MedCrave
Step into the World of Research
International Journal of Pregnancy & Child Birth

Research Article

Open Access
CrossMark

Hysterosalpingography for tubal patency after methotrexate therapy for ectopic pregnancy

Abstract

Introduction: Ectopic pregnancy is a serious cause of tubal loss or dysfunction among women in the reproductive age. Medical treatment is a commonly prescribed management under certain circumstances. It is associated with a high success rate, but tubal affection is a result. This study evaluated the effect of medical treatment on patients with unruptured tubal pregnancy.

Materials and methods: This was a prospective cohort study conducted at the Obstetrics and Gynecology Department of Suez Canal University Hospitals, from January 2016 to June 2019. We recruited Fifty- six patients with unruptured tubal pregnancy.All patients were managed with medical treatment, methotrexate therapy. After confirmation of successful medical treatment, hysterosalpingography was done three months after treatment for the evaluation of tubal patency.The outcome measure was the rate of tubal patency after medical treatment for unruptured tubal ectopic pregnancy.

Results: The present study revealed that 71.4% of patients (40 cases) had patent tubes, and 28.6% had blocked tubes. Moreover, 21.4% of patients have ipsilateral tubal block only, 3.6% have a contralateral tubal block, and 3.6% have a bilateral tubal block. Significant risk factors for tubal block were history suggestive of PID, acute PID hospitalization, and history of septic miscarriage (p value < 0.05).

Conclusion: Methotrexate provided successful fertility-preserving treatment for women with unruptured ectopic pregnancy, yet associated with tubal block.

Keywords: ectopic pregnancy, tubal ectopic pregnancy, risk factors, methotrexate, tubal patency, hystero-salpingography

Volume 6 Issue 3 - 2020

Ahmed A Aboelroose, Ahmed M Fakhr Eldein, Waleed A Sayed Ahmed, Omima T Taha
Department of Obstetrics and Gynecology, Suez Canal University, Egypt

Correspondence: Omima Tharwat Taha, Lecturer of Obstetrics and Gynecology, Department of Obstetrics and Gynecology, Faculty of Medicine, Suez Canal University, Address: ring road, kilo 4.5, Ismailia, Egypt,
Email omimatharat@yahoo.com

Received: April 25, 2020 | **Published:** June 22, 2020

Abbreviations: IUCD, intra-uterine contraceptive device; PID, pelvic inflammatory disease; EP, ectopic pregnancy

Key message

Medical treatment for ectopic tubal pregnancy is an effective modality of treatment. It may be associated with tubal destruction. This needed to be evaluated with hystero-salpingography in our population with the results of high rates of tubal patency. Patient counseling should include the possibility of (28%) tubal block after medical treatment.

Introduction

Ectopic pregnancy (EP) is defined as a conceptus implanted outside the natural uterine cavity. The most common site of implantation is within the fallopian tube (95.5%), followed by ovarian (3.2%) and abdominal (1.3%) sites.[1] Worldwide, EP represents the first cause of maternal death in early pregnancy.[2] In African developing countries, studies have reported that case mortality rates due to EP (1–3%) were ten times higher than that reported in the developed countries.[3]

Methotrexate is a chemotherapeutic drug -folic acid antagonist- and acts as an antimetabolite, by combining with the enzyme tetrahydrofolate reductase. It inhibits the synthesis of purine and pyrimidine bases, essential for the formation of DNA and RNA. Its action is exerted on cells with fast replication, including the trophoblastic cells of pregnancy.[4] Systemic methotrexate is a safe and effective treatment for EP. Methotrexate avoids anesthesia and is less invasive, and less costly than surgery.[5] Methotrexate has contributed to alleviating some of the disease burden of ectopic pregnancy, where it affords approximately 25% of women a nonsurgical and fertility-preserving treatment option.[6]

Varying results are present regarding tubal patency after methotrexate treatment of unruptured ectopic pregnancy with lacking published studies held in Egypt; hence we conducted this study to fill that gap of data and give an overview about tubal patency after using medical treatment for ectopic pregnancy instead of surgical methods.

Materials and methods

This was a prospective cohort study conducted after approval of our research ethics committee. It was carried out in the Obstetrics and Gynecology emergency ward in Suez Canal University hospitals upon 56 women with unruptured tubal ectopic pregnancy. We recruited all patients from January 2016- January 2019 with ectopic pregnancy upon the criteria for medical treatment according to NICE guidelines: a) no significant pain, b) unruptured ectopic tubal pregnancy with an adnexal mass smaller than 35 mm with no visible heartbeat, c) serum HCG levels less than 1500IU/L, d) no intrauterine pregnancy, and e) able to return for follow up.[7] Patients who refused to participate in the study or were unable to continue the follow-up program were excluded. Diagnosis of ectopic pregnancy was made using a transvaginal ultrasound examination. Criteria for diagnosis included an adnexal mass, empty uterine cavity, and extaruterine gestational sac with or without cardiac activity combined with serum HCG level

for correlation.[8] A full history was taken from the patients, including personal data as age, gravidity, parity, history of previous ectopic pregnancy, history of previous pelvic operation, history of IUCD (intra-uterine contraceptive device) usage, history suggestive of prior pelvic inflammatory disease (PID), and history of septic miscarriage.

