Medical management of unruptured ectopic pregnancy by methotrexate: A five years experience at tertiary care hospital

Manisha Munemane*1 and Anil Munemane2

1Senior Consultant, OBGY., Aditya Birla Memorial Hospital, Chinchwad, Pune, Maharashtra, India
2Associate Professor, Department of Pathology, Rural Medical College, Loni, Maharashtra, India

* Correspondence Info:
Dr. Anil Munemane, MBBS, MD.
Associate Professor,
Department of Pathology
Rural Medical College
Loni, Maharashtra, India.
E-mail: amunemane@yahoo.co.in

Abstract
Background: Medical treatment of ectopic pregnancy with methotrexate has been considered as an alternative to surgical intervention.
Aims and objectives: The present was carried with an aim to determine the role of methotrexate in management of ectopic pregnancy.
Materials and methods: The present study was carried out for a period of 5 years (September 2007 to August 2012) in a tertiary care hospital. It included a total of 128 patients of unruptured ectopic pregnancies. The medical management was done with methotrexate. Time taken for complete β human chorionic gonadotrophin (β hCG) resolution was recorded. The negative β hCG result indicated an endpoint of successful outcome.
Results: Out of 128 cases where Methotrexate was used, 4 required surgery. In remaining 124 cases, there were no side effects. Complete β hCG resolution was achieved in 28 -35 days. Subsequent tubal patency & reproductive functions were comparable to that of surgical management.
Conclusion: From our study, it can be concluded that methotrexate can be recommended as safe and effective drug for management of unruptured ectopic pregnancies.
Keywords: Methotrexate, unruptured ectopic Pregnancy, medical management, β hCG

1. Introduction
An Ectopic Pregnancy refers to the pregnancy occurring outside the uterine cavity usually in fallopian tube. 1 It is a potentially life threatening condition.

Currently over 90% of ectopic pregnancies can be visualized on transvaginal Scan (TVS) and hence early ectopic pregnancies can often be detected in asymptomatic patients. High resolution TVS along with rapid immunoassay of serum β hCG allows the early diagnosis of ectopic pregnancy and therefore early medical treatment can be administered in most of the cases.2 The overall success rate of medical treatment in properly selected cases is reported to be about 90 %.3

Methotrexate is a folic acid antagonist widely used for treatment of neoplasia, severe psoriasis & rheumatoid arthritis. It inhibits DNA synthesis & cell reproduction primarily in actively proliferating cells such as malignant cells,
The dose of methotrexate used to treat ectopic pregnancy (50mg/m² or 1mg/kg) is relatively low. Leucovorin (folinic acid) is also given to bypass the metabolic block induced by methotrexate and thus rescue normal cells from toxicity.

The present study was carried in tertiary care hospital with an aim to determine the role of methotrexate in medical management of unruptured ectopic pregnancy.

2. Material & Method

A study was conducted at Aditya Birla Memorial Hospital, Pune, from September 2007- August 2012. Patients with unruptured ectopic pregnancy were included in the study. The diagnosis of unruptured ectopic pregnancy was made when ultra sonographic examination revealed empty uterine cavity, adnexal mass < 3cm with no fetal heart activity and no free fluid. Serum βhCG levels were also estimated. The inclusion criteria for the study were

1) Heamodynamically stable patient
2) βhCG < 3000 IU/L
3) No evidence of rupture on USG.
4) Normal liver & renal function.
5) Patient reliability for follow up.

The patients not fulfilling the above criteria were excluded from the study. The patients were informed about the drug and those who agreed were included in the study. An informed consent was obtained from the patient. The regular follow up of the patients was done until serum βhCG level returns to normal.

These patients were treated with 50 mg of intramuscular (IM) methotrexate (Single or multiple doses) depending on decrease in βhCG levels. Maximum of three doses of methotrexate are given. If the BHCG level falls <15 percent between weekly measurement after a third dose then surgical intervention was done. βhCG levels were measured on day 3 and 6 then weekly until they were less than 5 IU/L. Complete blood count, liver and renal function tests were carried out on day 3 & day 6.

Treatment success was defined as resolution of βhCG level to less than 5 IU/L. Treatment failure was defined as the need for surgical intervention for any reason. The most efficient approach to therapy is administration of a single IM dose of methotrexate (1mg/kg).

3. Results

In the present study out of 128 patients, 82(64%) presented with abdominal pain, 38 (29%) had vaginal bleeding while remaining presented with both symptoms.

As shown in Figure 1. Out of 128 patients, 114(89.1%) required only single dose of methotrexate & 14 (10.9%) patients needed more than one dose out of which 12 required two doses & 2 required three doses.

Out of 128 patients, 124 (97%) were successfully medically managed by methotrexate whereas, 4 (3%) required surgical intervention.
Normal βhCG levels were achieved in 28-35 days in 122 patients while 2 patients took 42 days for their βhCG to return to normal.

4. Discussion

Unruptured ectopic pregnancy can be effectively managed by methotrexate if the diagnosis can be made earlier non invasively. Approximately 35% of women with ectopic pregnancy are eligible for medical treatment. In these women treatment with methotraxte is as effective as laprosopic salpingostomy and results similar success rates for tubal patency & future intrauterine pregnancy.

This study supports the use of methotrexate as a safe & highly effective alternative treatment of tubal ectopic pregnancies with success rate of 97%. This highly efficacious result was obtained with strict adherence of our selection criteria. Our experience with this method of treatment showed a negligible side effects and it allows short hospital stay.

Adverse reactions to methotrexate are usually mild and self limiting. The most common are stomatitis and conjunctivitis. Rare side effects include gastritis, enteritis, dermatitis, alopecia, elevated liver enzymes and bone marrow suppression. In our study no major side effects were seen. Side effects were relatively minor and transient. Our Patients tolerated methotrexate therapy well. It may be due to careful evaluation of patients before starting methotrexate therapy.

There is no evidence of adverse effect of methotrexate treatment on future pregnancies. Attempts to conceive may be resumed after the βhCG level is undetectable. The incidence of recurrent ectopic pregnancy is approximately 15% and rises to 30 % following two ectopic pregnancies. The risk of recurrence appears to be same for both medical & surgical therapies.

The reasons for change towards methotrexate therapy are minimal intervention, less morbidity and lower cost implications. Diagnosing the condition earlier in natural history has changed the management option. The classical presentation with collapsed ectopic women has become less common when good facilities for early diagnosis are available.

Early ectopic pregnancies tend to be smaller & have lower base line β hCG level thus more time is available for conservative management.

5. Conclusions

We conclude that the medical management with intramuscular methotrexate is a safe and cost effective alternative than the surgical intervention in the unruptured ectopic pregnancies which avoids surgical and anesthetic complications.

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