Elmer Press

Original Article

J Clin Gynecol Obstet • 2012;1(4-5):67-70

The Prognostic Value of Tubal Patency Test After Medical Treatment of an Ectopic Pregnancy

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Abstract

Background: Ectopic pregnancy (EP) is defined as the abnormal implantation of the blastocyst outside the uterine endometrium. The most common site of implantation is the Fallopian tube. The effect of different management strategies on subsequent fertility following tubal ectopic pregnancy is unknown. Some women who have had ectopic pregnancies will have difficulty becoming pregnant again. The aim of this study is to evaluate the tubal patency after successful medical treatment of an un-ruptured tubal ectopic pregnancy with systemic methotrexate (MTX).

Methods: This is an observational retrospective study carried out on 72 women diagnosed as un-ruptured tubal ectopic pregnancy. Systemic treatment with a single dose methotrexate (50 mg/m^2 intramuscularly) was used for 32 women and 40 cases underwent surgery. Hysterosalpingography (HSG) was performed on 30 patients (successfully managed with methotrexate) and 40 cases that underwent unilateral salpingectomy (as initial treatment).

Results: The medical treatment with single dose MTX for EP was effective (93.8%) as a primary treatment. In the MTX group, the HSG findings from the ipsilateral tube showed that 83.3% the diseased tubes were open and 16.7% were obstructed. The contralateral tube was patent in 93.3% and obstructed in 6.7%. In salpingectomy group the contralateral tube was patent in 82.5% and obstructed in 17.5%.

Conclusions: For an un-ruptured tubal EP, the medical treatment with MTX is effective. Routine HSG following medical treatment does not seem necessary but might be considered in selected risk cases.

Manuscript accepted for publication October 4, 2012

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doi: http://dx.doi.org/10.4021/jcgo48w

Keywords: Ectopic pregnancy; Methotrexate; Hysterosalpingography; Infertility

Introduction

Ectopic pregnancy continues to be a major cause of morbidity and mortality in reproductive-age women. The most common site of implantation is the Fallopian tube (in the ampullary section, fimbrial end or isthmus) but can also be interstitial, ovarian, abdominal and cervical, or on the site of a previous cesarean section scar [1].The prevalence of ectopic pregnancy appears to be rising, in part because of earlier, more accurate diagnosis of pregnancies. Further, an increased incidence of sexually transmitted infections, earlier diagnosis of pelvic inflammatory disease resulting in tubal damage but not complete blockage, and the rise in the number of ectopic pregnancies resulting from assisted reproductive technologies (ART) may account for the overall increase [2]. Although the classic treatment of ectopic pregnancy is surgical, early diagnosis allows the implementation of a medical treatment for most women with un-ruptured ectopic pregnancy [3]. Medical therapy of ectopic pregnancy is appealing over surgical options for a number of reasons, including eliminating morbidity from surgery and general anesthesia, potentially less tubal damage, and less cost and need for hospitalization. Several medical treatments have been used such as prostaglandins, actinomycin, etoposide, hyperosmolar glucose, anti-hCG antibodies, potassium chloride, or mifepristone. However, the treatment with methotrexate has shown better results and is presently considered the first option for medical therapy [4]. The effect of different management strategies on subsequent fertility following tubal ectopic pregnancy is unknown. Some small studies have shown that tubal patency and future reproductive outcomes are significantly improved in women managed expectantly compared with those who underwent surgery [5, 6]. The main concern following management of an EP is the risk of recurrence and future fertility outcome. Fertility outcome for these patients can be evaluated by hysterosalpingography (HSG) or

Table 1. Single Dose Methotrexate Protocol for the Treatment of Ectopic Pregnancy

Day	Test	Therapy or procedure
1	beta-hCG, CBC, blood type and screen AST, BUN, creatinine	MTX 50 mg/m^2 IM
4	beta-hCG	
7	beta-hCG	Repeat MTX if day 7 hCG < 15% lower than day 4 hCG

beta-hCG, beta human chorionic gonadotrophin; CBC, complete blood count; AST, aspartate aminotransferase; BUN, blood urea nitrogen; MTX, methotrexate.

future pregnancy [7]. HSG is the radiographic evaluation of the uterine cavity and fallopian tubes after the administration of a radio-opaque medium through the cervical canal. It is a safe and inexpensive procedure, being the most cost-effective method in the study of the Fallopian tubes [8, 9].

