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Maternal Morbidity and Associated Fetomaternal Outcomes in Women With Twin Pregnancies

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EDITORIAL

TUMOR SUPPRESSOR MIRNAS ARE DOWNREGULATED IN BCR-ABL AND TMPRSS2-ERG POSITIVE CANCER CELLS: TIME TO TRANSLATE CELL TYPE SPECIFIC STUDIES

Ammad Ahmad Farooq and Hilal Şehitoğlu

Research over the years has progressively shown substantial broadening in miRNA regulation of signaling landscape. Increasingly it is being realized that an individual miRNA may post-transcriptionally regulate over one hundred different mRNAs. It is noteworthy that overwhelmingly increasing data on miRNA biology has revolutionized current understanding of cancer cells and recently cancer-targeted miRNA drug -MRX34, has entered into Phase I clinical trials in patients with advanced hepatocellular carcinoma. Emergent themes have started to shed light on targeting of individual key targets by miRNAs thus promoting and suppressing carcinogenesis. Mechanistically, orchestrated modulation of target batteries, and reconstitution of signaling cascades in fusion positive cancer cells has recently gained tremendous appreciation. It is getting sequentially more understandable that leukemic cells carrying BCR-ABL are difficult to target because of rewiring of intracellular signaling cascades. Likewise, substantial fraction of information has been added into prostate cancer biology and it is now evident that prostate cancer cells harbor a fusion transcript TMPRSS2-ERG. In this editorial we will attempt to provide an overview obtained from cell type specific pieces of information regarding miRNA regulation of cell proliferation in BCR-ABL and TMPRSS2-ERG carrying cancer cells.

There are some direct pieces of evidence which substantiate tumor suppressing role of miRNAs in BCR-ABL positive cancer cells. Overexpression of miR-203 in T315I mutant BaF3-BCR/ABL cells inhibited cell growth and colony formation ability.[1] Interestingly, there is a contemporary study that suggests epigenetic silencing of miR-203 and BCR-ABL positive cancer cells treated with imatinib demonstrated upregulation of miR-203.[2] There are some other miRNAs which are downregulated in leukemic cells and enforced expression of miR-29b in K562 cells resulted in remarkable suppression of cellular growth.[3] In accordance with similar approach, enforced expression of miR-30a in K562 cells resulted in growth inhibition.[4] Significantly reduced cell proliferation and substantially enhanced apoptosis was noted in CD34+ CML stem/progenitor cells upon enforced expression of miR-326.[5]

Prostate cancer biology was further complicated after identification of a fusion transcript TMPRSS2-ERG in prostate cancer cells formed by chromosomal translocations that juxtapose the androgen-sensitive TMPRSS2 gene promoter to the oncogenic ETS-family transcription factor ERG. Experimentally verified data is more detailed and convincing related to miRNA regulation in BCR-ABL carrying leukemic cells as compared to dysregulation of miRNA subsets in TMPRSS2-ERG positive prostate cancer cells. miR-200c was found to be downregulated in TMPRSS2-ERG positive prostate cancer cells and reconstruction assays revealed considerably reduced cell migration and invasive potential of cancer cells.[6]

It is relevant to mention that tumor suppressor miRNAs are lost in cancer cells and rapidly emerging studies are pointing towards underlying mechanisms which suppress expression of miRNAs in BCR-ABL and TMPRSS2-ERG carrying cancer cells. Better understanding of the mechanisms and comprehensive analysis of role of miRNAs in xenografted mice will be helpful in getting fuller information of miRNA biology.

Previous study has shown that CB17. SCID/SCID mice inoculated with scrambled miRNA transfected Ba/F3 Bcr-Abl cells succumbed within 1425 days. The mice inoculated with Ba/F3 Bcr-Abl cells transfected with shRNA against Bcr-Abl junction survived between 45 and 60 days. However there was notably enhanced survival of CB17. SCID/SCID mice inoculated with single, double and triple miRNA mimics transfected Ba/F3 Bcr-Abl cells.[7]

As there is considerable advancement in translational oncology and we are heading towards personalized medicine, information related to miRNA clusters in fusion positive cancer cells will be helpful in designing and testing antisense nucleotides for inhibition of over-expressed oncogenic miRNAs. Moreover, sense nucleotides could be used to reconstitute cancer cells with tumor suppressive miRNAs.

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Original Article

Randomized Clinical Trial Comparing Local Anesthesia with Spinal Anesthesia for Intestinal Stoma Reversal

Habib Ahmed, Mansoor Ahmad Qureshi and Muhammad Tariq Siddique

Objective: To compare the outcome of local anesthesia versus spinal anesthesia in intestinal stoma reversal..

Material and Methods: It was randomized clinical trial with 64 patients, undergoing reversal of ileostomies and colostomies. Procedure was performed either under local anesthesia plus sedation (n=32) or spinal anesthesia (n=32). The duration of the operation, conversion or supplementation of the anesthetic technique, time spent in the post-anesthesia recovery room, postoperative complications and length of hospital stay were analyzed.

Results: Duration of operation and time spent in post operative recovery room was less in patients operated under local anesthesia. Conversion to general anesthesia was only needed in spinal anesthesia group. Post operative complications were less in local anesthesia group. Mean length of hospital stay was almost equal in both groups.

Conclusion: Intestinal stoma reversal under local anesthesia and sedation is safe and more effective than same procedure under spinal anesthesia.

Key words: intestinal stoma reversal, local anesthesia, spinal anesthesia.

Introduction

Only rare cases of ostomy surgery can be found before the 1700s. Throughout the 18th century, accepted management of abdominal wounds with intestinal perforation was to close the open abdominal wound and hope for the best. This was, not surprisingly, associated with extremely high mortality rates.[1] The earliest stomas were actually fistulas that developed spontaneously following penetrating abdominal wounds or incarcerated hernias.[2] On observing the high survival rates in case of spontaneous fistula development, surgeons started constructing planned stomas.[3,4] Surgeons in the mid to late 19th century used diverting colostomy to manage bowel obstruction. During the early 20th century, proximal stoma was used to protect a distal anastomosis and to reduce postoperative complications. Stoma management was further advanced in the 1920s with the development of a rubber appliance that could be belted and glued into place.[3,5] The next major advance came in the mid-1950s, when Dr Bryan Brooke pioneered surgical maturation of the stoma, which provided a protruding stoma while eliminating the complications related to spontaneous maturation.[5-7]

The temporary stoma creation and reversal is associated with certain complications,[8] but advantages clearly outweigh the disadvantages. Age of patient, urgency of surgery, diagnosis and mode of presentation of the patient are the factors affecting the morbidity and mortality.[9]

Reversal of stoma is traditionally performed under general or spinal anesthesia. Recent studies show that local anesthesia offers a safe and effective alternative to general or spinal anesthesia for reversal of stoma.[10-12]

Purpose of this study was to compare the outcome local anesthesia versus spinal anesthesia in intestinal stoma reversal.

Material and Methods

It was a randomized control trial carried at a surgical special unit of Services Hospital Lahore, from March, 2007 to February, 2009. Sixty four patients aged 18 years and above, undergoing reversal of ileostomies and colostomies were included. Informed consent taken. Following patients were excluded from the study;

- Patients with hypersensitivity to local anesthetics.
- Patients with psychiatric disorders.
- Obese patients (BMI >30 kg/m).[2]
- Patients with para-stomal hernias.
- Patients with ileostomy/colostomy with mucous fistula, separated by ≥ 10 cm.
- Patients with coagulopathy
- Patients with spinal injuries.

Distal loopogram was done in all patients to exclude

any obstruction in distal segment. Mechanical bowel preparation was done. All patients were kept nothing per oral from midnight before surgery. Pre operative antibiotics (inj. ceftriaxone 1gm and metronidazole 500 mg) were given and two doses were given post operatively. Patients were randomized equally in group A and B. In group A, patients received midazolam intravenously (0.03 mg/kg), 10 minutes before the operation, and stoma reversal was done under local anesthesia (2% lidocaine and 0.5% bupivacain). The surgery was monitored by an anesthesiologist. In group B, the procedure was done under spinal anesthesia. The operative technique was standardized. The entire mucosal-cutaneous junction was taken down and the adhesions between the bowel and the anterior abdominal wall were freed with sharp dissection. Continuity was then restored by vicryl suture in two layers. After return of the bowel into the abdominal cavity, the abdominal wall defect, the subcutaneous tissue and skin were closed. The duration of the operation, conversion or supplementation of the anesthetic technique, time spent in the post-anesthesia recovery room, postoperative complications and length of hospital stay were analyzed.

Results

The postoperative follow-up lasted for 30 days. Patient's comparative data is shown in table below.

Table-1: Patients comparative data.

Sample Variables	Local Anesthesia (n=32)	Spinal anesthesia (n=32)
Mean Age (years)	35	20
Gender (M:F)	18:14	17:15
Type of stoma		
Ileostomy	22	21
Transverse colostomy	02	03
Sigmoid Colostomy	06	08

Table-2: Operative and Post operative variables.

	Local Anesthesia (n=32)	Spinal anesthesia (n=32)
Mean duration of operation	92 min	124 min
Time spent in recovery	34 min	92 min
Anesthesia conversion to G.A.	Nil	2 (6.25%)
Post operative complications	6 (18.75%)	10 (31.25%)
Mean hospital stay	4.33 days	4.53 Days

Table-3: Comparison of post operative complications.

Complications	Local Anesthesia (n=32)	Spinal anesthesia (n=32)
Spinal headache	Nil	3 (9.38%)
Urine retention	Nil	2 (6.25%)
Illness	01	2 6(25%)
Wound infection	03	2 (6.25%)
Abddominal wall haematoma	01	Nil
Entero-cutaneous fistula	01	Nil
Intestinal obstruction	Nil	01 (3.12%)
Total	06 (18.75%)	10 (31.25%)

Discussion

The mean duration of operation in group A was 92 min, versus 124 min in group B. More time in spinal anesthesia group was mainly due to IV preloading, giving spinal prick under strict aseptic measures and waiting for the onset of anesthesia effect. In addition local infiltration of fluid in local anesthesia helps in tissue dissection. Vaz et al have shown mean operative time 105 min and 146 min in local and spinal anesthesia groups respectively10, while in another study mean operative time with local anesthesia was 133 min13. Wong et al.[14] have concluded that if operations lasts more than 120 minutes, the morbidity will increase. We have calculated the mean time spent by patients in the recovery room as 34 min versus 92 min in group A and B. The said time was 36.8 min versus 145 min in study by Vaz et al.[10]

We noted that all patients in group A tolerated the anesthesia well, while in group B, two patients (6.25%) had to be converted to general anesthesia. Cantele et al[11] noted in series of 14 patients operated under local anesthesia, that tolerance was excellent in 9 patients, good in 3 and average in 2. In another study by Vaz et al, conversion to general anesthesia was needed in 3/25 (12%) patients being operated under spinal anesthesia, while no conversion was needed in patients being operated under local anesthesia plus sedation.[10] Abreu et al have shown similar results.[15]

Post operative complications were in 6 patients (18.75%) in group A, versus 10 (31.25%) in group B. This major difference was mainly due to complications of anesthesia technique itself, while there was no complication of local anesthesia.

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Picture Quiz

What is the diagnosis?

Answer on Page No. 183

Original Article

Evaluation of Lipids and Lipoprotein Levels in Opium And Heroin Addicts in Punjabi Population

Akif Qasim, Nakhshab Choudhry, Sadia Mahmood, Iqra Riaz, Muhammad Faheem ul Haq and Nadia Adnan

Objective: The present study was conducted to assess lipid and lipoprotein levels in opium (50 subjects) and heroin-addicted men (50 subjects) against non-opium and non-heroin addicted men (25 healthy individuals) as control subjects from Punjabi population.

Material and Methods: The biochemical estimations: total lipids, total lipids, TC, TGs, HDL, LDL, VLDL and Chylomicron levels were carried out on fully automatic clinical chemistry analyzer on 12hour fasting blood samples. The variables for each group were presented as means± standard deviations. Results were considered statistically significant if $p \leq 0.05$ for the biochemical parameters.

