

SINGLE DOSE METHOTREXATE IN ECTOPIC PREGNANCY

Saadia Sharif, Ameelia Sadaqat, Shamayela Hanif and Rabia Noor

Objective: To evaluate the efficacy of a single dose of MTX for ectopic pregnancy management.

Material and Methods: 37 patients were carefully selected according to inclusion criteria. β -hCG was done at diagnosis and at day 7. A single IM dose of MTX was given & patients were kept admitted till recovery.

Results: Out of the 37 patients, 5 patients had ruptured ectopic pregnancy in spite of taking MTX. 26 had single dose and had a time of ectopic pregnancy resolution averaging 26.4 days. The remaining 6 patients received an additional dose of MTX with the time resolution of 35 days.

Conclusion: The successful medical management of ectopic pregnancy was seen in 26 patients (81%) in whom β -hCG levels became negative after administration of single MTX.

Key words: MTX, Ectopic Pregnancy, β -hCG

Introduction

Ectopic pregnancy occurs when embryo fails to implant in its physiological location within the uterine cavity. Ectopic pregnancy rate in industrialized countries has considerably increased over the last few decades, especially USA where the incidence of ectopic pregnancy rose from 4.5/1000 pregnancies in 1970 to 19.7/1000 in 1992.¹ Embryos that do not implant in the uterine wall are generally unable to develop normally. In addition an ectopic pregnancy can cause rupture of the organ on which they are implanted typically the fallopian tube. Rupture can result in shock and possibly death.^{2,3,4} Fortunately, the ability to diagnose, monitor and treat ectopic pregnancy reduces the risk of life threatening complications.^{5,6}

Management of ectopic pregnancy follows the following three approaches;

1. Expectant Management
2. Medical Treatment
3. Surgical Treatment

Medical treatment with Methotrexate (MTX) is one of the most important developments in the management of this disorder. This conservative approach to treatment has overcome surgical

treatment in most cases.^{7,8} The two most commonly used protocols for MTX administration are single dose and multiple dose. The overall rate of resolution of ectopic pregnancy is about 90% for both single dose and multiple dose protocols and rates of side effects are almost similar.^{9,10,11} Success is highly correlated with pretreatment β -hCG, as high as 92% with β -hCG < 5000 IU/l and 98% with β -hCG < 1000 IU/l.^{12,13,14}

The purpose of this study was to evaluate the effectiveness of a single dose of MTX for ectopic pregnancy treatment in a sample of patients care fully selected according to strict inclusion criteria.

Material and Methods

All patients admitted to department of Obstetrics and Gynaecology of Fatima Memorial Hospital Lahore with ectopic pregnancy diagnosis between 1st Nov 2005 to 1st April 2007 were included in the study, provided that they fell in the inclusion criteria as mentioned in **Table 1**. All patients gave their informed consent before the start of study and remained admitted till the β -hCG levels started falling.

Table-1: Inclusion and exclusion criteria

Inclusion criteria	Exclusion Criteria
Pregnancy diameter < 4cm	Tubal rupture
Pretreatment serum β -hCG concentration <3000 IU/l	Hemoperitoneum >100ml
Hemochromes, platelets, renal parameters and liver function test in normal range	Pregnancy Diameter >4cm
Hemodynamically stable	Breast feeding
	Immuno deficiency
	Active pulmonary disease

The risk factors, parity and clinical features are given in **Table 2, 3** and **4**.

On admission β -hCG, complete blood examination, urinalysis, RPM, LFTS, blood group and Rhesus factor were performed for all patients. After investigations, administration of MTX intra muscularly in a single dose of 50mg/m² was given. β -hCG was repeated on day 7. If the β -hCG level on day 7 was at least 25% lower than that on day 0, the patients were followed up for further decline in β -hCG. If the β -hCG on day 7 was the same or higher than day 0, the patients received a second 50 mg/m² dose of MTX. Follow up β -hCG levels were performed weekly until they were negative (5 IU/l). Single dose MTX was considered successful when β -hCG levels decreased until they became negative following the administration of one or more MTX doses. The side effects of MTX were also evaluated. Finally, the time to ectopic pregnancy resolution was also evaluated which was defined as the total number of days from the administration of MTX until β -hCG became negative.

Table-2: Risk Factors (n=37)

Risk Factors	Number of Patients
Intrauterine copper device	1
Previous abdominal/pelvic surgery	6
Previous tubal surgery	0
History of IVF	0
Previous history of ectopic pregnancy	4
Pelvic inflammatory disease	5
Previous history of D & C	7

Table-3: Parity (n=37)

Parity	Number of Patients
Primipara	13
Nullipara	07
Multipara	14
Grand multipara	03

Table-4: Gestational Age at Diagnosis (n = 37)

4 - 6 weeks	6- 8 weeks	> 8 weeks
14	16	07

Table-5: Mean β -hCG level at diagnosis & Day 7(n = 37).