Patients eligible for the study received a single dose of methotrexate 1mg/ kg — body weight as an intramuscular injection. Patients were followed up using serum beta- HCG levels that were taken two times in the first week (days 4 and 7) after treatment and then one serum HCG measurement per week until a negative result is obtained. If HCG levels plateau or rise, patients were reevaluated, and further treatment was considered (either another dose of methotrexate or surgical treatment).[7] Hystero-salpingography was done for patients with successful medical therapy after three months.

Results

Table 1 and 2 show demographic information and frequency of risk factors for ectopic pregnancy in the study participants, respectively. Table (3) illustrated that there were statistically significant relationships between history of PID, acute PID hospitalization, and history of septic miscarriage and tubal block. In contrast, there were no statistically significant relationships either between history of pelvic operation or history of previous ipsilateral ectopic pregnancy with tubal block. Ten of 16 (62.5%) patients with blocked tube had never used the IUCD, while 2 used IUCD in the past and 4 at the time of diagnosis of EP. Patient who used IUCD in the past had lower incidence of tubal blockage, only 2 out of 24 (Table 4). Forty patients (71.4%) had patent tubes, while 16 (28.6%) had blocked tubes. Twelve out of 56 (21.4%) patients had ipsilateral tubal block, 2 (3.6%) had contralateral tubal block, and 2 (3.6%) had a bilateral tubal block (Figure 1). Seventy five percent of the patients had a proximal block, 12.5% had a distal block, and 12.5 % had both proximal and distal blockage (Figure 2). Additionally, 7.1 % of patients (4 cases) had hydrosalpinx.

Table 1 Demographic data of participant females (n=56)

Age (mean±sd)		**30.04±6.03**
Gravidity (median, range)		3 (1-5)
Parity (median, range)		2 (0-4)
Infertility n (%)	Primary	4 (7.1%)
	Secondary	10 (17.9%)

Table 2 Frequency distribution table of risk factors of ectopic pregnancy (n=56)

Risk factors	**No. (%)**
History suggestive of PID	16 (28.6%)
Acute PID hospitalization	6 (10.7%)
History of ectopic pregnancy	10 (17.9%)
History of a septic Miscarriage	10 (17.9%)
History of pelvic operation	42 (75%)
Ovarian cystectomy	1 (1.79%)
Myomectomy	2 (3.57%)
cesarean section	39 (69.64%)
IUD usage	
Never used	24 (42.9%)
Used in the past	24 (42.9%)
Used at the time of EP	8 (14.3%)

IUCD, intrauterine device; PID, pelvic inflammatory disease; EP, ectopic pregnancy

Table 3 Risk factors of ectopic pregnancy and tubal block (n=56)

Risk factors	**Tubal block**		**p-value**
	Patent (n=40)	**Blocked (n=16)**	**(Statistics)**
	No. (%)	**No. (%)**	
History suggestive of PID	8 (20%)	8 (50%)	0.047*a
Acute PID hospitalization	2 (5%)	4 (25%)	0.049*a
History of ipsilateral ectopic pregnancy	6 (15%)	4 (25%)	0.448
History of a septic miscarriage	4 (10%)	6 (37.5%)	0.024*a
History of pelvic operation	30 (75%)	12 (75%)	1.000 a

Fischer exact test (normal cells<5 are more than 20 %),*Statistically significant at p<0.05

Table 4 IUCD usage and tubal block (n=56)

IUCD usage	**Total No.**	**Tubal block**		**p-value**
		Patent (n=40)	**Blocked (n=16)**	**(Statistics)**
		No. (%)	**No. (%)**	
Never used	24	14 (35%)	10 (62.5%)	
Used in the past	24	22 (55%)	2 (12.5%)	0.013*
Used at the time of EP.	8	4 (10%)	4 (25%)	

*Statistically significant at p<0.05 using the Chi-square test, EPis an ectopic pregnancy

Citation: Aboelroose AA, Eldein AMF, Ahmed WAS, et al. Hysterosalpingography for tubal patency after methotrexate therapy for ectopic pregnancy. *Int J Pregn & Chi Birth.* 2020;6(3):76–79. DOI: 10.15406/ipcb.2020.06.00201

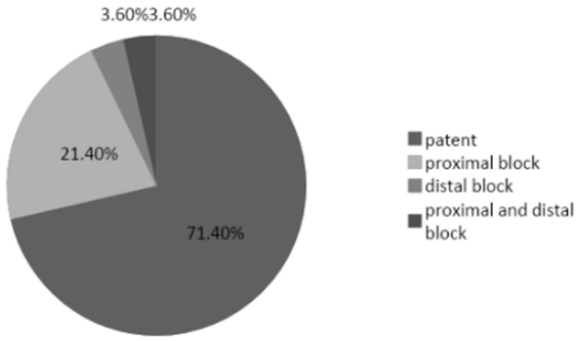

Figure 1 Frequency distribution of tubal patency.

