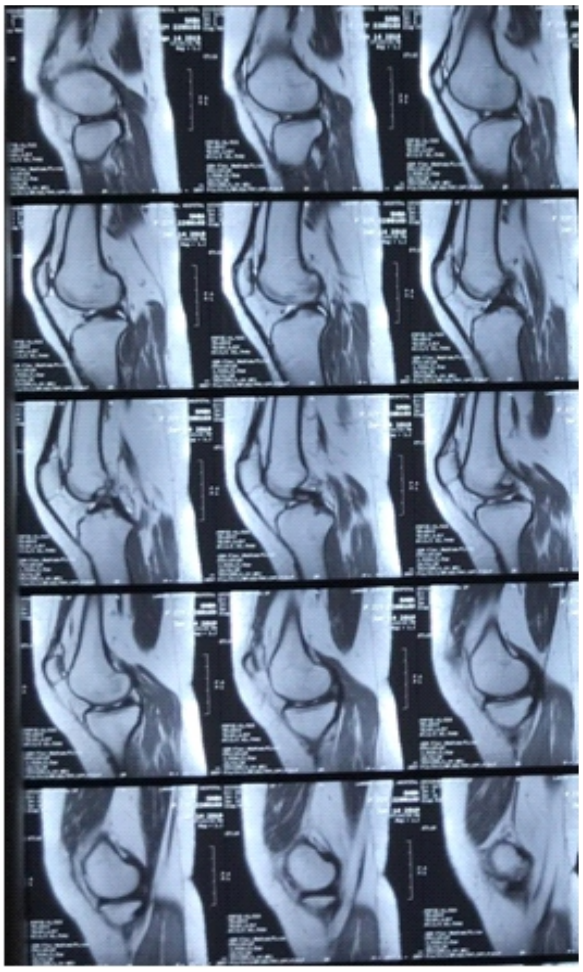

Fig-1: MRI Knee joint.

tissue defect due to massive swelling. andSLR test was negative despite the fat fracture. This case highlights the spectrum of injury that is possible, and difficulty in diagnosing a fat fracture. Furthermore, this case describes a patientwho presented with medial and anterior knee pain.

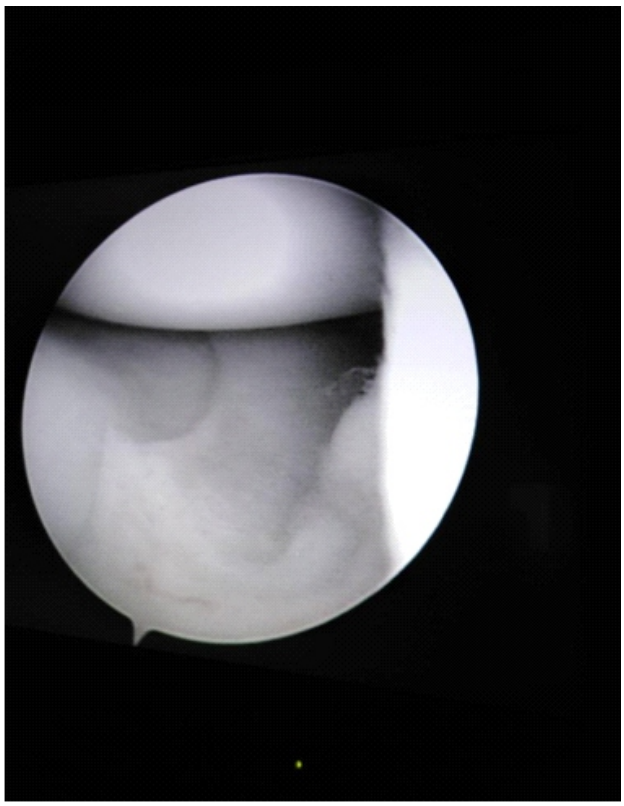

Fig-2: Arthroscopy of knee joint.

The swelling due to fat fracture spread into the medial part of patellar tendon, which can be confused with swelling from an injury to the medial-sided soft tissues. Operative management is not always required for such cases and conservative measures may not be as effective as those in a patellar contusion or ligamentous sprain, arthroscopic treatment is ideal to treat such cases **(Fig-2).**

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ZAHID RAFIQUE, HAFIZA SUMAIRA REHMAN, ASMARA ASRAR, IMRANA HAMID, AJWAD TARIQ AND M SHAHZAD HAFEEZ

Initial Expericne of Multi-Detector Computed Tomography Angiography for Cerebral Vascular Pathology in Pubic Sector hospital. (CR)