Results: Our study concluded that the cholesterol, triglyceride and Very Low Density Lipoprotein levels were higher in opium addicts than heroin addicts. Total lipid levels were decreased significantly in heroin addicts as compared to control subjects. However, no significant difference in High Density Lipoprotein and Chylomicron levels was noted in heroin and opium addicts in comparison to controls.

Conclusion: It may therefore be suggested that opium addicts are at higher risk to develop atherosclerosis leading to Ischemic heart disease than heroin addicts.

Key words: heroin, opium, ischemic heart disease, hyperlipidemia.

Introduction

One of the causes of death between 15 to 45 years of age is Heroin and Opium addiction. The 2006 national assessment report on problem of drug abuse in Pakistan, estimated that there are 628,000 opiate users. Of these, around 482,000 (77 percent) are heroin users. This is an alarmingly high rate. This heroin consumption costs around $1.2 billion every year, according to the estimates given by United Nations Office on Drugs and Crime (UNODC). Although, pain relief is the primary and justified use of opioids, this usage comes with the risk of producing physical and sometimes psychological dependence. Drug addiction is defined as a state of psychological or physical dependence, resulting from the interaction between a living organism and a drug, which forces the person to take the drug on a continuous or periodic basis in order to experience the effects and to avoid the discomfort of its absence.[1] Opiates are drugs which cause severe physical and psychological dependence with tolerance. Opium is included in naturally occurring opiates but heroin is a semi-synthetic opiate.

Opium is the air-dried milky exudate obtained by incising the unripe capsules of *Papaver somniferum L.* or its variety *album De Candolle* (Fam. *Papaveraceae*). Opium yields not less than 9.5 percent of anhydrous morphine. Powdered Opium is dried at temperature less than 70°C to reduce it to a very fine powder. Powdered Opium yields 10.0 to 10.5 percent of anhydrous morphine. It may contain any of the diluents permitted for powdered extracts, with the exception of starch.[2] Opium contains approximately 5-20 percent nonalkaloidal constituents such as water, about 20 percent various sugars, and several simple organic acids, including fumaric acid, lactic acid, oxaloacetic acid, and meconic acid.[3] Furthermore, it contains approximately 10-20 percent alkaloid constituents. While, more than 40 individual alkaloids have been isolated, only five of these alkaloids account for all of the quantitative alkaloid content in opium. These include the morphinans morphine (8-17 percent), codeine (0.7-5 percent), thebaine (0.1 - 2.5 percent); the benzylisoquinoline papaverine (0.5-1.5 percent) and the phthalideisoquinoline noscapine (narcotine) (1-10 percent).[4,5,6]

Heroin (also known as Diamorphine) is a compound synthesized by adding two acetyl groups to morphine. It is 3,6-diacetyl ester of morphine. Heroin is significantly more lipophilic than morphine and is therefore better transported and absorbed into the brain after injection. Heroin is rapidly hydrolyzed to 6-monoacetylmorphine, and then to morphine. Even the 6-monoester is more lipophilic than morphine, and thus better able to enter the brain.[3,7] Hence, heroin has a greater addiction potential than opium because of its euphoriant property and its rapid onset

of action. veuphoriant property and its rapid onset of action. Ischemic Heart Disease (IHD) is the single most common cause of death as of 2012,[8] placing a major economic and resource burden on health systems. There are many risk factors for IHD. Hyperlipidemia is one of the major risk factors that causes atherosclerosis and may lead to IHD.[9] Lipids are transported through the plasma compartment as lipoproteins. Major constituents of lipoproteins are triglycerides (TGs), cholesterol, cholesterol esters, phospholipids and apolipoproteins. The plasma lipoproteins are chylomicrons, very low-density lipoprotein (VLDL), low-density lipoprotein (LDL) and high-density lipoprotein (HDL).[10] Abnormal metabolism of some lipid fragments leads to various complications like atherosclerosis and coronary artery diseases (CAD).[11] The TG have been observed to be the major lipid content in atheromatous plaques supporting the preexisting view that a large number of myocardial infarction patients also exhibit hypertriglyceridemia.[12]

Furthermore, raised serum concentration of cholesterol, low-density lipoprotein cholesterol (LDL-C) and low serum concentration of high-density lipoprotein cholesterol (HDL-C) are all associated with an increased risk of coronary atherosclerosis.[13,14] Similarly, evidence also suggests that dyslipidemia is one of the major risk factors of CAD. Dyslipidemia is constituted as high level serum total cholesterol (TC), LDL-C, TGs, and low levels of HDL-C.[15,16] The prevalence of dyslipidemia may vary across population groups according to nationality, ethnicity, genetics, and socio-cultural and economic factors. The lifestyle and diet changes also significantly influence dyslipidemia.[17] A notion appears to prevail that opium can reduce serum lipids and hence the risk of IHD is reduced in opium addicts.[18] The present study was conducted to compare the lipid and lipoprotein levels in opium and heroin-addicted men with lipid and lipoprotein levels in non-opium and non-heroin addicted men from Pakistani population. The biochemical factors evaluated were total lipids, TC, TGs, HDL, LDL, VLDL and Chylomicrons. This study was designed to evaluate and compare the levels of lipids and lipoproteins in opium and heroin addicts.

Materials and Methods

The study was conducted to assess changes in lipid profile in heroin and opium male addicts. Subjects were chosen from psychiatry wards of Mayo and Services Hospitals. Investigations were carried out on fifty subjects of each group i.e. Heroin and Opium addicts. Twenty five healthy males of the same age groups were enlisted as controls. Duration of their addiction ranged from one to ten years. After twelve hours overnight fast, 6-8ml of blood were drawn from the patients and controls by venipuncture, in 10 cc disposable syringes and allowed to clot. Serum was separated by centrifugation at 3000 5000rpm.The biochemical estimations: total lipids, total lipids, TC, TGs, HDL, LDL, VLDL and Chylomicron levels were carried out on fully automatic clinically chemistry analyzer. The variables for each group were presented as means±standard deviations. Results were considered statistically significant if $p \leq 0.05$ for the biochemical parameters.

Results

Values of lipid profile are same sized in following tables. **(Table-1)**

Discussion

The importance of present study is to evaluate and compare the levels of lipids and lipoproteins in opium and heroin addicts, and to elaborate their

Table-1: The comparison of biochemical factors between the case (Heroin & Opium addicts) and control groups. Mean ± SD is given. Figures in parenthesis indicate number of cases in each group.

Biochemical Paramerters	Heroin Addicrs (Mean Values)	Opium Addicts (Mean Values)	Control Subjects (Mean Values)	P-Value
a. Triglylerids	155±35	223±62	227±61	<0.05
b. Total Cholesterol	153±39	248±53	193±27	<0.05
c. Total Lipids	4.8±1.06	7.5±1.2	7.0±1.7	<0.05
d. High density lipoproteins	33±7	36±6.3	34±4	<0.05
e. Low density lipoproteins	330±84.30	525±157.00	350±99.30	<0.05
f. Very low density lopoproteins	239±94.2	262±98	165±73	<0.05
g. Chylomicrons	210±89.1	229±93	195±85	<0.05

effects on atherosclerosis, IHD, and therefore on the quality of life. Cholesterol and phospholipids are the major lipid constituents of atherosclerotic lesion. A number of studies in the past have shown atherosclerosis.[19,20] The biochemical factors evaluated from the sera of heroin addicted, opium addicted and control subjects are shown in table. The results suggest a significant difference in cholesterol values between both groups i.e. opium and heroin addicts ($P < 0.05$). It is quite evident from our results that the levels of cholesterol in opium addicts are significantly higher than levels of cholesterol found in controls. Our findings regarding higher cholesterol levels in opium addicts are consistent with the studies conducted on morphine-pelleted rats maintained on a normal diet.21 However, these findings were not in agreement with other reports.[22-25] These changes in serum cholesterol levels can be explained on the basis that the persons taking opium reside mostly within the walled city of Lahore. The high serum cholesterol levels may however be explained by the fact that this section of population is known for their high cholesterol diet. On the other hand, this increase in serum values of cholesterol may have been caused by lipolytic effect of opioids.[26] Therefore, the higher levels of cholesterol observed in opium addicts during this study may suggest atherosclerotic changes in opium addicts as compared to heroin addicts. In this study, cholesterol levels were observed to be significantly lower in heroin addicts than in controls, which are consistent with other reports in humans.[22-25] Lower serum cholesterol levels in the heroin addicts may be the result of anorexia that is observed in heroin addicts because of the euophoriant effect of heroin.

The levels of TGs are higher in opium addicts than in the heroin addicts. The mean values of TGs are 223±62 in opium addicts, 155±35 in heroin addicts corresponding with 227±61 values of control subjects. Comparing the TG values in opium addicts and control subjects, no significant difference in TG levels is noticed and this trend is consistent with other studies.[18,22] However, it is quite evident from our results that the TG levels in heroin addicts are significantly lower than the TG levels found in control subjects and this contrasts sharply with another study which showed higher values of serum TGs in heroin addicts.[27] However, the low levels of TGs in heroin addicts as compared to opium addicts may be explained by the observation that heroin addicts are of relatively lean built as compared to opium addicts. Therefore, these obese subjects have more adipose tissue deposition than the lean built heroin addicts.[28,29] The higher adipose tissue deposition therefore appears to be an indication of high serum TG levels. In another study, it was further confirmed that lipoprotein lipase activity in a single fat cell was significantly higher in obese persons than lean control subjects, suggesting that the TG levels are high in obese persons.[30] In conclusion, eating habits, paucity of physical exercise and excessive somnolence in this particular class of opium addicts may be responsible for higher levels of TGs.

The mean values of both TC (248±53) and TGs (223±62) are higher in opium addicts than the heroin addicts in whom the mean TC levels are 153±39 and mean TGs levels are 155±35. It has been documented previously that hyperlipidemia is one of the major risk factors causing atherosclerosis and may lead to IHD.[9] In conclusion, opium addicts are more likely to develop atherosclerosis and IHD than heroin addicts based on the higher levels of both TC and TGs in opium addicts.

VLDL is assembled in the liver from TGs, cholesterol, and apolipoproteins. VLDL is converted in the bloodstream to LDL. VLDL functions as body's internal transport mechanism for lipids. Since VLDL depicts mostly the levels of TGs so the changes in VLDL levels are expected to reflect the changes in serum TG levels of these patients. The levels of VLDL in opium addicts are the highest (mean values 262±98), followed by VLDL levels in heroin addicts (values 239 ± 94.2) and lowest in the control (values 165±73) subjects.

The role of high plasma VLDL cholesterol level has been established beyond controversy, in atherosclerosis in both mice[31] and humans.[32] Increased VLDL levels in this study point towards higher incidence of atherosclerosis in cases of opium addicts. The possibility of formation of atherosclerosis in heroin addicts is less due to lower levels of VLDL whether it is due to dietary habits or increased activity after taking the drug.

However, it is reported that difference in LDL-C as well as in VLDL-C between opium addicts and control groups were not significant in both, men[33] and normolipidemic mouse[34] which is in contrast to our results. The preventive role of HDL levels in the development of IHD has already been established. In our study HDL levels are highest in opium addicts (36±6.3) as compared to heroin addicts (33±7) and controls (34±4). However, these changes are not consistent with previous studies.[18,25]

The mean serum levels of total lipids in opium addicts (7.5±1.2) are higher than mean serum levels of total lipids in heroin addicts (4.8±1.06) and mean serum levels of total lipids in controls (7.0±1.7). It is evident from our results that total lipids levels are decreased significantly in heroin addicts as compared to control subjects in accordance with other studies.[35] which may be explained by anorexia and lean frame that is characteristic of heroin addicts. The mean chylomicron levels are higher in opium addicts (229±93) as compared to heroin addicts (210±89.1) and controls (195±8). Although this is not a significant difference but these minor elevations in the levels of chylomicrons in opium taking group may be due to intake of diet high in lipids.

Conclusion

In conclusion, our findings showed that opium had an impact on the serum levels of TC, TGs and VLDL that are higher in opium addicts than heroin addicts. The total lipid levels were decreased significantly in heroin addicts as compared to control subjects. Furthermore, the changes in the levels of HDL and Chylomicrons in heroin and opium addicts were not significant in comparison to control subjects during this study. Therefore, it may be suggested that opium addicts are at a higher risk of developing atherosclerosis and Ischemic heart disease than heroin addicts.