	Mean β -hCG levels IU/l	Range
Diagnosis	10122	385 – 93186
Day 7	2893	112 – 11038

Table-6: Treatment Features (n = 37).

No. of Pts.	MTX doses	Resolution (days)
26	01	26.4
06	02	35

Table-7: Side Effects (n = 37)

Side Effects	Number of Patients
Abdominal pain	18
Nausea, Vomiting	09
Fatigue	04
Skin sensitivity	0
Sore mouth	0
Hair loss	0
Low blood counts	0
Pneumonitis	0

Results

During this period, 37 patients with ectopic pregnancy, matching the inclusion criteria were treated with MTX. The parity is summarized in Table 3. Mean gestational age at diagnosis of ectopic pregnancy was 12.3 days. In all patients, ultrasound imaging suggested ectopic pregnancy with an average pregnancy diameter smaller than or equal to 4 cm. A yolk sac was visible in 9 cases. No embryonic cardiac activity was detected in included patients. Mean β -hCG levels at diagnosis and at day 7 are given in **table 5**.

On day 4 β -hCG was not taken as it is supposed that elevated levels will be present as a result of break down of trophoblastic tissue. Out of 37 patients 5 (13%) had ruptured ectopic; out of 32 remaining patients 6 (18%) received a second dose and time of resolution was about 35 days.

The medical treatment with a single dose was successful in 26 (81%) patients being defined as a decrease in β -hCG levels until they became negative without additional MTX doses and without surgery. All the patients remained admitted and 18 had lower abdominal pain occurring 2 days after treatment. The

pain regressed without surgery or any other treatment. No patient developed rash or GIT symptoms.

Discussion

The success rate with single dose MTX was about 89% in a review of previously published studies. Single dose appears to be as effective as multi dose regimen with additional advantage of requiring less MTX and hence less side effects.

This study provides further evidence in favor of single dose MTX; more over the success rate is 81%. This might be explained by low average serum concentration of β -hCG. In addition the cardiac

activity which is thought to be a factor for failure of therapy was excluded in this study. The single most important factor responsible for the success is low concentration of β -hCG as success is inversely proportional to β -hCG concentration. In addition the help of modern diagnostics such as more rapid and sensitive β -hCG and transvaginal ultrasound, early diagnosis is possible today.

*Department of Obstetrics and Gynaecology
Fatima Memorial Hospital Lahore*

theesculapio@hotmail.com

www.sims.edu.pk/esculapio.html

References

- 1 From the Centers for Disease Control and Prevention. Ectopic Pregnancy-United States, 1990-1992. JAMA 1995; 273:533-3.
- 2 Potter MB, Lepine LA, Jameison DJ. Predictors of success with methotrexate treatment of tubal pregnancy at Grady Memorial Hospital. Am J Obstet Gynecol 2003; 188:1192-4.
- 3 Lipscomb GH, Stovall TG, Ling FW. Non surgical treatment of ectopic pregnancy. N Engl J Med 2000; 343:1325-9.
- 4 Yao M, Tulandi T. Current status of surgical and non-surgical treatment of ectopic pregnancy. Fertil Steril 1997; 67:421-33.
- 5 Gamzu R, Almog B, Levin Y, Pauzner D. The ultrasonographic appearance of tubal pregnancy in patients treated with methotrexate. Hum Reprod 2002; 17:2585-7.
- 6 Bisharah M, Tulandi T. Practical management of ectopic pregnancy. In: Reproductive endocrinology and infertility. Current trends and developments. Tan SL and Tulandi T, Marcel Dekker, New York, 2003,225.
- 7 Pescetto G, De Cecco L, Pecorari D, Ragni N. Ginecologia e Obstetricia 2001; 2:1777-82.
- 8 Sowter MC, Farquhar CM, Petrie KJ, Gudex GA. A randomized trial comparing single dose systemic methotrexate and laproscopic surgery for the treatment of ectopic pregnancy. Br J Obstet Gynecol 2001; 108:192-203.
- 9 Kelly H, Harvey D, Moll S. A cautionary tale: fatal outcome of methotrexate therapy given for management of ectopic pregnancy. Obstet Gynecol 2006; 107:439-41.
- 10 Lipscomb GH, Givens VM, Meyer NL, Bran D. Comparison of multi dose and single dose methotrexate protocols for the treatment of ectopic pregnancy. Am J Obstet Gynecol 2005; 192:1844-48.
- 11 Stovall TJ, Ling FW. Single dose methotrexate: an expanded clinical trial. Am J Obstet Gynecol 1993; 168:1762-5.
- 12 Alleyassin A, Khademi A, Aghahussani M. Comparison of multi dose and single dose administration of methotrexate: a prospective, randomized clinical trial. Fertil Steril 2006; 85:1661-6.
- 13 Medical management of tubal pregnancy. ACOG practice Bulletin#3. American College of Obstetricians & Gynaecologists, 1998.
- 14 Barnhart KT, Gosman G, Asnby R. The medical management of ectopic pregnancy: A meta analysis comparing single dose