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A study on medical management of ectopic pregnancy using methotrexate

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Abstract
Ectopic pregnancy is defined as one where fertilised ovum implants outside the normal uterine cavity the main sites for implantation include tubes, ovaries, cervix, rudimentary horn of a bicornuate uterus and cesarean scar. Risk factors being PID tuberculosis of pelvis, use of progesterone contraception, endometriosis of tube, congenital anomalies of tube. Diagnosis is being made by TVS and serum beta HCG. Treatment depends on hemodynamic stability of patient. In unstable patients surgical management is best but in stable patients medical management with methotrexate is done. Our study is aimed at medical management of ectopic.
Methodology and results: 70 unruptured ectopic patients were included in study. 12 patients were kept for observation. 58 patients were selected for medical management i.e. methotrexate treatment. No. Of patients with Successful single dose methotrexate treatment were 42 (72.4%) No. Of patients required multidose methotrexate were 10(17.24%) No. Of patients with failed methotrexate treatment and requiring surgical intervention were 2(3.4%) No. Of patients with tubal rupture 4(6.8%).
Conclusion: Medical management of patients with ectopic pregnancy who are hemodynamic stability with methotrexate offers promising results and avoids surgical morbidity and offers a good obstetric future to the patients.

Keywords: medical management, ectopic pregnancy, methotrexate

Introduction
Ectopic pregnancy is one where ovum implants outside the normal uterine cavity. The common sites for implantation are tubal (90%) Ovarian, cornual, abdominal, cervical, cesarean scar ectopic. Most Common predisposing factors for ectopic pregnancy are PID, congenital anomalies of tube, previous tubal surgery, use of progesteronal contraceptives Tuberculosis of tube, use of emergency contraceptives, transperitoneal migration of ovum, endometriosis of tube and long term infertility [1, 2].
When a women on progesterone only contraceptives conceives an ectopic Pregnancy should always be considered [3, 4, 5].
Nowadays the incidence of ectopic pregnancy is on rise because of early diagnosis, use of artificial reproductive techniques (ART) and increased incidence of PID. Ectopic pregnancy can present as ruptured ectopic which manifests as acute abdomen, subacute or chronic ectopic. Diagnosis of ectopic is made on the basis of TVS and serum Beta HCG and since 1980 this has made diagnosis of ectopic easier [1]. A paired serum Beta HCG is taken at least 48 hours apart, if serum beta HCG increases less than 66% then ectopic is suspected. TVS should make out Gestational sac when beta HCG is 1500 I. U/ml, if it fails to detect intrauterine gestational sac at this discriminatory zone of beta HCG then laparoscopy is advised.
Use of colour doppler TVS assess increased blood flow in adnexal mass indicating active trophoblastic tissue in adnexa Which correlates with beta HCG titre (Kurjak *et al*. 1994). There are different modalities of treatment for ectopic pregnancy depending on beta HCG titres and clinical condition of patient. Conservative and medical management saves a woman from surgical morbidity and at the same time saves her tube. Medical management of ectopic with methotrexate has been found to safe and effective [6]. Depending on the size of ectopic and beta HCG levels methotrexate can be given as single or multidose regimen.

Methodology
It was a prospective study carried over a period of one year August 2016-May 2017.

Seventy (70) unruptured ectopic pregnancy were included in this study. Diagnosis was made by TVS.
All baseline investigations were done CBC, KFT, LFT, measurement of height and weight.

Inclusion criteria
1. Patients with stable, unruptured ectopic diagnosed by TVS.
2. Beta HCG titre <10000miu/ml.
3. Size of ectopic mass <4 cm.
4. Absence of fetal cardiac activity.
5. Patient giving consent for medical treatment.

Exclusion criteria
1. Patient who are unstable with hemoperitoneum.
2. Size of sac >4cm with cardiac activity with cardiac activity present.

Now patients were divided based on their beta HCG level, those With beta HCG level <500mi.u/ml, where kept for observation and their beta HCG was repeated after 48hours, their beta HCG showed a falling titre and had complete resolution. Patients whose beta HCG >500 but < 5000 we're given a single dose of methotrexate regimen 50mg/metre square (calculated on the basis of height and weight). Beta HCG was measured on day 4 and day 7. 15% or more fall in beta HCG between day 4 and day 7 was considered satisfactory and successful. If there was <15% fall in beta HCG then methotrexate was repeated on day 7 and beta HCG was measured between day 7 and day 11.
Those with beta HCG >5000 we're given multidose regimen (1mg/kg) on day 1,3,5,7 with folinic acid rescue on day 2, 4, 6, 8. Beta HCG was detected in between days 15% or more of fall in between the days was considered satisfactory. After administration of methotrexate patients were instructed to avoid vitamins, folic acid, travel, NSAIDS, exposure to sunlight.

Results
No. Of patients with unruptured ectopic pregnancy = 70.
No. Of patients kept for observation with beta HCG <500 = 12.
Resolution of ectopic = 12 patients 100%.
No. Of patients kept for medical management = 58.
No. Of patients with successful single dose methotrexate therapy = 42 (72.4%).
No. patients requiring more than one dose of methotrexate = 10 (17.24%).
No. Of patients with failed medical therapy requiring surgical Intervention = 2 (3.4%).
No. Of patients with tubal rupture requiring emergency laparotomy = 4 (6.8%).

Discussion
Ectopic pregnancy is a major cause of maternal mortality and morbidity in first trimester of pregnancy. Nowadays because of better antenatal care and USG facilities mortality due to ectopic pregnancy has reduced a lot. There are various treatment modalities for ectopic pregnancy observation, treatment, surgical.
Medical treatment for ectopic introduced since 1980 [1] has facilitated management of ectopic pregnancy. Medical treatment with methotrexate either as single dose or multiple doses has helped to manage patients even without exposing them to surgical management. In earlier times multidose dose was used but later because of refinement and modification single dose therapy is nowadays preferred and that too on OPD basis [6, 7]. Medical treatment with methotrexate has many advantages as it is effective, less costly, simple and preferable to surgery (Das *et al*. 2001) Methotrexate is given on the basis of body weight and height from which surface area is calculated. In single dose therapy 50mg/metre square is given on day zero and beta HCG is measured on day 4 and day 7. If beta HCG decreases by 15% or more from day 4 to day 7 then beta HCG is done weekly till it becomes negative. If there is <15% decrease from day 4 to day 7 then a repeat dose of methotrexate is given on day 7 and beta HCG is measured between day 7 to day 11.This is known as Second dose regimen. Single dose methotrexate treatment has got less side effects however Glock *et al*. [8] reported more side effects like nausea, diarrhea, dryness of mouth even with single dose of methotrexate.
In multidose regimen methotrexate is given in dose of 1 mg/kg on day 1,3,5,7 with folinic acid on day 2, 4, 6, 8. In our study 58 patients were kept for medical management. In our study Single dose of methotrexate was successful in 72.4% of patients, 17.24% patient's required 2 dose regimen or multidose regimen. In our study there were 2 patients (3.4%) that required surgical intervention despite giving medical management. 4 patients were those had that tubal rupture and required emergency surgery.

Conclusion
With the introduction of use of methotrexate in management of ectopic, we have been able to manage ectopic patients even on OPD basis. Although failure is there with use of this period but still it is number one treatment option for hemodynamic stable ectopic patients with beta HCG <10000.
Use of medical management offers a better obstetric future to the patient and saves her from surgical morbidity.

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