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Original Article

COMPARISION OF HEMODYNAMIC CHANGES CAUSED BY 2 UNITS VERSUS 5 UNITS OF OXYTOCIN DURING ELECTIVE CAESARIAN SECTION UNDER SPINAL ANAESTHESIA

Afroza Abbas, Humaira Akram and Bushra Farooq

Objective: To compare the effects of 2 units and 5 units bolus doses of oxytocin on heart rate and mean arterial pressure during elective caesarian section under spinal anaesthesia.

Material and Methods: Randomized control study ,conducted over 6 months period on 150 patients at Maula Baksh Teaching Hospital Sargodha by dividing into 2 groups(group A & group B),through lottery method for randomization of oxytocin allocation.

Results: In our study, majority of the patients i.e. 45.33%(n=34) in Group-A and 38.67%(n=29) in Group-B were between 26-30 years of age, mean ± SD was calculated as 27.85±3.54 years.,while 60%(n=45) in group A and 56%(n=42) in group B were between 37-39 wks of gestation ,mean ± SD was calculated as 38.63±4.61wks.Blood loss in both groups shows insignificant difference by recording 187.43±18.65 ml in Group-A and 194.24±21.47 ml in Group-B, comparison of tachycardia in both groups was done which shows 32%(n=24) in Group-A and 61.33%(n=46) in Group-B while which shows a significant difference in both groups while hypotension was recorded as 4%(n=3) in Group-A and 17.33%(n=13) in Group-B, p value was calculated as <0.01.

Conclusion: We concluded that frequency of tachycardia and hypotension in patients administered with 2 IU bolus dose of oxytocin is significantly lesser as compared to 5IU bolus dose and there is no difference in the incidence of postpartum haemorrhage.

Key words: caesarean section, postpartum haemorrhage, prevention, oxytocin, 2 units, 5 units bolus, hypotension, tachycardia.

Introduction

Oxytocin is the most commonly used uterotonic agent in obstetrics. It is routinely administered after both normal and operative delivery to initiate and maintain adequate uterine contractility for minimizing blood loss and preventing postpartum haemorrhage. Several regimens of oxytocin have been tested during caesarean delivery (CD) with variable wanted (uterotonic) and unwanted (cardiovascular) effects. It is a common practice to administer oxytocin as an intravenous (IV) bolus followed by IV infusion for adequate uterine contraction. Larg doses of oxytocin injected rapidly is known to produce various adverse effects such as hypotension, nausea, vomiting, chest pain, headache, flushing, myocardial ischemia, ST-T segment changes, pulmonary edema, severe water intoxication, and convulsion.

Material & Methods

Randomized control study ,conducted over 6 months period on 150 patients at Maula baksh teaching hospital Sargodha by dividing into 2 groups(group A & group B),through lottery method for random- ization of oxytocin allocation, by non probability purposive sampling ,from 1.11.2012 to 30.4.2013.

Results

iA total of 150 (75 in each group) after fulfilling the inclusion/exclusion criteria were enrolled to compare the effect of 2 units and 5 units bolus doses of oxytocin on heart rate and mean arterial pressure during elective caesarean section under spinal anaesthesia and to compare the effect of 2 units and 5 unit bolus doses of oxytocin on amount of blood loss during elective caesarean section under spinal anaesthesia.

Age distribution of the patients was done which showed that 30.67%(n=23) in Group-A and 36%(n=27) in Group-B were between 20-25 years of age, 45.33%(n=34) in Group-A and 38.67%(n=29) in Group-B were between 26-30 years of age, while only 24%(n=18) in Group-A and 25.33%(n=19) in Group-B were between 31-35 years of age, mean and sd was calculated as Mean + SD: 27.85+3.54 years.

Blood loss in both groups was recorded which showed that in Group-A 187.43+18.65 ml while in Group-B 194.24+21.47 ml blood was lost.

Gestational age distribution of the patients was done which showed that 60%(n=45) in group A and

56%(n=42) in group B were between 37-39 wks of gestation,40%(n=30) in group A and 44%(n=33) in group B were between 39 1-41 wks of gestation. Mean and SD was calculated as mean ±SD 38.63±4.61wks. Comparison of tachycardia in both groups was done which showed 32%(n=24) in Group-A and 61.33%(n=46) in Group-B while 68%(n=51) in Group-A and 36.67% (n=29) in Group-B had no findings of tachycardia, p value was calculated as 0.000 which shows a significant difference in both groups. we compared hypotension in both groups, it shows 4%(n=3) in Group-A and 17.33%(n=13) in Group-B while remaining 96%(n=72) in Group-A and 82.67%(n=62) in Group-B had no hypotension, p value was calculated as 0.01.

Table-1: Blood loss, hypotension and tachycardia in both groups (n=150).

	Group-A (n=75)	Group-B (n=75)
Blood Loss (ml±SD)	187.43±18.65	194.23± 21.47
Tachycardia		
Yes	24 (32%)	46 (61.33%)
No	51 (68%)	29 (38.67%)
Hypotension		
Yes	03 (04%)	13 (17.33%)
No	72 (96%)	62 (82.67%)

Discussion

There are no practice guidelines regarding oxytocin dosage and optimal dose remains unclear. It is common practice in Pakistan to use 5 or 10 IU intra venous bolus dose of oxytocin during elective caesarean delivery. However, we planned this study to compare the haemodynamic effects of 2 and 5IU boluses of oxytocin to determine which dose is associated with lesser haemodynamic disturbances without compromising sufficient uterine contraction, so that we can change our practice for safety of the patients and provide published data as none is available in this regard in our country.

In our study, majority of the patients i.e. 45.33%(n=34) in Group-A and 38.67%(n=29) in Group-B were between 26-30 years of age, mean ± SD was calculated as 27.85+3.54 years,while 60%(n=45) in group A and 56%(n=42) in group B were between 37-39 wks of gestation mean±SD was calculated as 38.63±4.61wks. Blood loss in both groups shows insignificant difference by recording 187.43+18.65 ml in Group-A and 194.24+21.47 ml in Group-B, comparison of tachycardia in both groups was done which shows 32%(n=24) in Group-A and 61.33%(n=46) in Group-B while which shows a significant difference in both groups while hypotension was recorded as 4%(n=3) in Group-A and 17.33%(n=13) in Group-B, p value was calculated as 0.01.

The findings of the study are in accordance with Sartain J B and co-workers, in their study after 1 min with 2IU oxytocin heart rate increased in 11 patients(27.5%) and mean arterial pressure decreased in none(0%) and with 5 IU heart rate increased in 23 patients(57%) and mean arterial pressure decreased in 6 patients(15%)respectively,[5] which shows that during elective caesarean delivery giving more than 5IU intra venous bolus of oxytocin is not advantageous in preventing post partum haemorrhage.

The guidelines of the Royal College of Obstetricians and Gynaecologists (UK) on caesarean section recommend a slow intravenous bolus dose of 5 IU of oxytocin after delivery of the infant. This dose is based on the principles of active management of the third stage of labour[12] and is consistent with practice across most of Europe and Australia.[13] In a survey of obstetricians and anaesthetists in the UK, the use of an oxytocin bolus was standard treatment, although the dose varied between 5 IU and 10 IU.[14] In settings where an oxytocin bolus is used routinely, an additional infusion of oxytocin may be required if haemorrhage occurs. This practice has led some obstetricians to use an additional infusion of oxytocin on a selective or routine basis for high risk cases, despite a lack of evidence to support this practice.[14]

While results of this study are in favour of a low dose i.e In which shows a significantly low rate of hypotension and tachycardia while the blood loss in both groups were similar and insignificant and the hypothesis of the study that "Incidence of tachycardia and hypotension with 2 IU bolus dose of oxytocin is less as compared to 5IU bolus dose and there is no difference in the incidence of postpartum haemorrhage" is justified.

Further trials on this comparison may authenticate the results of the current study and we can change our practice for safety of the patients.

Conclusion

The frequency of tachycardia and hypotension in patients administered with 2 IU bolus dose of oxytocin is significantly lesser as compared to 5IU bolus dose and there is no difference in the incidence of postpartum haemorrhage.

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CORRIGENDUM

Esculapio
Journal of Services Institute of Medical Sciences, Lahore
Volume 08, Issue 04, Oct - Dec. 2012

In Original Article,
"Frequency of Helicobacter Pylori (H. Pylori) in Patients of Acid Peptic Disease "
By Ikram ur Rahim and Omar Ahsan page # 165. The correspondence address was printed
Department of ENT/Akhtar Saeed Trust Teaching Hospital, Lahore

Now **Volume 08, Issue 04, Oct - Dec. 2012** Page No. 165 should be read as follows:
Department of Medicine/Akhtar Saeed Trust Teaching Hospital, Lahore

Original Article

Frequency of Pseudomembranous Colitis in Antibiotic Associated Diarrhea

Salman Javed and Attique Abubakar

Objectives: The objective of this study is to determine the frequency of Pseudomembranous colitis in antibiotic associated diarrhoea in tertiary care hospital.

Methods: Two hundred and fifty patients, who fulfilled the inclusion criteria, were enrolled in the study. The antibiotic being taken by the patients was documented. No specific therapy or diet for the prevention of diarrhea was prescribed, except for the withdrawal of antibiotic and introduction of antiperistaltic agent. After 3 days of starting diarrhea, stool culture for Clostridium difficile infection was done and if it was found to be positive then patients were subjected to sigmoidoscopy/colonoscopy to confirm the presence of pseudomembranous colitis.

Results: Out of two hundred and fifty patients, 159 patients (63.6%) were, 12-40 years old, 59 patients (19.6%) were between 41-60 years of age while 42 patients (16.8%) were between 61-70 years of age. 130 patients (52.0%) were male and remaining 120 patients (48.0%) were female. Stool culture for Clostridium was positive in 63 patients (25.2% of total) and negative in 187 patients (74.8% of total). Pseudomembranous colitis was noted in 31 patients (12.4%) on lower GI endoscopy.

Conclusions: Considerable number of antibiotic associated diarrhea cases were found to have evidence of Pseudomembranous colitis.

Keywords: pseudomembranous colitis, diarrhea and antibiotic associated diarrhea.

Introduction

Antibiotic-associated diarrhea (AAD) is defined as the diarrhea that occurs in association with the administration of antibiotics after excluding other causes of diarrhea. It can be a significant problem for patients needing antibiotic therapy. It can affect patient compliance resulting in incomplete duration of therapy and development of microbial resistance[1]. Frequency of Antibiotic-associated diarrhoea varies from 5-39 % depending on the antibiotic type.[2]

Clostridium Difficile infection is responsible for approximately 20% cases of Antibiotic-associated diarrhea.[3,4] Pseudomembranous colitis (PMC) is characterized by inflammation of colonic wall with inflammatory debris and cells and distinctive patches of yellowish gray exudates, ulcerations or ovoid plaques, separated by normal or hyperemic mucosa. PMC complicates about 50 % cases of *Clostridium Difficile* infection and about 10 % cases of Antibiotic-associated diarrhea.[3,4]

Klebsiella pneumonia, Staphylococcus *aureus*, *Candida* albicans, and candida tropicalis might also contribute to the development of Antibiotic-associated diarrhea.[5] Up to 5% of healthy adults and majority of infants and children are asymptomatic carriers of *Clostridium Difficile*.[3,4]

Clostridium difficile is a Gram-positive spore bearing anaerobic bacteria and is commonly present in the stools of 5 % of healthy adults and in about 15-70 % of infants.[3,5] The majority of hospitalized patients infected by *C. difficile* are asymptomatic carriers who serve as silent reservoirs in hospital environment.[6] However *C. difficile*-associated disease (CDAD) is a serious condition with mortality up to 25 % in frail elderly people[7] and is now recognized as the primary cause of hospital acquired colitis in patients who receive antibiotics, chemotherapeutics or other drugs that alter their normal flora. *C. difficile* infection was initially considered as a consequence of antibiotic intake and not as a life threatening disease. During the recent outbreaks of CDAD in the West, a higher number of cases involving toxic megacolon, colectomy or death have been reported.[8] The mutant hypervirulent strain was typed as NAP1/BI/027 (North American PFGE type I/restriction endonuclease analysis BI/ribotype 027).[9] It was found to produce greater than 16 times toxin A and 23 times toxin B in addition to the binary toxin.[10]

C. difficile is also being reported more frequently even from non hospital-based settings, such as from the community.[11] Domestic as well as wild animals are probably transmitting this as the same ribotypes found in them were found to be associated with human infection.