TAHIRA NISHTAR, NOSHEEN NOOR, TABISH AHMED AND M. AFTAB

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Diagnostic Accuracy of Right Liver Lobe Diameter/ Albumin ratio for Non-invasive Detection of Esophageal Varices in Hepatitis C Related Cirrhosis. (OA)

SANA AHMED, NOMA SARWAR, SHAHZAD HAFEEZ, NASIR ABBAS, NAZ AKRAM AND ROHMA AHMED

Correlation between Mean Platelet Volume and Severity of Acute Diarrhea in Children. (OA)

MUHAMMAD FAHEEM AFZAL, SARA KHALID, KHAWAJA AMJAD HASSAN AND ASIF HANIF

Microscopic Anatomy of Aging Human Prostate Histological Architecture of BPH. (OA)

MUHAMMAD AMIN, SHAISTA ALI AND SAMAR ASHRAF

Assessment of Knowledge Regarding IMNCI among Final Year Medical Students of Fatima Jinnah Medical University. (OA)

FOUZIA JSHAQ,HASNAIN ABID, SUMMAIRA NAVEED, ASMA ANWAR, TAYYABA RAHAT,RASHID MAHMOOD AND MUHAMMAD RAFIQUE

Ultra Sonic Dissection in Modified Radical Mastectomy. (OA)

FASIHA MUNAWWAR, ATIF ASHRAF JANJUA, LMDAD AHMED, HASSAN SHAUKAT, KIRAN SARFARAZ AND ABDUL BASIL

Assessment of Physical Characteristics and Fecal Contamination of Drinking Water in Tertiary Care Hospitals of Lahore. (OA)

ASIFA HUSSAIN, FAREEDA NASIR KHAN, ANJUM RAZZAQ, MUHAMMAD UMAR FAROOQ, HAFIZ SHAHID LATIF AND FAISAL MUSHTAQ

Correlation of Serum Adiponectin with Lipid profile in Diabetic and Non Diabetic Rats. (OA)

HAFIZA HINA PASHA, AYESHA SADIQA, SAUDA USMANI, SAIMA TABASSUM AND HAMID JAVAID QURESHI

Patient satisfaction Questionnaire: A Tool towards Quality Improvement of Health Care services. (OA)

ASIF IQBAL, LFFAT NOUREEN, NAEEM LIAQAT, NAVERA JAVED, AYESHA ANWAR, MIAN MUHAMMAD BILAL, SHOAIB HASSAN TARRAR AND SHARIQ IQBAL RAI

Frequency of Heparin-induced Thromocytopenia in Patients Treated with Un-fractionated vs. Low Molecular-weight Heparin. (OA)

M. RASHID, ALI RAZA, M. SHAHZAD CHAUDHRY, ASTHMA MUNIR, M. SHAHZAD HAFEEZ AND AMTIAZ AHMAD

Savary-Guilliard Dilators for Management of Corrosive Esophageal Strictures without using Fluoroscope: Five -year Experience in Pakistani Population. (OA)

MAHMOOD AHMAD, YASIR MAHMUD, SIDRA RASHEED, NAEEM AFZAL, NASEER UMER AND MUHAMMAD ARIF NADEEM

Attitude and Trends of Undergraduate Medical Students towards Blood Donations in Services Institute of Medical Sciences, Lahore. (OA)

TABASSUM ISLAM, MAHRUKH ASLAM, MARIUM SHABIR, SHABBAR HUSSAIN CHANGAZI, SAMIULLAH BHATTI AND QAMAR ASHFAQ AHMAD

Hypovitaminosis-D : A Predictive Risk Marker for Preeclampsia in 3rd Trimester of Pregnancy. (OA)

RIDA FATIMA, MUHAMMAD SHAFIQ, MUHARRUNAD AMMAR YASER, MUHAMMAD ALI, SAMIA JAWED, RANA KHURRUM AFTAB AND FARHAT JAZ

Effectiveness of Combination of Zinc and Lactulose versus Lactulose Alone to Decrease Recurrence of Hepatic Encephalopathy in Patients with Hepatic Cirrhosis. (OA)

MUHAMMAD AWAIS, AHMAD MANAN, BILAL AZIZ, TAZEEN NAZAR, AMBREEN BUTT, BILQUIS SHABBIR AND M. SHAHZAD HAFEEZ

Increased Risk of Cardiovascular Disease in Women Exposed to Biomass Fuel during Cooking. (OA)

NABIHA SAEED, MAHAM LJAZ, ABDUL HANAN SAEED, MUNIZA SAEED, M. SHAFIQ, AND M. ZAIN UL ABADIN

Frequency of Etiological Agents of Accidental Poisoning in Children Presenting in Emergency of a Tertiary Care Hospital. (OA)

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