

Original Article

EFFICACY OF SYSTEMIC METHOTREXATE IN UNRUPTURED TUBAL PREGNANCY

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Objective: To observe the efficacy of systemic methotrexate for the treatment of unruptured tubal pregnancy.

Material and Methods: It was a descriptive study carried out over a period of 6 months from 01-10-2012 to 31-03-2013 in the department of obstetrics and gynaecology unit III, Services Hospital, Lahore. A total of 65 cases were included in this study. Patients were given single dose of injection methotrexate $50\text{mg}/\text{m}^2$ intramuscularly and β -hCG level was assessed at 4th and 7th day for each patient. In those patients in which β -hCG level did not fall more than 15% on day 4th and 7th were surgically treated by doing laparotomy.

Results: Among 65 patients, age distribution showed 7 patients (10.8%) were less than 20 years of age, 41 patients (63%) were between 20-30 years and 17 patients (26.2%) were between 30-40 years of age. Mean age was 29.7 ± 4.9 years. According to distribution of parity, 17 women (26.2%) were primigravida, 38 women (58.4%) were para 2-4 while 10 women were para 5-7. Out of 65 women, 11 (16.9%) presented at <6 weeks of gestation and 54 (83.1%) at 6-8 weeks of gestational age. Mean gestational age was 6.7 ± 1.9 weeks. Efficacy of methotrexate for the treatment of unruptured tubal pregnancy observed in 44 women (67.7%) in term of fall in β -hCG level > 15%.

Conclusion: Methotrexate is an effective medical management for ectopic pregnancies in a society where tubal conservation is of utmost importance.

Keywords: Unruptured tubal pregnancy, β -hCG, Systemic methotrexate.

Introduction

Ectopic pregnancy is defined as implantation of conceptus at a site other than the uterine cavity. It is a leading cause of early pregnancy related deaths. Fortunately, after the advent of transvaginal ultrasonography and β -hCG tests, the incidence rate of ruptured fallopian tubes and case fatality rates declined.¹

In developing countries, the reported ectopic pregnancy case fatality rate is around 1-3 % (10 times higher than those reported in developed countries).² Early diagnosis gives us possibility to apply the best treatment with fewer complications.³ However, transvaginal ultrasonography and β -hCG tests are not readily available in all government hospitals in developing countries like Pakistan. Hence, ectopic pregnancy continues to be a life threatening and fatal condition, requiring emergency intervention including laparotomy/salpingectomy.⁴

For the treatment of very early stages of ectopic pregnancy, systemic methotrexate should be preferred for its simplicity, low cost and effectiveness. Single dose of systemic methotrexate

$50\text{mg}/\text{m}^2$ with success rate of 81% and open surgery (salpingectomy) are the two best options for the treatment of uncomplicated ectopic pregnancy.⁵

The rationale of my study is to observe the efficacy of systemic methotrexate for the treatment of unruptured tubal pregnancy in our population. It will help in tubal preservation and saving the patients from surgery thereby reducing maternal morbidity and mortality.

Material and Methods

This was a descriptive case study carried out in obstetrics and gynaecology department at Services Institute of Medical Sciences/ Services Hospital, Lahore over a period of 6 months from 01-10-2012 till 31-3-2013. All patients who attended antenatal clinic or admitted through emergency fulfilling inclusion criteria were included in study. Inclusion criteria was women aged 15-40 years, clinically stable with unruptured tubal pregnancy assessed by symptoms and signs, serum β -hCG level was less than 3000 I.U/L and on ultrasonography size of the tubal pregnancy less than 3cm and absent cardiac activity. Patients with contraindication to methotrexate injection like liver and renal dysfunction

Total number of 65 patients fulfilling the inclusion criteria were selected for the study. Patients were admitted and a proforma was filled in for data collection. After informed consent, her biodata (name, age, parity) was noted and detailed history was taken. Those fulfilling the inclusion criteria were given intramuscular single dose of injection methotrexate. Serum β -hCG levels were assessed at 4th and 7th day. Those patients in which β -hCG level did not fall more than 15% on day 4th and 7th were surgically treated by doing laparotomy. SPSS version 11 was used for data analysis. Quantitative variables like patients age, gestational age, parity, and β -hCG levels were presented by mean \pm SD. Qualitative variables like treatment efficacy were presented by calculating frequency and percentage.