Material And Methods

It was a cross sectional study, done in emergency department, OPD and Indoor Department of Medical Unit-III of Services Hospital Lahore. Sampling was done by purposive non-probability technique. Study was conducted for six months. Two hundred and fifty patients of antibiotic associated diarrhea were enrolled in this study. Patients who took even a single dose of antibiotic and developed diarrhea at least 3 days afterwards and no history of diarrhea in preceding 2 weeks before starting antibiotics was included in this study. Patients having other causes of chronic diarrhea like IBS, inflammatory bowel diseases, Celiac disease, colorectal carcinoma, thyrotoxicosis and diabetes mellitus, which were diagnosed on the basis of previous history and laboratory test and use of laxatives were excluded. The antibiotic being taken by the patients was documented. No specific therapy or diet for the prevention of diarrhea was prescribed, except for the withdrawal of antibiotic and introduction of antiperistaltic agent. After 3 days of starting diarrhea, stool culture for Clostridium difficile infection was done, if it was found to be positive then patient were subjected to sigmoidoscopy/colonoscopy to confirm the presence of Pseudomembranous colitis. The data was entered and analyzed by SPSS version 10.0.

Results

Out of 250 patients, 159 patients (63.6%) were 12-40 years old, 59 patients (19.6%) were 41-60 years of age while 42 patients (16.8%) were between 61-70 years of age. Mean age of patients was 36.94 (±16.239) 130 patients (52.0%) were male and remaining 120 patients (48.0%) were female. In this study most offending drug for PMC causation was found to be Clindamycin (19.3% of patients taking the drug developed this condition). Erythromycin and Ceftriaxone were among the second and third culprit agents respectively. Stool culture for Clostridium was positive in 63 patients (25.2% of total) and negative in 187 patients (74.8% of total). Pseudomembranous colitis was noted in 31 patients (12.4%) lower GI endoscopy.

Table-1: Frequency of Pseudomembranous colitis and sex distribution.

	Number (n=250)	%
Age (Years)		
12-40	159	63.6
41-60	49	19.6
61-70	42	16.8
Sex Distribution		
Male	130	52.0
Female	120	48.0

Table-2: Distribution of pseudomembranous colitis with respect to the use of different Antibiotics.

Antibiotic Name	No. of patients who used the antibiotic	No. of patients who developed pseudomembranous colitis (n)
Clindamyoine	52	10 (19.33%)
Erythromyoine	28	04 (14.28%)
Co-amoucicilin	62	04 (6.45%)
Ciprofloxcacin	44	05 (11.36%)
Ceftriazone	24	03 (12.5%)
Clarithromicin	28	03 (10.71%)
Amoxicillin	12	01 (8.33%)

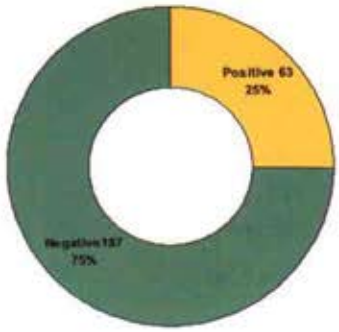

Fig-1: Stool Culture results in Patients with Antibiotic Associated Diarrhea.

Discussion

The diagnosis of Pseudomembranous colitis in this study was based upon the presence of positive sigmoidoscopic/colonoscopic findings in patients with antibiotic associated diarrhea with positive stool culture for clostridium. Using this criterion, out of two fifty patients, 31 were found to have Pseudomembranous colitis. In our region, there are limited studies on *C. difficile*-Associated Diarrhea, (CDAD) probably due to the lack of technology and the difficulty in culturing the pathogen.

This is the first study in Pakistan that reports the frequency of Pseudomembranous colitis and CDAD among patients with antibiotic associated diarrhea. Available reports from India estimate the prevalence

of CDAD of about 15-30 % in patients taking antibiotics[15-19]. Gupta & Jadav[20] reported 25.3 per cent isolation of *C.difficile* from diarrheal patients of all age groups. Vaishnavi *et al*[7] reported 30 per cent positivity for *C. difficile* toxin in hospitalized patients. When only adult population was investigated, the positivity for *C. difficile* toxin was 19.4 per cent in the antibiotic receiving hospitalized patients[21]. Some studies from United States reveal the frequency of Clostridium difficile infection of about 20-25% and of Pseudomembranous colitis of about 10% in patients of antibiotic associated diarrhea.[3,4] These findings are comparable with our results where frequency of CDAD among patients with AAD was noted 25.2% and of PMC about 12.4%. Kang *et al*[22] reported that *C. difficile*-associated diarrhoea was more common in the post transplantation period in India than in developed countries. Vaishnavi *et al*[23] reported the association of *C. perfringens* with antibiotic associated diarrhoea either by itself or in synergy with *C. difficile* infection. Balamurugan *et al*[24] reported overgrowth of *C. difficile* in the stool of Indian patients with ulcerative colitis compared to healthy controls using real time PCR. Due to difference in demographic profile, injudicious use of antibiotics in our community, depressed nutritional and immunological status, and global emergence of resistant strain (BI/NAP1/027), our population has more propensity of acquiring CDAD. In addition to this due to poor sanitary condition and insufficient supply of clean drinking water, feco-oral transmission of infections is common. Prevention of *C. difficile* infection is challenging. A change in antibiotic policy and implementation of standard infection control measures reduces the incidence of *C. difficile* symptomatic infections. Combined approach, involving effective control measures, the use of rapid and sensitive techniques for laboratory diagnosis as well as prudent use of antibiotics, is necessary to reduce morbidity and mortality due to *C. difficile* associated infections in hospitalized patients. It certainly highlights the importance of public awareness regarding the judicious use of antibiotics. We urge the clinicians that while advising antibiotics, they must have a high index of clinical suspicion of PMC, if the patients subsequently develop diarrhea after taking therapy. Furthermore, screening tests can be incorporated for general population, if this clinical problem would found to be significantly high in future large scale, probability studies. This may reduce morbidity and mortality associated with this grave but treatable condition. There are a few limitations to the study results. Firstly, this study was conducted on small scale. Sampling of the patients was done by non-probability purposive method. Therefore the results obtained cannot be generalized. We only analyzed the association of PMC with different antibiotics but preference or percentage of patients receiving a particular antibiotic many influence this results, as there may be over prescription of certain antibiotics. To overcome the above mentioned problems following suggestions should be taken into consideration:

1. A large scale, population based study is needed to achieve results, which can be applied to general population.
2. Sampling should be done by probability techniques. Many of the patients who had been diagnosed as cases of antibiotic associated diarrhea and pseudomembranous colitis did not have knowledge of their problem and subsequent complications. So it is suggested that screening for pseudomembranous colitis should be done meticulously.

Conclusion

Based on the results obtained from our study, it is concluded that considerable number of antibiotic associated diarrhea cases were found to have evidence of Pseudomembranous colitis. Early detection of Pseudomembranous colitis is of vital importance, as with appropriate care we can reduce morbidity and mortality. The results of this study support our objectives. A large scale population based study is required for achieving significant results, which can be generalized. Following features can be highlighted from study:

1. *C. difficile* associated disease is a growing nosocomial and public health problem.
2. Pseudomembranous colitis is an important complication of antibiotic associated diarrhea.
3. Most culprit drug was found to be Clindamycine followed by Erythromycine and Ceftriaxone respectively.
4. Clinical suspicion is more important because stool assays for diagnosing CDAD are not widely available. Hospitalized patients receiving antibiotics for their ailments are at greater risk of acquiring.
5. Infection control procedures that should be followed to prevent spread of the CDAD include environmental hygiene, use of phenolic disinfectant washing hands with ordinary soap and water or using 0.03 percent Triclosan and isolating patients with CDAD.

6. Preventing *C. Difficile* infection offers a potentially significant improvement in patient's outcomes, as well as a reduction in hospital, costs and resource expenditures.

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Original Article

ROLE OF C-REACTIVE PROTEIN IN DIAGNOSIS OF ACUTE APPENDICITIS

Abdul Basit Qureshi, Ahmad Raza and Sajid Mukhtar

Objective: The objective of this study is to determine the role of C-reactive protein in the diagnosis of acute appendicitis.

Material and Methods: Seventy patients with suspicion of acute appendicitis were collected for this study. The patients were collected on the basis of history, clinical examination and laboratory investigations. Operation was done in all patients and appendix was sent for histopathology. Histopathology was considered as gold standard.

Results: The mean age of patients was 22.40±7.95 years. The mean C-reactive protein of the patients was 21.64±19.63µg/ml. There were 14.3% patients of C-reactive protein range of less than 6µg/ml and 85.7% patients of C-reactive protein range of more than 6µg/ml. In the histopathology findings, there were 94.3% patients of acutely inflamed appendix and 5.7% patients of normal appendix. The sensitivity was found to be 86%, specificity 91%, and positive predictive value 86%, negative predictive value 87% and accuracy 89%.

Conclusion: A normal pre-operative serum CRP measurement in patients with suspected acute appendicitis is most likely associated with a normal appendix. Deferring surgery in the patients would probably reduce the rate of unnecessary appendicectomies.

Key words: acute appendicitis, c-reactive protein, appendix.

Introduction

Acute appendicitis is one of the most common intra-abdominal infections seen in patients presenting with acute abdomen in the surgical departments.[1] The reported lifetime prevalence is as high as one in seven.[2] According to an estimate 6% of population will suffer from acute appendicitis during their lifetime.[3] The peak age group is 12 to 30 years in both sexes but slightly more common in males.[4]

Acute appendicitis remains an up to date issue, being the most frequent cause of surgical acute abdomen round the globe.[5] Appendectomy is one of the commonest procedures in surgery.[6] Despite the recent advances in diagnostic medicine, the diagnosis of appendicitis is still doubtful in a number of cases.[7] Diagnostic accuracy of acute appendicitis remains insufficient with an unacceptable high rate of unnecessary operations.[8] Inspite of various investigations used to improve the accuracy of diagnosis the rate of normal appendices removed is still about 15-30%.[6] Improving the diagnosis of acute appendicitis in order to prevent unnecessary surgery is crucial.[9] Majority of clinicians rely on their clinical examination strengthened by the laboratory tests.[7] Laboratory measurements such as leukocyte count and C-reactive protein (CRP) concentration are commonly used as diagnostic aids in patients with suspected acute appendicitis.[10]

C-reactive protein measurement has been shown to give valuable information in the diagnosis of acute appendicitis.[11] An elevated level of C-reactive protein, is one of the many downstream indicators of inflammation.[12] C-reactive protein is an acute phase protein that is produced in large amounts by hepatocytes during an acute inflammatory process.[13] C-reactive protein levels serve as an early marker of the magnitude of inflammation in events such as acute appendicitis.[12] C-reactive protein measurement can increase the diagnostic accuracy in acute appendicitis.[14] A normal pre-operative serum CRP measurement in patients with suspected acute appendicitis is most likely associated with a normal appendix and deferring surgery in this group of patients might reduce the rate of unnecessary appendectomies.[15]

The role of inflammatory markers in the diagnosis of acute appendicitis has not been clearly defined. Laboratory tests of the white cell count, neutrophil count and C-reactive protein are more effective in supporting a clinical diagnosis of acute appendicitis in patients with typical clinical features than in excluding the diagnosis.[17]

The purpose of this study was to analyze the diagnostic accuracy of CRP and its possible advantage in diagnosing acute appendicitis in patients presenting with pain in right iliac fossa.

