

Ectopic pregnancy managed medically at St. Paul's Hospital Millennium Medical College, Addis Ababa, Ethiopia

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Abstract

Background: Ectopic pregnancy, a pregnancy in which the embryo implants outside the endometrial cavity, is an important cause of maternal mortality, especially in developing countries. It can be managed medically using methotrexate. In Ethiopia, limited evidence exists regarding the treatment outcome of this approach.

Methods: This retrospective study was conducted based on medical records of ectopic pregnancies managed medically using methotrexate. The data of women who had unruptured ectopic pregnancy and who were managed medically in the study period at St. Paul's Hospital Millennium Medical College were included. Data were extracted from patients' medical records and analysed using SPSS software.

Results: During the 5-year period 2015 to 2019, 81 women with unruptured ectopic pregnancy were managed medically using methotrexate with 93.8% (n=76) success. Methotrexate was administered intramuscularly to all patients in either single dose or multiple doses. Five out of the 81 patients underwent surgical intervention for either ectopic rupture or persistent ectopic mass. There were no fatal complications.

Conclusion: Methotrexate is a successful and safe alternative to surgical management of unruptured ectopic pregnancy in our settings. It should be given a trial in patients who meet the selection criteria in a setting ready for emergency surgical intervention and blood transfusions.

Key words: Ectopic pregnancy, methotrexate, medical management, beta hCG, Addis Ababa.

Introduction

An ectopic pregnancy (EP) results from implantation outside the uterine cavity.^[1] It is an obstetric emergency. Undiagnosed it leads to rupture and haemorrhage. Despite the improvement in diagnostic techniques haemorrhage from EP remains the leading cause of pregnancy-related maternal mortality in the first trimester, accounting for 4% of all such deaths.^[2] The recurrence rate is as high as 15%.^[3,4] Studies in Ethiopia reported a higher incidence among 20 to 29-year-olds and unmarried and nulliparous women.^[1,5,6] Ethiopia is among the countries with a high incidence with the EP being the leading cause of death in the first trimester.^[7,8]

Research indicates that medical management of EP is a possible alternative to surgery. Methotrexate (MTX) seems to be the preferred medication. Medical management avoids the complications of surgery and anaesthesia and reduces costs. Most of these studies were conducted in developed countries with different settings and practices.^[9]

Medical management using MTX is being practiced in some referral hospitals in Ethiopia but there is no information on effectiveness. Studies conducted on EP in Ethiopia [1,5,6] have not addressed its surgical or medical management outcomes. This study focused on treatment outcomes, with the hope that the results will inform decisions on the management of unruptured EP, as well as being a reference for future research.

Methodology

This retrospective study was based on medical records of EP patients managed medically using MTX at St. Paul’s Hospital Millennium Medical College from January 1st 2015 to December 31st 2019. All patients with unruptured EP, who were given MTX (50mg/dose by intramuscular injection) as initial treatment, were included. Medical record numbers were extracted from the medical registry books in wards and emergency outpatients. The patients’ charts were retrieved and data were extracted, using a structured and pretested format, and after confirmation of accuracy and completeness, were analysed using SPSS software.

Results

Eighty-one patients had been managed using MTX. The diagnosis of EP was made with trans-abdominal and transvaginal sonography and serum beta human chorionic gonadotropin (hCG). Table 1 shows that most of the women (60.5%) were aged 20 to 29 years, with only four (4.9 %) under 20 years; most were married (86%), 39% were nulliparous, 26.0% each were para 1 and para 2 and above. None had a recorded history of pelvic inflammatory disease. Twelve women (14.8%) had a history of EP for which unilateral salpingectomy was done, and 13 (16%) had at least one abortion.

Three patients (3.7%) presented with abdominal pain only. The remainder presented with either amenorrhoea alone or with lower abdominal pain. None had vaginal bleeding. The gestational age of the fetus was below eight weeks in 40.7% (n=33) and equal or greater than 8 weeks in 45.7% (n= 37) based on the last menstrual period (LMP). Eleven patients had unknown LMP dates but claimed to have had amenorrhoea for not more than two months.

The pre-treatment serum beta hCG levels for most of the patients (70.4%) was below 5,000 iu, with the levels above 10,000 iu for 8.6%. No foetal cardiac activity was seen on ultrasound for all patients and the gestational sac (GS) diameter was below 3.5 cm for most (93.8%). One patient had a GS diameter above 4 cm.

MTX was given intramuscularly to all patients in either a single dose (60.5%) or multiple doses if the beta hCG did not reduce (39.5%). Leucovorin, a drug to alleviate

Table 1. Details of the pre-treatment patients’ information (N=81)

Variables	n (%)	
Maternal age groups (years)	below 20	4 (4.9)
	20 – 29	49 (60.5)
	30 and above	28 (34.6%)
Marital status	Single	11 (14)
	Married	70 (86)
Parity	Nulliparous	39 (48.1)
	Para 1	21 (26.0)
	Para 2 or greater	21 (26.0)
Gestational age (weeks)	< 8	33 (40.7)
	>8	37 (45.7)
	Unknown	11 (13.6)
History of abortion	Nil	68 (84)
	1	8 (9.9)
	2	2 (2.5)
	3 or more	3 (3.6)
History of EP	Yes	12 (14.8)
	No	69 (85.2)
Presenting complaint	Amenorrhoea	42 (51.9)
	Abdominal pain	3 (3.7)
	Both	36 (44.4)
Gestational sac diameter	< 3.5cm	76 (93.8)
	3.5 - 4cm	4 (4.9)
	> 4cm	1 (1.2)
Foetal cardiac activity on ultrasound	Present	0 (0)
	Absent	81 (100)
Pre-treatment Serum beta hCG i.u.	< 1,000	23 (28.4)
	1000 - <5,000	34 (42)
	5,000 - 10,000	17 (21)
	>10,000	7 (8.6)

side effects of methotrexate, was given to all patients who had multiple doses. However, only two patients had mild vomiting.