The aim of this study is to evaluate if there is a residual effect on tubal patency after successful systemic methotrexate treatment of un-ruptured tubal ectopic pregnancy.

Patients and Methods

This is an observational retrospective study carried out at obstetrics and gynecology departments; Zagazig university hospitals, Egypt, in the period from June 2009 to May 2010. During this period 72 women were diagnosed as unruptured tubal ectopic pregnancy. Systemic treatment with a single dose methotrexate (50 mg/m^2 intramuscularly) was used for 32 women and 40 cases underwent surgery. HSG was performed on 30 patients (successfully managed with methotrexate) and 40 cases that underwent unilateral salpingectomy (as initial treatment). Two patients in the salpingectomy group were missed during follow up. All women were informed about the study. A written consent was obtained from all patients after the entire management and procedure was described.

Diagnosis of ectopic pregnancy

According to our unit's protocol, ectopic pregnancy was diagnosed by means of patient's history and examination, transvaginal ultrasound examination (by evaluating the cavity of the uterus in order to exclude intrauterine pregnancy and viewing an image characteristic of an extraovarian adnexal mass using a 7.5-MHz transvaginal probe (Toshiba, Nemio XG SSA-580A) and peripheral blood sample was taken to measure the levels of serum β-HCG on admission and 48 hour later to be used in the analysis and diagnosis.

Methotrexate treatment for ectopic pregnancy

The inclusion criteria [10] for treatment with methotrexate (MTX) were: hemodynamic stability without evidence of active bleeding or hemoperitoneum, desire of future progeny, absence of contraindications for MTX, gestational sac with maximum diameter of < 3.5 cm, stable or rising beta-hCG levels with peak values of < 15,000 mIU/mL and no embryonic cardiac motion. Contraindications to Methotrexate therapy [10] were: hepatic dysfunction (aspartate aminotransferase level > 2 times normal), renal disease (serum creatinine level > 1.5 mg/dL), active peptic ulcer disease, blood dyscrasia (leukocyte count < 3000 cells/μL or platelet count < 100,000/μL), known MTX sensitivity and breastfeeding. The patients who satisfied the selection criteria were treated with a single intramuscular dose of MTX (50 mg/m^2) as showed in Table 1. The formula used for assessment of body surface area in square meters was: (height (cm) + weight (Kg) − 60)/100. Patients with declining beta-hCG levels between days four and seven were monitored as outpatients weekly until their beta-hCG levels were below 5 mIU/mL. Hospitalization was indicated for cases with significant abdominal pain, or suspected tubal rupture. The treatment was considered to be a successful when the levels of beta-hCG became negative (< 5 mUI/mL), and to be a failure when surgery was necessary.

Hysterosalpingography

HSG was performed in immediate postmenstrual phase, 3 months after the successful medical treatment for the EP (when the levels of beta-hCG became negative and the image of an extraovarian adnexal mass disappears at transvaginal ultrasound). Before the procedure was done, a pregnancy was ruled out, vaginal infections were treated and doxycycline prophylaxis was recommended to all patients. Because patients may experience cramping during the HSG, women were advised to take a nonsteroidal anti-inflammatory drug one hour prior to the procedure. The procedure was per-

Table 2. The Ipsilateral and Contralateral Tube Patency Following Methotrexate Treatment and Salpingectomy

Hystsalpingography	Ipsilateral tube Obstruction Patency	Contralateral tube Obstruction Patency	Total
MTX	5 (16.7%), 25 (83.3%)	2 (6.7%), 28 (93.3%)	30
salpingectomy	-	7 (17.5%), 33 (82.5%)	40

formed with a sterile technique, with a single-tooth tenaculum applied to align the cervical canal and uterine cavity. Approximately 10 mL of water soluble contrast medium was injected through a cannula. Fluoroscopic examination was performed during the injection with patient repositioning as necessary. The examination was performed, read, and interpreted by a radiologist.