Material and Methods

It was Cross sectional comparative study, done at surgical unit 1 services hospital Lahore from June 2006 to November 2006. Seventy patients with clinical suspicion of acute appendicitis were included in the study by Non-probability convenience sampling. All patients with right iliac fossa pain, having suspicion of acute appendicitis on the basis of history and clinical examination, patients of both genders, age of 12 years and above were include in the study. Exclusion criteria was, pregnant patients, patients with a mass in right iliac fossa, known cases of right sided renal calculi, patients with hepatic dysfunction. All seventy patients with suspicion of acute appendicitis fulfilling the inclusion criteria were enrolled from the emergency department of Surgical Unit-I Services Hospital Lahore. Informed consent was obtained from the patients.

Detailed history of present illness was recorded. Symptoms of the patients e.g., site of onset, duration of onset, radiation, nausea, vomiting, fever anorexia, and diarrhea were noted. The signs of acute appendecitis e.g., tenderness, muscle guarding, rebound tenderness, rovsing sing, psoas sign and obturator sign were also noted. The laboratory investigations e.g., complete blood count, urine examination, C-reactive protein and abdominal ultrasonography were also done. Operation was done and appendix was sent for histopathology. Histopathology was considered as gold standard to establish the diagnosis of acute appendicitis.

All this information was collected through prescribed Proforma.

The collected data was entered into SPSS version 11 and analyzed accordingly. The study variables to be analyzed were age, sex, presenting complaints, symptoms, examination findings, haemoglobin, C-reactive protein, white blood cell, ultrasonography findings, histopathology findings, and operative findings. Descriptive statistics was calculated. Means and standard deviations were calculated for age, haemoglobin, white blood cell and C-reactive protein. Proportions and percentage was calculated for sex, presenting complaints, symptoms, examination findings, ultrasonography findings, histopathology findings and operative findings. Role of C-reactive protein was determined by calculating sensitivity, specificity, positive predictive value, negative predictive value and accuracy. Histopathology was taken as a gold standard to establish the diagnosis of acute appendicitis.

Results

The mean age of patients was 22.40±7.95 years. There were 37 (52.9%) patients of age range of 12-20 years, 22 (31.4%) patients of age range of 21-30 years, 10 (14.3%) patients of age range of 31-40 years and 1 (1.4%) patients of age range of 41-50 years of age. There were 32 (45.7%) males and 38 (54.3%) females.

The mean C-reactive protein of the patients was 21.64±19.63µg/ml. There were 10 (14.3%) patients of C-reactive protein range of less than 6µg/ml and 60 (85.7%) patients of C-reactive protein range of more than 6µg/ml **(Table 1).**

In the ultrasound findings, there were 20 (28.5%) patients of inflamed appendix and 50 (71.5%) patients of normal. scan. In the histopathology findings, there were 66 (94.3%) patients of acutely inflamed appendix, and 4 (5.7%) patients of normal appendix **(Table 2).**

In the operative findings, there were 66 (94.3%) patients of acutely inflamed appendix, 2 (2.9%) patients of perforated appendix and 2 (2.9%) patients of normal appendix. The sensitivity was found to be 86%, specificity was found to be 91%, positive predictive value was found to be 86%, negative predictive value was found to be 87% and accuracy was found to be 89%. **(Table-3)**

Table-1: Distribution of patients by signs and symptoms (n=70).

Sign and Syptoms	No	%	No	%
Radiation	518	25.7	52	74.3
Vomiting	33	47.1	37	52.9
Anorexia	56	80.0	14	20.0
Fever	19	27.1	51	72.9
Diarrhoea	05	7.1	65	92.9
Nausea	31	44.3	39	55.7
Tenderness	70	100.0	0	0

Rebound Tenderness	64	91.4	06	8.6
Muscle Guarding	32	45.7	38	54.3
Rovsing Sign	09	12.9	61	87.1
Psoas Sign	0	0	70	100.0
Obturator Sign	0	0	70	100.0

Table-2: Distribution of patients by C-reactive protein (n=70).

C-reactive protein (ug/ml)	No	Percentage
<6	10	14.3
>6	60	85.7
Mean±SD	2.64±19.63	

Table-3: Distribution of patients by histopathology (n=70).

Histopatholgy findings	No	Percentage
Acutely inflamed appendix	66	94.3
Normal Appendix	04	5.7
Total	70	100.0

Table-4: Comparison of C-reactive protein versus histopathology (n=70)

C-reactive Protein	Histopathology (gold standard)		
	Positive	Negative	Total
Positive	60 (TP)	6 (FP)	66
Negative	10 (FN)	64 (TN)	74
Total	70	70	140

Key: *TP: True Positive, FP: False Positive, FN: False Negative, TN: True Negative*

Discussion

Appendicectomy for suspected acute appendicitis is a common procedure. The rate of normal appendices unnecessarily removed remains as high as 15-30% despite several techniques and investigations used to improve the diagnostic accuracy. Many studies investigated the role of raised C-reactive protein in improving the diagnosis of acute appendicitis. In patients with histopathologically proven acute appendicitis both the WBC count and serum CRP level were significantly raised.[18]

In our study the mean age of the patients was 22.40±7.95 years which is comparable to the study of Jehangir et al[19] in which mean age of patients was 20 years. In the study of Khan et al[20] the mean age of the patients was 24 years which is also comparable with our study. In our study 45.7% of patients were male and 54.3% were females. As compared with the study of Stefanutti et al[21], there were 55% males and 45% females which were comparable with our results. In our study, CRP was high in 85.7% patients and low in 14.3% patients and mean CRP was 21.64±19.63µg/ml. According to Iqbal[22] CRP was high in 61% and low in 39% with mean 14.53±13.16µg/ml. In another study of Fernando et al[23] CRP was high in 78% of cases included in the study. So our results are comparable with the study of Fernando et al.[24] In a study of Asfar et al[18] serum C-reactive protein level was normal in 16.7% explorations. As compared with our study, the C-reactive protein was normal in 14.3% patients which is comparable with the above study.

Another study conducted by Amalesh et al[6] described that C-reactive protein was normal/negative in 7.3% patients and positive in 92.7% patients. As in our study CRP was high in 85.7% patients and CRP was low in 14.3% patients, which is not different with the study of Amalesh et al[6], the minor difference is due to number of patients, as our sample is much less as compared to the number of patients of Amalesh et al.[6]

In our study, on the basis of histopathology report, there were 94.3% positive appendicitis and 5.7% negative appendicitis patients. As compared with the study of Amalesh et al[6] on the histopathology report was normal/negative in 17% patients and 83% positive patients, which is not different with above study. The minor difference is due to number of patients, as our sample is much less as compared to above study's number of patients.

In our study, the sensitivity was found to be 86%, specificity was found to be 91%, positive predictive value was found to be 86%, negative predictive value was found to be 87% and accuracy was found to be 89%. As compared with the study of Alamesh et al[6] the specificity and sensitivity was 42% and 91% respectively. The predictive value of a positive (raised CRP) and negative (normal CRP) test is 88% and 48%

respectively. According to the study of Asfar et al[18] the specificity and sensitivity of serum CRP was 86.6% and 93.6%, respectively.[18] As compared with our study the specificity and sensitivity was 91% and 86% which is comparable with the above study. In another study conducted by Shoshtari et al[16] 89.7% had acute appendicitis whereas 10.3% were normal with no sign of inflammation on histological examination. Whereas in our study, 94.3% were positive appendicitis and 5.7% were negative appendicitis patients, which were same and comparable with the above study. In a study conducted by Shoshtari et al[16] sensitivity was 80%, specificity was 89.7%, positive predictive value was 97.5% and accuracy was 88.7% patients. While in our study, sensitivity was 86%, specificity was 91%, positive predictive value was 86%, and accuracy was 89%. So our results are same and comparable with the above study.

Conclusion

A normal pre-operative serum CRP measurement in patients with suspected acute appendicitis is most likely associated with a normal appendix. Deferring surgery in the patients would probably reduce the rate of unnecessary appendicectomies.

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Original Article

IMPACT OF PESTICIDES ON RENAL FUNCTION TESTS IN COLLABORATION WITH LIVER FUNCTION TESTS AMONG WORKERS OF PESTICIDE FORMULATION AND PACKING PLANTS IN PAKISTAN

Muhammad Fahim ul Haq, Sadia Mahmood, Nakhshab choudhry, Shama akram, Tazeem Shahbaz, Riffat Yasmin and Nadia Adnan

Objective: To evaluate the impact of pesticides on renal function tests in collaboration with liver function tests among workers of pesticide formulation and packing plants in Pakistan.

Material and Methods: One hundred workers, 20-50 years of age, working at different pesticide formulation and packing units for at least one year were included in this study. One hundred healthy age and sex matched industrial workers were taken as controls. Renal function tests i.e. blood urea nitrogen, serum creatinine and liver function tests i.e. alkaline phosphatase, alanine transaminase, aspartate transaminase, gamma glutamyl transferase, total bilirubin, and direct bilirubin, were performed. Screening for hepatitis B and C virus was also done to confirm that all the samples included in current study were negative for Hepatitis B and C virus.

Results: In current study, mean blood urea nitrogen value for 100 control subjects was 8.37 mg/dl while that of 100 pesticide industrial workers was 12.70 mg/dl. Mean serum creatinine value of 100 controls was 0.65 mg/dl and that of patient population was 0.98 mg/dl. These results revealed that all the hundred pesticide industrial workers had normal blood urea nitrogen and serum creatinine levels but on the higher side as compared to control subjects. P value was significantly high. The results of liver function tests in serum samples of control subjects were within normal range. Liver function tests of 80 pesticides industrial workers out of 100 were within normal range whereas 20 workers had abnormally raised levels.

Conclusion: Pesticide exposure among workers of pesticide plants might cause liver toxicity.

Key words: pesticide industrial workers, renal function tests, liver function tests.

Introduction

Pesticide is defined as any substance intended for preventing, destroying, attracting, repelling or controlling any pest including unwanted species of plants or animals during production, storage, transport, distribution and processing of food, agricultural commodities or animal feed.[1]

The increasing and injudicious use of chemical pesticides is recognized to be a potential hazard to both humans and animals.[2] Presently on an average, fifty thousand tons of pesticides are used in Pakistan annually.[3] Number of local pesticide formulation and repacking plants has also increased considerably, according to the increased need. About 70% of the total pesticides are formulated locally.

A large number of workers are directly exposed to pesticides at formulation or repacking plants. These workers are not aware of the hazardous effects of these pesticides and therefore handle the pesticides in a casual way without following any safety measures. Functions of different body organs including liver and kidneys maybe disturbed due to exposure to pesticides.[4]

Liver is one of the most important organs in the human body. Liver functioning is evaluated on the basis of levels of different enzymes in the blood, i.e. alkaline phosphatase (ALP), alanine transaminase (ALT), aspartate transaminase (AST), gamma glutamyl transferase (GGT), total bilirubin (TBil) and direct bilirubin (DBil).[5] The kidneys are vital organs that perform a variety of important functions. In a clinical laboratory, blood urea nitrogen (BUN) and serum creatinine (Cr) are used in assessment of renal function.

Significant negative impact of pesticide exposure on various liver and renal functions in human beings has been reported by many researchers. Azmi *et. al.* (2005), at Baqai University, Karachi studied the effect of pesticide residues on general health and different enzyme levels, in the blood of farmers from Gadap (rural area) Karachi. A significant increase in ALP, ALT and AST levels was reported.[6]

Ozucelik DN *et. al.* (2004), Department of emergency medicine Hacettepe university Ankara, Turkey, reported a case of toxicity following unintentional Dichlorodiphenyltrichloroethane (DDT) ingestion, the patient developed severe metabolic acidosis and acute renal failure (ARF) which was diagnosed on second day of ingestion with a BUN level of 47 mg/dl and Cr level of 6.4 mg/dl.[7]

High levels of ALP, ALT, AST and low level of GGT were also reported by Naqvi *et. al.* in the blood of farm workers from Gadab in Pakistan during 2007.[8]

Safety standards for workers at pesticides formulation and repacking plants in Pakistan generally do not meet with the international standards. Now when the pesticide formulation industry is expanding at a rapid pace, health of the workers must be safeguarded. Assessment of different liver and renal function tests are an important tool to assess the impact of exposure of workers to pesticides.

