Study of single dose methotrexate for treatment of tubal pregnancy

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ABSTRACT

Introduction: Ectopic pregnancy (EP) occurs in ∼1% of pregnant women, and may seriously compromise women’s health. Systemic administration of methotrexate (MTX), has gained acceptance in selected patients.

Objective: The propose of this Descriptive analysis study was to determine the success rate of single dose methotrexate (MTX) protocol for the treatment of un ruptured tubal ectopic pregnancy.

Method: This retrospective study included 139 patients with ectopic pregnancy who were treated with MTX therapy (single dose protocol 50 mg/kg, Intra muscularly) during the years 2009-2010. data analyzed through SPSS software version 13.

Main and secondary outcome measures:
Decline of plasma human chorionic gonadotropin < 15% on the 4th day of MTX administration, mean of primary β-hCG level, need to additional dose of MTX, need to surgery, presence of free fluid in culdesac, length of hospitalization, mean of gestational and maternal age, mean of ectopic mass size.

**Result:** The success rate was 64%, mean of primary β-hCG level was 523.72±674.13 MIU/ml, need to additional dose 23.74%, need to surgery 21.6%, free fluid was observed in 23% of patients, mean hospitalization was 6.46% days, mean of maternal age 27.74 years and mean of gestational age was 5.97±1.82 weeks and mean of ectopic mass size was 2.45±0.79 cm.

**Conclusion:** In women with an ectopic pregnancy medical treatment with single dose MTX tends to be successful options.

**Keywords:** MTX, ectopic tubal pregnancy, success rate

**Introduction**

Davidson 1, believes that research in the medical field is growing very rapidly. Other authors provide similar inputs 2.

Ectopic pregnancy (EP) is a pregnancy in which the fertilized ovum implants outside the uterine cavity. Its incidence has increased from 0.5 per 100 pregnancies 30 years ago to the present day of 2 per 100 pregnancies 1,2. risk of ectopic pregnancy is 3 fold in IVF cycles 3. EP is potentially a life threatening condition in first trimester and also is the most important cause of maternal mortality and morbidity 4. Despite this, risk of maternal death due to ectopic pregnancy has decreased due to early diagnosis 5. Greater awareness of risk factors and improved technology (biochemical markers and ultrasonography) allow ectopic pregnancy to be identified before the development of life-threatening events 6. EP affects young woman and the commonest presenting symptom is abdominal pain 7. Before any clinical symptoms of rupture have occurred, early diagnosis of EP is now possible by specific assays of the β-subunit of human chronic gonadotropin (hCG) and high resolution ultrasonography with vaginal probes 8. This increases the chance of success of medical treatment and minimizes the morbidity and mortality created by this health problem 7. Linear salpingotomy by laparoscopy remains the treatment of choice for tubal pregnancy (pouly et al 1986) and represent a significant advance over laparotomy in the duration of hospitalization, delay of recovery and health service costs (vermesh et al 1989) lundorff et al 1991. This procedure carries a risk of persistent trophoblast and of repeated tubal pregnancy 8. Although treatment is still primarily surgical, management with methotrexate is a viable and potentially cost-effective alternative. Medical treatment of ectopic pregnancy with methotrexate has been shown to be effective and safe in carefully selected patients. It is no
longer considered experimental therapy. MTX has been administrated by I.M or I.V injection with one to four doses. (tanaka et al 1982, ory et al 1986, Stovall et al , 1991, 1993 ) when appropriate inclusion criteria are used (fermandez et al , 1991) methotrexate failure rates have been similar to those reported in previous series of laparoscopic surgery (pouly et al 1986), more over follow up and reproductive outcomes have been similar in both treatments (pouly et al, Stovall 1993). Therefore the present study was conducted to determine our institutional success rate with single-dose intramuscular methotrexate injection for the treatment of ectopic pregnancy.

Material and Method

Over a period of two years (2009-2010) a descriptive analytic study was conducted in the maternity research center department of obstetrics and gynecology in Imam Reza teaching hospitals Kermanshah University of medical sciences. Population study was those women who presented with the clinical pictures of EP. Diagnosis was confirmed by sensitive β-hCG assay and transvaginal ultrasound. 139 patients included the study inclusion criteria for conservative management was hemodynamic stability, ectopic mass size less than 4 centimeter in transvaginal ultrasound (TVS), serum β-hCG level less than 10/000 mIU/ml, absence of free fluid in pelvic cavity, Morrison space and desire of the patients for future fertility. Those with ruptured EP, visualization of fetal heart in ectopic mass, hemoperitoneum, hepatic, kidney, and platelet (PTL) dysfunction were excluded from the study. More over those patients with WBC < 2000 mm³, PTL< 10⁵ µl, creatinine <1.5 mg/d were excluded. Single intramuscular injection of methotrexate (1mg/kg body weight) was given to eligible patients. A second dose was given to those cases in which decrease in β-hCG between days 4 and 7 is less than 15 percent. Successful treatment was defined as decrease of β-hCG level more than 15% between days 4 and 7 of MTX injection without any need further intervention. Possible signs of methotrexate toxicity like leucopenia, thrombocytopenia, raised hepatic enzymes and raised blood urea and creatinine level were noted carefully. The patients were warned that the therapy might fail in 5-10 % of cases and result in surgery. Folic acid was avoided during treatment phase. Outcome measures were success rate of single dose methotrexate injection. Additional variable studied were need to additional dose of MTX, need for alternative methods of management, success rate with respect to mean of ectopic mass size and mean of β-hCG level and presence of free fluid in pelvic cavity. Data were entered in to SPSS software version 13 and analyzed. Indicator of percentage, mean, standard deviation, one-dimensional and two-dimensional tables as the number and percentage were used.