Results

During the study period, a total of 65 patients were included. Age distribution showed 7 patients (10.8%) were less than 20 years of age, 41 patients (63%) were between 20 -30 years and 17 patients (26.2%) were between 30-40 years of age. Mean age was 29.7 ± 4.9 years (**Table-1**). According to distribution of parity, 17 women (26.2%) were primigravida, 38 women (58.4%) were para 2 - 4 while 10 women were para 5 - 7 (**Table-2**). Out of 65 women, 11 (16.9%) presented at < 6 weeks of gestation and 54 (83.1%) at 6-8 weeks of gestational age. Mean gestational age was 6.7 ± 1.9 weeks (**Table-3**). Efficacy of methotrexate for the treatment of unruptured tubal pregnancy observed in 44 women (67.7%) in terms of fall in β -hCG level > 15% (**Table-4**).

Table-1: Age distribution of cases (Mean \pm SD= 29.7 ± 4.9).

Age (years)	no	(%)
<20	07	10.8
20 -320	41	63.0
31- 40	17	26.2
Total	65	100.0

Table-2: Distribution of cases parity .

Parity	no	(%)
Primigravida	22	33.9
P2-4	38	58.4
P5-7	05	07.7
Total	65	100.0

Table-3: Distribution of cases by gestational age (Mean \pm SD= 6.7 ± 1.9).

Gastational age	no	(%)
<6	11	16.9
6-8	54	83.1
Total	65	100.0

Table-4: Efficacy in terms of fall in β -hCG level >15% .

Efficacy	no	(%)
Yes	44	67.7
No	21	32.3
Total	65	100.0

Discussion

The prevalence of ectopic pregnancy has increased over the last few years and accounts for 2% of all pregnancies in the United States.⁷ Although this is mostly attributable to the increasing prevalence of fallopian tube diseases. More accurate detection of ectopic pregnancy has been made possible by the association of β -hCG and transvaginal ultrasonography.⁸

Some women have aggressive ectopic pregnancies that are clearly visible on ultrasound; with high β -hCG levels, short amenorrhea duration and accurate clinical courses. However other women have latent ectopic pregnancy with low β -hCG levels, longer time interval since the last menstrual period and present fewer symptoms. In screening for ectopic pregnancy, serial β -hCG measurements are important when the levels are less than 2000 I.U/L and when transvaginal ultrasound is used to rule out intrauterine pregnancy.⁹ Methotrexate is an anti-metabolite that interferes with DNA synthesis by inhibiting the action of *dihydrofolate reductase*. It interrupts the synthesis of purine nucleotide thymidylate. In an earlier study it was reported that when methotrexate was injected locally, the serum concentration changes were lower than those when methotrexate was given intramuscularly. These findings may reflect decreased bioavailability of methotrexate captured directly by target trophoblastic cells leading to high tissue concentrations and better efficacy. Single dose methotrexate appears effective not requiring citrovorum recovery and has better patient compliance. Treatment success is inversely related to β -hCG concentration.¹⁰

In our study, efficacy rate of single dose of methotrexate was 67.7%, in terms of fall in β -hCG level more than 15%. Results of current study are close to the following studies: Dhar et al² reported success rate of 65% for methotrexate treatment for ectopic pregnancy. Another study carried out in 2006 on efficacy of systemic methotrexate for the treatment of unruptured tubal pregnancy was found to be effective in 73.3%. Fletcher et al observed in their study 'the medically treated group', the success rate was 68%.⁶

Conclusion

Methotrexate is an effective management for ectopic pregnancies where tubal conservation is of utmost importance. It offers several benefits over surgical treatment. It is less invasive, less expensive, can be given on an outpatient basis and does not need expertise. Future reproductive expectations are better with higher intrauterine pregnancy rates and lower ectopic pregnancy rates subsequently.

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