Review of literature has shown that a number of studies have previously been conducted regarding the effect of pesticides on farmers but not in the workers of pesticides industry who are continuously exposed to the pesticides. Keeping in view the importance of the subject, present study was designed to evaluate impact of exposure to pesticides on different liver and renal function tests among workers of pesticide formulation and packing plants in Pakistan.

Materials and Methods

In this cross-sectional, case control study, one hundred workers in the age group of 20-50 years working at different pesticide formulation and packing units for at least one year were included.

One hundred healthy age and sex matched workers (other than pesticide workers) with no history of exposure to pesticides were taken as control.

Individuals, who were known diabetic, hypertensive, smoker, obese, having previous history of jaundice or positive cases of hepatitis B or C were excluded from the study. 6-8 ml of blood samples were drawn and brought to the laboratory. Sera were immediately separated by centrifugation at 3000 rpm for five minutes and were transferred to eppendorf tubes and kept frozen at -2 to -4°C.

Biochemical tests ALP, ALT, AST, GGT, TBil, DBil, BUN and S. Cr were estimated on Dade Dimension RxL (Siemens Healthcare Diagnostic Inc. Delaware, USA) fully automatic clinical chemistry analyzer. Screening for hepatitis B and C virus was done by immunochromatographic technique.

Results of BUN and S. Cr were expressed as mean s SD. Data was analyzed by using SPSS version 18. A p value of less than 0.05 was considered statistically significant.

Results

Data of 100 pesticides industrial workers were taken and it was found that LFTs of 80 workers out of 100 were within the normal range whereas 20 workers had abnormally raised level of LFTs. The results of LFTs in serum samples of control subjects were within normal range. The results of RFTs of all the control subjects as well as pesticide industrial workers were within the normal range. Results are summarized in **table no 1,2.**

Renal Function Tests:

Blood Urea Nitrogen

Normal range for BUN in serum is 5 to 18 mg/dl. In current study, mean BUN value for 100 control subjects was 8.37 mg/dl ± 1.74 **(Table 1)**. Regarding 100 pesticide industrial workers mean BUN value was 12.70 mg/dl with SD ± 2.28 and 95% confidence interval of 8.15 to 17.25. The aforesaid mean BUN value was within normal range but slightly on the higher side. Out of above 100 pesticide industrial workers, 80 workers (having normal LFT's level) had mean BUN level of 12.77 mg/dl, ± 2.31 which was slightly on the higher side as compared to control workers group **(Table 2)**. Mean BUN value for rest of 20 pesticide industry workers (having abnormal LFT's level) was 12.40 mg/dl ± 2.16 **(Table 2)**. P value was significant on comparison of control group with both pesticide industrial workers group having normal and abnormal LFT's **(Table 2)**. On the other hand P value was not significant on comparison of both pesticide industrial workers group having normal and abnormal LFT's.

Serum Creatinine

Normal values of Cr are 0.5 to 1.3 mg/dl. In current study, serum of 100 control subjects indicated mean Serum Creatinine value of 0.65 mg/dl ± 0.15 **(Table 1)**. Mean Serum Creatinine value for 100 pesticide industrial workers was 0.98 mg/dl ±0.13 with SD ± 0.98 and 95% confidence interval of 0.73 to 1.25, which was within normal range but on the higher side. Out of 100 pesticides industrial workers mean Serum Creatinine level for 80 workers (having normal LFT's level) was 0.96 mg/dl ± 0.11 i.e. within normal limits **(Table 2)**. Mean Serum Creatinine value for rest of 20 industrial workers (having abnormal LFT's level) was 1.06 mg/dl ± 0.15 **(Table 2)**. P value was significant on comparison of control group with both pesticide industrial workers group having normal and abnormal LFT's.

Discussion

The present study was carried out to evaluate the impact of exposure to pesticides on LFT's and RFT's among workers of pesticides industry. It was observed that the entire control group had LFT's

Table-1: Pesticide industrial workers having normal and abnormal LFT's jointly.

RFT's	Control Subjects (n=100)			Pesticide industrial workers (n=100)		
	Mean	±SD	C.I 95%	Mean	±SD	C.I 95%
BUN (mg/dl)	8.37	1.74	802 - 8.71	12.7	2.28	8.15 - 17.25
S.Cr (mg/dl)	0.65	0.15	0.63 - 0.68	0.13	0.13	0.73 - 1.25

Table-2(a): Pesticide industrial workers having normal LFT's(n=80).

RFT's	Control Subjects (n=100)		Pesticide industrial workers		
	Mean	±SD	Mean±SD	C.I 95%	P value
BUN (mg/dl)	8.37	1.74	12.71± 231	3.08-4.99	P<0.00
S.Cr (mg/dl)	0.65	0.15	0.96 ± 0.11	0.27-0.33	P<0.00

Table-2(b): Pesticide industrial workers having abnormal LFT's(n=20).

BUN (mg/dl)	8.37	1.74	12.4± 2.16	3.15-4.91	P<0.00
S.Cr (mg/dl)	0.65	0.15	1.06± 0.15	0.10-0.71	P<0.00

And RFT's not only within normal limits but also on the lower side of normal levels. Out of 100 pesticide industry workers, blood samples of 80 workers showed normal level of LFT's and RFT's, however, slightly on the higher side except GGT which was slightly on the lower side as compared to control subjects. Other 20 pesticide industry workers had raised levels of ALP, ALT and AST whereas GGT level was slightly on the lower side but within normal range and the other tests i.e., TBil, DBil and RFT's were within normal range but close to upper limits of normal levels. High ALP level in serum has also been reported by previous researchers such as Srivastave et. al. (1991),[9] Paulino et. al. (1996),[10] Srivastava and Malik (2000),[11] Mani et. al. (2001),[12] Altuntas et. al. (2002),[13] and Kaur and Dhanju (2004)[14] in personnel involved in spraying. High level of ALT and AST has also been noted in the serum of the persons exposed to pesticides by different research scientists; Misra et. al. (1985),[15] Carvalho (1991),[16] Kossmann and Magner (1992),[17] Katoh et. al. (1998),[18] Kacker et. al. (1999),[19] Venkaterswarlu et. al. (2000),[20] El-Sakka et. al. (2002),[21] Sahin et. al. (2002),[22] Rahman and Siddiqui (2003),[23] Choudary et. al. (2003),[24] Kaur and Dhanju (2004).[14] In Pakistan, studies have been conducted by Naqvi et. al. (2007)[8] at Karachi and they reported that there was significant increase in the liver enzyme levels in the persons exposed to pesticides and they complained about liver and kidney dysfunction and respiratory tract infection. Also target persons of above research work were the males/females involved in spraying of pesticides in the field. However, the complaints reported by spraying personnel were more than the complaints from the workers of current study. This is probably due to higher exposure of the farmers and spraying personnel to pesticides, as pesticides become more volatile with addition of water. High level of GGT was not observed in any pesticide industry worker. In current study low level of GGT in serum of pesticide industry workers as compared to control subjects was noted. However, GGT level was within the normal range. This Lower Level of GGT probably showed that these workers were exposed directly to the pesticides. Above results are in conformity with the findings of Enan et. al. (1992)[25], Garcia and Mourelle (1984)[26] and Ranjbar et. al. (2002)[27] who reported low level of GGT in various persons exposed to different pesticides or involved in pesticide spraying. TBil and DBil in both groups were not only within the normal range but were also comparatively close to upper normal limit in pesticide industrial workers. High Bilirubin level after exposure to pesticides has also been reported in previous studies by Queoraz ML et. al. (1998)[28], Kacker R et. al. (1999)[19], Azmi et. al. (2005).[4] RFTs i.e., BUN and Creatinine of all the 100 pesticides workers were found to be within normal range but on the higher side as compared to control subjects. It was also observed that in chronic exposure there was no significant change but acute severe exposure led to acute renal failure, as was reported in a case in Turkey following unintentional DDT ingestion, where the patient developed severe metabolic acidosis and acute renal failure.[7]

Conclusion

Pesticide exposure among workers of pesticide plants might cause liver toxicity.

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Answer Picture Quiz

Impetigo

Diagnostic features are:

- Its apparently epidemic character in many cases.
- The antecedent febrile condition.
- Its attacking children.
- The origin from isolated vesicles which tend to enlarge into blebs and to become pustular, the blebs having a depressed centre, and it may be a well-defined, slightly raised, rounded edge.
- The isolation of the spots; the uniform character of the eruption & its general and scattered condition.
- Its frequent seat and commencement about the face or head.
- The circular, flat, granular, yellow crusts looking as if stuck on.
- Its contagious nature and inoculability.
- Its frequently following in the wake of vaccination.
- The absence of pain, and especially troublesome itching at night.

Original Article

Maternal Morbidity and Associated Fetomaternal Outcomes in Women With Twin Pregnanies

Afshan Ambreen, Samina Khurshid, Misbah Khurshid and Amna Fatima

Objective: Multiple pregnancies still warrants special attention as it is associated with increasing risk for mother and fetus. Preterm delivery increases the risk for baby. This study was conducted to evaluate the risks of pregnancy complications and associated fetal and maternal outcome in women with twin pregnancies.

Material and Methods: It was one year observational study from 1st January 2012 till 31st December, 2012 at department of obstetrics and gynecology Fatima Memorial Hospital, Lahore. All women admitted to the labour ward with twin pregnancies after 28weeks of gestation were included in the study. Main outcome measures were maternal complications (i.e., anaemia, preterm labour, pregnancy induced hypertension, postpartum hemorrhage etc)and perinatal morbidity and mortality. All data collected was analysed using SPSS-16.

Results: Majority of women 78(78%) were unbooked and only 22(22%) were booked, 56(56%) women presented with preterm labor, anemia was found in 72(72%) patients and hypertension in 33(33%) patients. Majority presented between 30-35weeks gestation and 30(30%) patients delivered at 36weeks and above. The most common cause of neonatal death was very low birth weight followed by sepsis and jaundice.

Conclusion: Multiple pregnancies are associated with increasing risk for the mother and fetus. Preterm delivery increases the risk for baby.

Key words: twin pregnancy, maternnal & child health care, postpartum complications..

Introduction

Multiple pregnancies are no longer a rare event, mostly due to widespread use of assisted reproductive techniques. Incidence of twin pregnancy is 2-3% of all live births; 30-60% of twins are born prematurely, this account for 7-12% of all deliveries, and 85% of all perinatal morbidity and mortality. Delivery before 37wks in singleton pregnancies occurs in 1-11% and the prematurity rate is between 8-10%.[1] Multiple pregnancies are associated with increased risk for the mother and fetus. A national study described major complication for twin pregnancy as preterm labour (84%), premature rupture of membranes (PROM) (84%), anemia (5-6%), pregnancy induced hypertension (31.2%), abruption placentae (6.2%) and post partum hemorrhage (12.5%).[2] The national study described that about half of twins were born with a birth weight of <2500grams.The most common cause of neonatal death was low birth weight(32.8%)followed by sepsis and jaundice. However the chances of survival for very small twin babies are higher than for very small singleton babies. Neonatal death due to very low birth weight was 32.8% for twin-1 and 34.4% for twin-2.Spontaneous vaginal delivery was more common for twin-1 (50%), for twin-2 it was 35%.LSCS rate was 43.6% while for twin-1and46.9% for twin-2[2]. Women with twin pregnancy had a higher incidence of GDM (3.98%) when compared with singleton pregnancies (2.32%).[3] The impact of monitoring relies on use of effective and timely intervention so that the problem must be avoided.[4] Birth weight and gestational age are important factors affecting perinatal morbidity and are most significant determinants of infant and childbirth morbidity. Close antenatal and intrapartum care are needed in order to improve outcome and decrease complications.[5]

Although considerable amount of literature already exists regarding twin pregnancies and associated outcomes, the incidence of twin pregnancy has greatly risen over past few years owing to the development and advancement in the assisted reproductive techniques with large proportion of infertile couples resorting to them. Thus reevaluating these patients may add more to existing knowledge. Also, with a very well equipped neonatal care unit at Fatima Memorial Hospital, we receive a lot of patients with twin pregnancies as routine due to risk of prematurity and subsequent requirement of neonatal care services from the periphery.