Results

One hundred thirty nine patients with the diagnosis of EP and single dose MTX treatment were enrolled in to the study. Of those 139 patients eighty nine patients (64%) were successfully treated .The mean age of women was 27.77 ± 5.52 years. mean of gestational age was 5.97± 1.82 weeks, mean of gravidity was 2.2 ± 1.31, the mean initial β-hCG level at the time of treatment was 523.72±674.13 mIU/ml. mean of ectopic mass size was 2.45± 0. 79 cm. success rate with respect to initial β-hCG level and ectopic mass size is shown in Fig 1 and 2.
There was free fluid in pelvic cavity in 23% of cases (32 out of 139 patients) success rate in those with and without free fluid was 34.4% and 72.9% respectively, this difference was statistically significant (P.Value=0.00).

Need to additional dose of MTX was 24.5% (34 out of 139), need to surgical operation 21.6% (30 out of 139). Need to additional dose of MTX was 66% (33 out of 50) in unsuccessful group, in successful group no patients need to additional dose of MTX or emergency laparotomy. 30 out of 50 patients (60%) of unsuccessful group underwent emergency laparotomy. Frequency of length of hospital stay is presented in table 1, mean of hospital stay was (6.46 day) most of the patients (39.56%) 55 out of 139 stayed in hospital for 4-6 days.

**Discussion**

Our findings suggest that among patients with unruptured tubal pregnancy treatment with single dose injection of methotrexate have success rate of 64% (89 out of 139 patients). Patients with lower serum β-hCG concentrations before treatment with MTX had significant higher success rate compared with those with higher levels (P.Value = 0.03) 76.8% in β-hCG level < 400 mIU/ml versus 55.6% in β-hCG level (400-600 mIU/ml) and 55.2% in β-hCG level > 600 mIU/ml.

In the study by Clara Merisio et al on 11 patients success rate with single dose of MTX was higher (90%) and similar to our study lower β-hCG level had significantly relation with success of treatment.

In the similar studies other series reported success rate of 73.3% by Mehmet Erdem on 30 patients and also by Soliman K.B while in our study success rate was 64%. Mehmet found 26.6% patients (8 patients) required second dose of MTX while in the present study 24 out of 139 patients 24.5% required second dose of MTX. With respect to β-hCG titer he also found higher success rate with lower β-hCG level. 78.2%, 50%, 33.3% success rate in β-hCG level less than 2000 mIU/ml, between 2000-4000 mIU/ml and more than 5000 mIU/ml respectively.

Mohammad Shebab, Bassam reported 84.82% success rate on 112 patients (95 out of 112) and 17 cases (15.17%) required to second dose of MTX, in 9 cases (8%) ruptured EP occurred. In successful group initial β-hCG level < 3000 mIU/ml and ectopic mass size < 3 cm was reported in 86% of cases, while in the present study there was not significantly meaningful relation between success rate and mean of ectopic mass size (P.Value = 0.018).

In the study carried out by MM Alshimiri on 77 cases success rate was 95% (73 patients) with mean initial β-hCG level 2592 MIU/ml and mean ectopic mass size 2.4 cm, while in our experience the mean of initial β-hCG level was 523.72 MIU/ml and mean ectopic mass size was 2.45 cm.

Similar to our study Martin C Sowter reported success rate of 65% (22 out of 34) and 9 cases (26%) required to second dose of MTX.
Lipscomb GH reported 81% success rate on 35 cases but in opposite to our study he found no significantly meaningful relation between success rate and presence of free fluid in culdesac however similar to our experience success rate was associated with initial β-hCG level. (98% success rate in β-hCG level < 1000 mIU/ml)\(^1\). 

Amelie Gervaise et al also reported success rate 65.1% (41 out of 63 patients) 19% of patients (12 patients) required to second dose of MTX and 8 out of these 12 patients (12.6%) underwent emergency laparotomy. In that study the mean initial β-hCG level was 1372 ± 2609 mIU/ml in successful group and 1936±1501 mIU/ml in unsuccessful group\(^1\). Similar to our study success rate of treatment in lower β-hCG level was significant Successful rate of 37.5% in β-hCG level equal or more than 2000 mIU/ml and 83% in β-hCG level < 2000 mIU/ml.

The primary strength of the present study is the large number of patients available for the study as well as referral of nearly all ectopic patients to Imam Reza Teaching hospital for diagnosis and treatment. Limitations of this study include retrospective nature of the study and the inherent bias presented when the initial decision for management are based both on patients preference and physicians recommendations.

**Conclusion**

We concluded single dose of MTX for treatment of ectopic tubal pregnancy is successful in 64% of patients and initial β-hCG level and presence of free fluid in culdesac are strong predictors of success of treatment .there was not any meaningful relation between ectopic mass size and success of treatment.

**Conflict of Interest:** None declared.

**References**

Table 1: Length of hospital stay

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Figure 1: Success rate with respect to β-hCG level.
Figure 2: Success rate with respect to mean ectopic mass size

![Success rate with respect to mean ectopic mass size](image-url)