Statistical analysis

The Fisher exact test with 5% significance level was applied to compare the tubal patency levels seen via HSG following MTX management and salpingectomy.

Results

A total number of 72 women were diagnosed as un-ruptured tubal ectopic pregnancy. The age of women (mean ± SD) was 29 ± 6 years. Parity ranged from 1 to 3. All women have no history of previous ectopic pregnancy. The initial treatment with a single dose intramuscular MTX was effective in 28 cases (87.5%) of the situations. In the failed 4 cases (12.5%), a second single dose intramuscular MTX treatment was offered. Treatment was failed only in two cases and managed by salpingectomy. The ipsilateral tube patency after MTX treatment was seen in 83.3% of the cases (25 out of 30). The contralateral tube patency levels were 93.3% and 82.5%, following methotrexate treatment and salpingectomy, respectively. The contralateral tube obstructions were 6.7% and 17.5% following MTX and salpingectomy, respectively. There was no significant difference between the groups as showed in Table 2.

Discussion

Evidence shows that fertility decreases following an EP [11]. It has been found that 10 to 50% of ectopic pregnancy has a subsequent ectopic pregnancy and 60 to 70% has fertility problems. Future fertility in these patients is dependent on several factors, including age, history of infertility, history of previous EP, tubal rupture, and contralateral tubal lesion [12, 13]. The subsequent pregnancy rate was also significantly influenced by the findings on the HSG, being higher in the patients with normal HSG. Thus, it seems reasonable to assess tubal permeability following a medical treatment of an EP in those women who are willing to have future pregnancy. The Practice Committee of the American Society for Reproductive Medicine published that MTX treatment was successful in 78-96% of selected patients [14]. It seems clear that in order to achieve comparable good results, compliance with patient selection criteria is essential. In our study the medical treatment with single dose MTX for EP was effective and safe (93.8%) as a primary treatment. In the MTX group, the HSG findings from the ipsilateral tube showed that 83.3% of the diseased tubes were patent and 16.7% were obstructed. Within the same group, the contralateral tube was patent in 93.3% and obstructed in 6.7%. HSG findings of bilateral tubal obstruction were found in 3.3% of women. The difference between the obstruction rates for the ipsilateral (16.7%) and contralateral tubes (6.7%) could be attributed to post-treatment sequelae of the tubal pregnancy. The contralateral tube obstruction may be a reflection of the tube disease prior to the tubal pregnancy. These patients almost presented history of tubal risk factor of infertility such as previous tubal pathology and/or pelvic surgery. In salpingectomy group, the contralateral tube was patent in 82.5% and obstructed in 17.5%. The contralateral tube obstruction rates in salpingectomy group 17.5% were more frequent than in MTX group 6.7% (but not significance). This could be attributed to that surgery may give rise to more occurrences of adhesions because of the peritoneal factor, thereby resulting increase the risk of recurrent ectopic pregnancy or decrease fecundity rate. Hence,the potential advantage of medical treatment of ectopic pregnancy is the avoidance of any iatrogenic injury to the Fallopian tubes, which may decrease the risk of recurrent ectopic pregnancy and improve the chance of successful intrauterine conception. In a fertile women seeking future pregnancy after successful medical treatment of an ectopic pregnancy, the HSG findings of a unilateral tubal obstruction would unlikely affect the initial expectant management .While women diagnosed bilateral tubal obstruction would probably benefit from HSG, being recommended for in vitro fertilization. These patients almost presented history of previous tubal risk factors of infertility. Therefore, HSG is

of beneficial prognostic value in such patients, in whom a prompt diagnosis of bilateral obstruction would result in adequate counseling towards early in vitro fertilization.

Conclusions

The medical treatment with MTX for EP is effective. Routine HSG following medical treatment for an EP does not seem necessary but might be considered in selected risk cases. We recommend further larger studies to confirm the present results.

Acknowledgement

We have to thanks all gynecologic residents who helped us throughout the study.

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