So with this large proportion of twin gestations presenting to us and an effective clinic for infertile couples; both males and females, I am interested to gain deeper insight into the issues related to twin pregnancies both to mothers and babies with a view to identify areas of critical care.

Objective

Determine maternal morbidity and associated maternal and fetal outcome in subjects with twin pregnancy.

Material And Methods

It is a cross-sectional descriptive study. It is conducted in the department of obstetrics and gynaecology, Fatima Memorial Hospital, Lahore. Non Probability purposive sampling was done. Subjects with twin pregnancy>28weeks (gestational age as confirmed by LMP & Dating) scan were included.100 women with twin pregnancy admitted through OPD and emergency were included in this study. An informed consent for using their data in research was obtained. History was taken from patients regarding age, parity, duration of gestation, and any associated risk factors. Examination and investigations were performed. Mode of delivery, Gestational age at the time of delivery and fetal outcome were noted. All this information was recorded on pre-designed Performa. The collected data was entered in SPSS version 16.0 and analyzed through its statistical package.

Results

A total of 6,645 patients were delivered during the study period out of which 100 women presented with twin pregnancy. Majority of the women belonged to age group 25-35 years, Most of the women were unbooked and only 25 (25%) was booked. Frequency of twin pregnancy wse 26% in primigravida, 24% in multi gravida and 50% in grand multigravida, Major maternal complications were preterm labor, anemia, premature rupture of membranes, PIH and post partum hemmoerhage. Antenatal steroids were given to all patients threatening to deliver prior to 34 weeks gestation. Mode of delivery was spontaneous, vertex vaginal delivery in 35% cases, while cessarian section was done in 65% of cases. When perinatal outcome was analysed, prematurity was the ,major problem in patients with twin pregnancy, 85% presented between 28-35 weeks of gestation. 15% came in labor at 36 weeks or above. 30% twin I had birth

Table-1: Distribution of age, parity etc.

Age distribution	"n"	"%"
20-25	20	20%
26-30	30	30%
31-35	36	36%
>35	14	14%
Parity		
Para 1	26	26%
2-4	14	14%
4-5	10	36%
5 and above	50	50%
Maternal Morbidity		
Anemia	28	28%
Pre term labor	20	20%
Premature rupture of membranes	14	14%
PIH	15	15%
GDM	9	9%
Placental abruption	5	4%
PPH	10	10%
Mode of Delivery		
SVD	35	35%
LSCS	65	65%
Gestational age at the time of delivery (in weeks)		
28-32	40	40%
33-35	45	45%
36 and above	15	15%
Fetal Morbidity		
Low birth weight	32	23%
Sepsis	29	29%
Jaundice	27	27%
RDS	12	12%
Perinatal Mortality		
TWIN I	36	36%
TWIN II	42	42%

weight between 1500-2500 grams and among twin II, 70% had birth weight between 1500-2500grams. Neonatal death due to very low birth weight was 36% for twin I and 42% for twin II, sepsis and jaundice were the commonest causes for neonatal death.

Discussion

Twin pregnancy is a high risk pregnancy associated with increased maternal morbidity and increased perinatal morbidity and mortality.[6] The incidence of twin pregnancy varies throughout the world. Most of the women were found in the age group between 31-40 years which shows that incidence of twin pregnancy is higher in older age group. Similar observation was found in the study conducted by Malik MS et al, Lahore.[7] Most studies have found that the incidence of twin pregnancy increased with advance maternal age uptil 35 years after which the rate declines.[8,9] Most of the women presented with preterm labor at less than 36 weeks and 15% were at gestational age of more than 36 weeks. Mean gestational age was 39 weeks in singletons, 35.8 weeks in twins and 32.5 weeks in triplets.[10] In the present study, most of the patients belong to parity 5 or above. Similar results were found in the study by Malik MS et al.[7] Most of the women were unbooked. (75%) only 25% were booked The same frequency of unbooked cases was found in the study conducted by Naqvi MM in 2003 where among 96% cases 65% patients were unbooked. During the antenatal period, anemia, preterm labor, PIH and abruption placentae were the major complicating factors. Same as in the study done by Anemia was the most common complication.[12]

Conclusion

Multiple pregnancies are associated with increased maternal and perinatal risk. There is a need for specialized pre natal care to reduce the complications and adverse outcomes in multiple pregnancies and the need for on going social and medical care beyond the pre natal and perinatal periods.

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Original Article

THE EFFICASY OF SUBMUCUS RESECTION OF HYPERTROPHIED INFERIOR TURBINATE IN NASAL OBSTRUCTION

Nadeem Raza, Muhammad Yousaf Saleemi, Muhammad Dawood Saleem, Ghulam Murtaza and Muhammad Tariq

Objective: To analyze the efficacy of submucous resection of inferior turbinate for symptomatic relief of nasal obstruction.

Material and Methods: Sixty (60) patients were included in the study who had inferior turbinal hypertrophy. All the patients had history of failed medical treatment. Follow up was carried out for one year for bleeding, synechie formation, nasal crusting and nasal obstruction.

Results: Submucus Resection of hypertrophied symptomatic inferior turbinate is an effective surgical procedure with minimal intraoperative and post operative complications and significant improvement in nasal patency.

Conclusion: Submucous resection of the hyper trophied symptomatic inferior turbinate is a very good surgical opetion for its turbinal reduction. Bleeding per-operative and post-operative is less in amount. Due to reduced chances of bone exposure bone necrosis, crusting and foul odour are minimal. As mucosal injury is not produced neither during surgery nor during packing, so minimal chances of adhesion formation. Removal of erectile submucosal tissue is precise and under direct vision so good satisfactory nasal airway patency. We recommend use of microdebrider assisted turbinoplasty for relief of nasal obstruction due to hypertrophic inferior turbinate.

Key words: nasal obstruction, rhinitis, inferior turbinal hypertrophy, submucous resection of inferior turbinate.

Introduction

Nasal obstruction is the most common complaint in an average rhinologic practice.[1] It has been estimated that as many as one third of the population has some nasal obstruction and as many as one quarter of these patients pursue surgical treatment.[2] When assessing individual symptoms of chronic rhino-sinusitis, nasal obstruction often ranks highest in patient-reported symptom severity.[3] The role of inferior turbinate pathology in the reduction of nasal airflow is well known.[4]

The main etiologies for nasal obstruction are septal deviation, hypertrophy of inferior and middle turbinate, nasal polyposis and hypertrophy of nasopharyngeal tonsils.[5] Among these etiologies, the inferior turbinal hypertrophy is the main cause of nasal obstruction.[6] Allergic rhinitis, vasomotor rhinitis and compensatory hypertrophy of inferior turbinate on the concave side of septal deviation figure as the main causes of inferior turbinate hypertrophy.[7] The nasal passages are complex structures that serve several functions like filtration, humidification, heating, olfaction and voice resonance. Humidification, filtration and heating (air conditioning) are greatly aided by turbinates. The inferior turbinate is a separate bony structure covered with nasal mucosa. Embryologically it develops from an endonasal prominence called maxilloturbinal prominence. Histologically, the inferior turbinate is composed of three layers, medial and lateral mucosal layers and central osseous layer. The thickness of medial layer is more than lateral layer, due to increased thickness of lamina propria. In the lamina propria lie venous sinusoids, seromucinous glands and immunocompetent cells. The venous sinusoids get engorged or constricted according to extent of vasodilatation or vasoconstriction in the veins and arteriovenous anastomosis. These vascular structures are constantly under the influence of autonomic nervous system. Chemical or microbial irritation leads to inflammatory response i.e activation of mast cells, basophils and other leukocytes, release of cytokines, chemokines and other chemical mediators. This leads to swelling of turbinates, primarily in the lamina propria where venous sinusoids reside. Enlargement of inferior turbinate is mainly due to swelling of the submucosa and rarely due to enlargement of the bone. This hypertrophy of inferior turbinate caused by dilatation of submucosal venous sinusoids is the cause in intrinsic rhinitis and responds to decongestants.[8]

Sometimes inferior turbinal enlargement is due to submucosal fibrosis. This does not respond to decongestants.[9]

In a few cases of inferior turbinal hypertrophy, the venous sinusoids become atonic and also do not respond to decongestants.[10] Internal nasal valve is the area of greatest nasal resistance. It is formed medially by nasal septum, inferiorly nasal floor and laterally by lower edge of upper lateral cartilage and anterior end of inferior turbinate. This valve is a dynamic valve, as swelling of the venous erectile tissue of the inferior turbinate and nasal septum can cause complete nasal obstruction.

Medical management of inferior turbinal hypertrophy includes antihistamines, sympatho mimetics, anticholinergics and steroids. These medications provide symptomatic relief but no permanent cure. When optimal medical management has been unsatisfactory in the relief of nasal obstruction, surgical intervention is warranted. The goals of surgical reduction of inferior turbinal hypertrophy are to maximize the nasal airway, preserve mucosal function and to minimize complications with reduction of submucosal and bony tissue.[11] Inferior turbinate reduction can be performed by various techniques that resect, displace or decrease the volume of the turbinate. Techniques of turbinate reduction include turbinectomy,[12] submucous turbinectomy,[13] inferior turbinoplasty,[14] Cryotherapy,[15] submucous electrosurgery[16] CO_2 laser turbinplasty.[17] No technique is perfect and each is associated with known short term and long term complications.[18] Inferior turbinate reduction with microdebrider offers advantages over other traditional techniques with regard to mucosal preservation, bleeding, crusting and other complications. We prospectively studied the efficacy of submucous resection of hypertrophoid inferior turbinate (Submucous Turbinectomy) on alleviating nasal obstruction and other complications.

Materials and Methods

A prospective study was performed in sixty patients who complained of nasal obstruction due to inferior turbinal hypertrophy. Inferior turbinal hypertrophy was graded I to III.

Grade -I: Mild enlargement, no obvious nasal obstru- ction.

Grade-II: Moderate enlargement, nasal obstruction.

Grade-III: Complete occlusion of nasal cavity, severe nasal obstruction.

A total of Sixty patients, between ages 18-50 with symptoms of moderate and severe nasal obstruction due to inferior turbinal hypertrophy in grade II & grade III, who were symptomatic on optional medical management were studied.

All patients were evaluated before surgery and after surgery. The patients were followed up to 1 year for assessment of symptoms, need for further medical and surgical intervention, post operative complications & influence of symptom relief on quality of life.

Surgical Technique

All cases were operated under general anesthesia with endotracheal intubation and throat pack. First 0.05% xylometazoline spray was done in the nasal cavity and then 0.05% xylometazoline soaked strip gauze was inserted into the nasal cavity. 2% xylocaine with 1: 200,000 adrenaline was injected in the submucosal plane after diluting it twice with 0.9% normal saline. After 05 minutes with number 15 blade a small incision was made on anterior (head) part of the inferior turbinate and a submucosal tunnel was made with sharp dissection on medial surface of the turbinate, then after elevating the mucosal flap from the bone of Inferior Turbinate from its medial, superior and inferior side, infracture was done with freer's elevator. Then with Takahashi's forceps bone was removed. Particular attention was paid to the safety of medial surface of the mucosal flap. Then lateralization of the turbinate was done with long nasal speculum.

Haemostasis was achieved with electrocautery if necessary. Incision was not stitched. Reduction in size was obvious. After operation nose was packed with glove finger packing which was removed after 24 hours. Post operatively antibiotics, analgesics and saline irrigation was advised for one week. Follow-up was done weekly for four weeks then fortnightly for four weeks then after every two months for one year. Complications like bleeding, crusting, foul odour, nasal obstruction and synechie formation were recorded.

Results

A total of Sixty patients, 27 Females and 33 males between ages 18-50 with symptoms of moderate and severe nasal obstruction due to inferior turbinal hypertrophy in grade II & grade III, who were symptomatic on optional medical management. 22 patients had unilateral and 38 patients had bilateral turbinoplasty. If necessary, septoplasty was done too. Follow-up was for 12 months. The main symptoms before the operation were nasal obstruction in 60 patients (100%), anterior nasal discharge in 40 patients (67%), post nasal drip in 28 patients (47%). After one year of post operative follow up 45 Patients (75%) reported satisfactory results

regarding nasal obstruction while 15 patients (25%) had mild degree of nasal obstruction. 38 patients (38%) had some degree of post operative complications in the form of mild nasal dryness in 13 patients, post nasal drip in 5 patients. Nasal crusting & foul odour was not complained by any patient. 5 patients had nasal synechia which were lysed.