Of the 81 patients, five (6.2%) underwent surgical intervention (two for ectopic rupture and three for persistent EP).

All with successful medical treatment (93.8%) were discharged within ten days. The serum beta hCG levels at the time of discharge were below 1,500 iu for most (90.8%).

Table 2. Details of the treatment and outcomes

Variables		n (%)
MTX dose protocol	1 dose	23 (28.4)
	2 doses	26 (32.1)
	3 doses	8 (9.9)
	4 doses	24 (29.6)
Leucovorin	Given	31 (38.2)
	Not given	50 (61.8)
Side effects	Yes	02 (2.6)
	No	74 (97.4)
Treatment outcome	Discharged	76 (93.8)
	Ruptured	2 (2.5)
	Persistent	3 (3.7)
Period of hospital stay	7 days or less	31 (40.8)
	>7 days	45 (59.2)
Serum Beta hCG on discharge	< 1,000	61 (80.3)
	1,000 - <1500	8 (10.5)
	> 1,500	7 (9.2)
Serum Beta hCG on the 1st visit	< 15 iu	20 (26.3)
	< 500 iu	45 (59.2)
	500 - < 1000 iu	11 (14.5)
Serum Beta hCG on 2nd visit	<15 iu	49 (64.5)
	15 iu - < 200 iu	27 (35.5)
	200 - < 500 iu	00 (0)
GS diameter on discharge	< 3.5 cm	76 (100)
	> 3.5 cm	00 (0)
GS diameter on the 1st visit	< 2 cm	76 (100)
	> 2 cm	00 (0)
GS diameter on the 2nd visit	< 0.5 cm	63 (82.9)
	0.5 - < 1 cm	13 (17.1)

The first post-treatment visit was after one week from discharge and the serum beta hCG levels were all below 1,000 iu with most below 500 iu and the gestational sac (GS) diameter reduced by more than 50% of the pre-treatment size. The second post-treatment visit a week later found serum beta hCG levels were below 200 iu for all patients. The GS had disappeared for most patients. See Table 2.

After 5 patients underwent surgical intervention, only 76 patients remained on treatment and follow up.

Discussion

The success of medical management of EP using MTX

was 93.8%.^[9] If selection criteria were strictly followed, we would have concluded that the treatment outcomes between single and multiple doses is comparable.^[9,10,11] Fifty three percent of patients in the single dose regimen group required a second dose of MTX, a rate higher than reported in India and Jordan.^[12,13] This was dictated by the unsatisfactory reduction of the serum level of beta hCG after the first. In this study, the failure rate was 6.2%, similar to a meta-analysis of previous studies^[9] but lower than reported in India.^[12] For the five patients for whom medical management was unsuccessful, the pre-treatment serum beta hCG levels were above 15,000 iu for three patients, while the GS size was above 4 cm for the fourth patient. The size of the ectopic mass and beta hCG levels were in the recommended ranges^[11,15] for medical treatment in only one patient who underwent surgery for ruptured EP.

Although such levels of serum beta hCG and the size of ectopic mass were reported to affect the success rate of medical management^[10,14,15], treatment using MTX was given a trial in these patients, probably because four of them had a unilateral salpingectomy for previous EP. None of them required blood transfusion. It is observed from this study that, the earlier the gestational age, the lower the pre-treatment serum hCG and the smaller the GS diameter, the more rapid the rate of decline of the serum hCG and the resolution of the ectopic mass and therefore, the earlier the hospital discharge. So the levels of serum beta hCG above 10,000 iu and the ectopic mass size greater than 3.5 cm were the identified factors affecting the success rate of this treatment.

Longer hospital stays (more than 7 days for 59% of patients) and costs for the medication (especially for those who completed all four doses) and serial investigations were the drawback of this treatment. There was no serious morbidity reported and no fatalities.

Conclusion

We have confirmed that MTX in our setting is a successful alternative to surgical management for patients with unruptured EP who meet certain criteria. We expect success rate to be higher if strict selection of patients were made based on these criteria.

Although treatment was successful in many patients whose pre-treatment serum beta hCG levels were above 5,000 iu, we agree with previous studies that reported serum beta hCG levels to be the most important determinant for treatment success and recommend levels of 5,000 iu or below to be used as the main selection criterion.

Our study included a small sample size and did not address long term outcomes of this treatment option. Therefore, we recommend that further research with larger numbers is undertaken with attention to long term outcomes. Early

detection of EP before tubal rupture gives the obstetrician an opportunity to give medical treatment a trial. We recommend proper counselling of patients at high risk for EP to seek early ante-natal attention.

Finally, we recommend this medical approach to be carried out in settings ready for emergency surgical intervention and blood transfusion. All patients were placed on follow-up.

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