Discussion

Inferior turbinate hypertrophy is one of the most common causes of nasal obstruction. When proper medical treatment, sympathomimetics (local & systemic), antihistamine (local & systemic), steroids (local & systemic) and saline nasal irrigation for prolonged period have failed in relieving the symptoms then surgical treatment for reduction in size of inferior turbinate is indicated. Numerous reports substantiate the usefulness of inferior turbinate surgery.[19] The ideal turbinal surgery is limited to the erectile submucosal tissue and the bony turbinate. Reduction of bone produces enough space while removal of submucosal tissue produces scarring and fibrosis which minimizes engorgement of the inferior turbinate in patients of intrinsic rhinitis. Mucosal preservation maintains air conditioning function of the inferior turbinate and also reduces crust formation. More than ten surgical techniques have been used to treat hypertrophy of the inferior turbinate but there is no completely effective treatment. However all of the techniques performed for turbinate reduction have potential of complications that fall into several categories.[20]

Surgical treatment for hypertrophied inferior turbinates includes techniques that resect partially or completely, displace it laterally or reduce its volume. One method is lateral outfracture, involves fracturing the insertion of the inferior turbinate at its attachment to the lateral nasal wall and then forcing it laterally with nasal speculum and nasal packing. This gives temporary relief as turbinate resumes its position eventually.[21] Electrocautery is used in two ways; either we do submucosal diathermy or superficial mucosal diathermy. Each results in fibrosis and reduction in size of the turbinate but significant risk includes necrosis of the turbinate bone, sequestrum formation, crusting and foul odour. More over this method is not effective in managing posterior end of hypertrophied inferior turbinate.[22]

Cryosurgery (cryoturbinectomy) can be used easily under local anesthesia in outpatient setting. It involves the application of a cryoprobe to the mucosal surface of the turbinate and freezing at -85 C° for 6075 seconds.[23] This affects more on goblet cells so reduces rhinorrhea, however results are temporary and variable, thus requires repeated applications.[24] Carbon Dioxide (CO_2) or Diode Laser turbinate reduction can also be performed under local anesthesia. This procedure results in little blood loss and post operative discomfort.[24] Disadvantage is eschar formation which can cause nasal obstruction or rarely haemorrhage with sloughing of eschar.[25] However this is not effective for bony hypertrophy. Another disadvantage is that equipment is expensive and requires additional expertise, training and safety precautions. Resection of the inferior turbinate partial or complete, although no longer widely performed, is still considered an option in turbinate reduction surgery. This results in increase in volume of the nasal airway and diameter of the nasal valve. This increase occurs at the expense of nasal physiology with decreased humidifying activity of the nasal mucosa, excess drying of nasal secretions and resultant crusting.[26] Therefore complication rate of bleeding, synechie formation and empty nose syndrome is high.[27] Another technique presently in use is radio frequency volumetric tissue reduction (RFVTR). Radio frequency heat is used to induce submucosal tissue destruction. The device, an electrode probe induces ionic agitation at the cellular level, heats the turbinate tissue with little heat dissipation. Thermal injury only extends 2-4 mm around the active portion of the electrode, thus only within deep mucosa, thus sparing damage to mucosal surface. The area of injury is replaced with scar producing fibroblasts. Scar contraction leads to reduction of turbinate volume and relief of nasal obstruction. The ideal turbinate surgery is limited to the erectile submucosal tissue and to the bony turbinate. The endoscopic approach to inferior turbinectomy provides complete visualization of the operating field, thus reduces risk of excessive or inadequate resection. Preservation of mucosal surface and debulking of the turbinal tissue is the main goal of surgery. Microdebrider only removes thick, erectile, vascular tissue of the turbinate and hypertrophic bony part, in a short time with minimal blood loss. Intra-operative and post-operative blood loss is minimal.[28] Per-operative bleeding site can be visualized and electrocoagulated with uni-polar cautery. Residual erectile tissue can be visualized and debrided. Post-operative packing with glove finger reduces mucosal damage and reduces adhesion formation. Bone exposure leads to crusting, foul Odour which is minimal in microdebrider assisted turbinoplasty.

Conclusion

Submucous Resection of the Hyper trophied Symptomatic Inferior Turbinate is a very good surgical opetion for its turbinal reduction. Bleeding per-operative and post-operative is less in amount. Due to reduced chances of bone exposure bone necrosis, crusting and foul odour are minimal. As mucosal injury is less than partial or complete resection of the turbinate, so less chances of adhesion formation. Removal of erectile submucosal tissue is precise and under direct vision so good satisfactory nasal airway patency. We recommend use of Submucous Resection of turbinate (Turbinoplasty) for relief of nasal obstruction due to hypertrophic inferior turbinate.

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Case Series

EWING'S SARCOMA CHEST

Nasir Iqbal, Javed Shakir and Saba Tahir Bokkhari

Abstract: The aim of this review article was to highlight clinical presentations, diagnosis and treatment approaches of thoracic cavity Ewing's sarcoma. This was a prospective study. Ewing's sarcoma is the second most frequent bone tumour among children and young adults. It comprises 10-15% of all bone tumours. Ewing's sarcoma arises intramedullary. The frequency of rib involvement follows that of the femur, the pelvic bones, the fibula, the humerus and the tibia.
Between January 1999 and December 2005, 5 patients of Ewing s sarcoma chest were dealt with. The age range was 6-12 years.
All the 5 patients had huge masses compressing the lung and other vital structures in the chest. One patient was on ventilatory support preoperatively. Thoracotomy was done in 3 patients prior to chemotherapy and later on after chemotherapy in 2 patients. Post operative stay range was 7-15 days. No hospital mortality occurred.
This article demonstrates the most effective and immediate treatment in case of Ewing's sarcoma chest. The three cases that had to be operated urgently before the chemotherapy survived and received chemo-radiation later on thus signifying the importance of timely and proper surgery. Referral to proper hospital is mandatory who cater these kinds of cases.
Key words: ewing sarcoma, thoracotomy.

Introduction

Ewing's sarcoma is named for James Ewing (1866-1943), the American pathologist who first described it.[4,5] It is a malignant tumour composed of small round cells. It originates in the bone and is characterized by the translocation of chromosomes 11 and 22. Approximately 15% of all cases of Ewing's sarcoma arise in the chest wall, most frequently from a rib (less often from the scapula).[2,6,7,8] The peak incidence occurs between the ages of 10 and 15 years.

There is a slight male: female preponderance (1.6:1). Clinical presentation includes pain and swelling of weeks or months duration.[1] Micro-metastatic disease is present in many at the time of diagnosis that can't always be seen on the CT & bone scans or bone marrow tests.

The general radiological appearance is a mass in the chest wall accompanied by destruction of the bone. Ewing's sarcoma is rarely extra osseous.[10]

Although bone involvement is an important characteristic, the soft tissue components may be much more extensive than the bony component.

Usually the Ewing's sarcoma is treated initially with chemotherapy, followed by surgical resection with or without radiation therapy. This malignant tumour is associated with a high rate of metastasis (75% of cases) and local recurrence. The overall 5 year survival rate is 50%.[9,11,12]

Materials and Methods

There were five patients of Ewing's sarcoma initially diagnosed by needle biopsy between January 1999 and December 2005, who were treated. All the patients presented with chest pain, shortness of breath and in one patient there was obvious external swelling on the chest wall. There were two females and three males.

The age range was 6-12 years. Three patients had to be operated immediately after the percutaneous biopsy as the respiratory distress was increasing. Two were operated after the initial chemotherapy.

Results

All the five patients had huge masses in the chest cavity compressing the lung and other vital structures. One patient was on ventilatory support preoperatively. Thoracotomy for excision of mass and the involved rib was done in all the cases. In three patients who underwent surgery prior to chemotherapy treatment had their chemotherapy treatment later on. In one patient there was recurrence after 6 months. For which Thoracotomy for excision of mass and adjacent rib excision was repeated. This patient also had additional radiotherapy treatment to the chest wall.

The post operative stay range was 7-15 days. There were no complications. No hospital morality occurred.

Discussion

Chest wall tumours of primitive neuroectodermal origin (PNET, Ewing's sarcoma) are rare and have a poor prognosis. Multimodality therapy has improved survival results, and long-term survival is possible. Evidence suggests that roughly 75% of the patients with Ewing's sarcoma present with localized disease. For those who present with metastatic disease the cure rate is 20 to 30 percent. The metastatic disease is to the lungs, bone and bone marrow.

Complete resection of the primary tumour of the chest wall is accomplished more frequently in resections performed after initial adjuvant chemotherapy compared with primary resections. Although thoracic tumours are frequently large and primary resection is often attempted.

In our study we had to do primary resection in three cases as they were having acute respiratory distress after the percutaneous biopsy from the chest. It was probably due to the bleeding in the large tumours after the biopsy, which was later confirmed at the time of thoracotomy.

Delayed resection resulted in a significant decrease in the proportion of patients requiring radiation therapy to the chest. Radiation therapy has been associated with the significant incidence of secondary tumours, pulmonary fibrosis and cardiomyopathy in these patients. Evaluation of the primary and metastatic sites is performed approximately every 10-12 weeks while on chemotherapy and at 3 to 4 months intervals during the first year following the completion of therapy.

Reevaluations are spaced to gradually or 5-6 years following the completion of therapy. Recurrence of primary disease is the major risk in the first 10 years from the time of diagnosis. Minimally invasive surgery has a role in planning the resection of malignant chest wall tumours in the pediatric population.[13,3]

Conclusion

This article demonstrates the most effective and immediate treatment in case of Ewing's sarcoma chest.

The three cases that had to be operated urgently before the chemotherapy survived and received chemo-radiation later on thus signifying the importance of timely and proper surgery. Referral to proper hospital is mandatory who cater these kinds of cases.

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C.M.E. Article

Normal Findings Mimicking Fractures

Apophysis

The greater and lesser trochanters are apophyses which fuse at 15-20 years of age

Lack of Fusion

Hyoid Bone fuse later in life usually by age 40; it is therefore common to see and unfused hyoid

Mach Line

"Mach Lines" are optical illusions which produce a black line where none exists; they are common at the base of the dens

Accessory Epiphyses

In a child, when in doubt, think of obtaining the opposite side for comparison

Synchondroses

3 main temporary joints in pelvis: ilio-pubic, ischio-pubic and ilio-ischial; bilateral and usually symmetric

Costovertebral Junction

Every rib attaches to the spine at the costo-vertebral junction; not to be confused with a fracture

Accessory Ossicle

Os Acetabuli Marginalis Superior
Normal variant
May be bilateral

Multiple Ossification Centers

The calcaneal apophysis frequently has multiple centers of ossification and appears denser than rest of calcaneous

Sesamoids

There are almost always sesamoids of the thumb; they are well-corticated and smooth-edged, unlike fractures

Accessory Ossicle

Os Trigonum-accessory ossicle just posterior to the talus normally found in 5-15% of people

Accessory Ossicle

Multiple ossification centers are common in epiphyses and are smooth and well-corticated

Apophysis

Apophysis of the 5th MT runs in a longitudinal direction; fractures are usually transverse

Normal Epipphyseal plate

Don't confuse the undulations of the humeral epiphyseal plate for a fracture

Bipartite Patella

Bipartite patella almost always affects the upper outer pole of patella; 57% are bilateral

Nutrient Channel (Canal)

Nutrient channels or canals run diagonally only in the cortices of certain bones

Normal Excrescence

Radial spur is normal variant occurring on the lateral aspect of the radius at the site of the physis

Normal Apophysis

The apophysis of the tibial tubercle (tuberosity) fuses at age 14-18 years

Limbus Vertebra

Most commonly affects antero-superior border of single vertebra in lumbar spine

Normal Excresence

This is a normal bony excresence from the scaphoid that can be mistaken for a fracture

Sesamoids

Sesamoids are ossicles embedded in a tendon that aid in movement; they are common in the feet and hands

Author Index

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