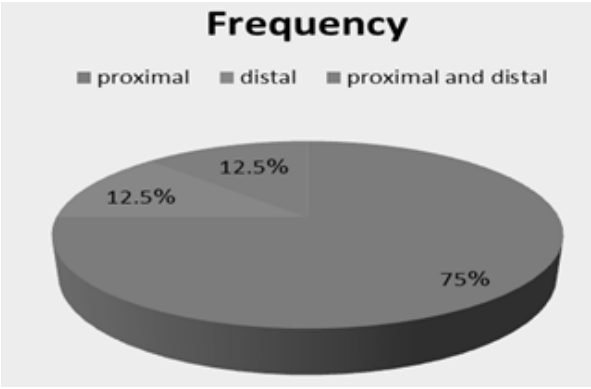

Figure 2 Frequency distribution of site of tubal block.

Discussion

The present study revealed that 71.4% of patients had patent tubes, and 28.6% had blocked tubes. Moreover, 21.4% of patients had ipsilateral tubal block only, 3.6% had a contralateral tubal block, and 3.6% had a bilateral tubal block. This can be due to the action of MTX therapy destroying cells in fast replication (like the trophoblastic cells), resulting in residual lesion/tissue remaining (remnants of conception) in the Fallopian tube, which may then occlude the tube.[9] Also, the inflammatory reaction occurring at the site of implantation may result in intratubal adhesions affecting tubal patency, explaining the occurrence of ipsilateral tubal block.However**,** acontralateral tubal block could probably be due to a tubal disease occurring before the current pregnancy as PID, salpingitis, or previous surgery.[10] The current study findings were consistent with a previously reported one, in which ipsilateral tube patency was as high as 84% after using methotrexate treatment, and the contralateral tubal patency was 97% [(9)]. Previous researchreported a general ipsilateral tubal patency rate of 66.7% (26/39) in women treated with methotrexate.[11]

In another study conducted earlier, higher rates of tubal patency were reported (97.5%) after combined systemic and local methotrexate therapy. This difference in results can be explained by different methods of treatment.[12] We postulated that tubal patency would depend on the size and site of EP, as well as the status of the tube before pregnancy; i.e., the larger the ectopic, the more liable the obstruction to occur. Also, ectopic pregnancies in the isthmus would be more likely to result in occlusion of the tube compared to EP in the ampulla (owing to its larger size and capacity). Also, if there was a risk factor for tubal occlusion (PID), this may facilitate tubal obstruction if EP occurred at that site. With regards to tubal block and PID, there was a significant relationship between them. Twenty percent and 50% of patients with patent and blocked tubes, respectively had PID. PID is an inflammatory process that destroys the tubal architecture and the ciliary function. It also, causes pelvic adhesions, leading to an increased risk of ectopic pregnancy. These findings were in agreement with previous research in which 30/155 patients with suspected acute PID had tubal occlusion and adnexal adhesions.[13] Moreover, in a study conducted in 2004, revealed that the most widely recognized cause of tubal factor infertility was tubal block caused by an infection (Neisseria gonorrhea or Chlamydia trachomatis). There is usually a time lag between acute PID and when women first consultation for fertility.[14] The results of that study emphasized the significant relationship between PID and tubal block, which was consistent with the current study results.

The present study revealed that 7.1% of patients had hydrosalpinx. It was more likely that tubal occlusion and subsequent hydrosalpinx were consequences of EP. These findings were consistent with the mentioned study,[15] which demonstrated that 9 (6.3%) of patients had tubal patency, but with defect, namely a non-obstructive hydrosalpinx. In the present study, parity range was (0-4) with a median of 2. The history of infertility (primary and secondary) was 25%. The history of previous ectopic pregnancy among patients was 17.9%. Also, the history of septic miscarriage was 17.9%. The history of pelvic operation was as high as 75% (1.79% had ovarian cystectomy, 3.57% had myomectomy, and 69.64% had cesarean section). Regarding IUCD usage, 42.9% of them had a history of IUCD use, and 14.3% were current users.

A previous study conducted in Egypt (2012)[16] showed that ectopic pregnancy was common among multiparous females with 1-3 deliveries (52%), as they have a higher rate of pelvic operations. History of PID was reported in 17% of patients. Also, 6% of cases had a history of infertility, and 5% had a history of using IUCD. A history of previous pelvic surgery was reported in 4%, one of them was tubal surgery (right salpingectomy due to hydrosalpinx), and no patient-reported history of last ectopic pregnancy. This variation of the results may be due to different sample sizes (1333 women) and diverse geographical regions (Ismailia and Assuit) with different rates of cesarean section. Besides, the objectives of both studies were different. In addition, another study showed that the most significant risk factor for an EP and fertility loss was a history of a previous EP (the recurrence rate of EP is 10% to 15% after the first EP and 30% after the second). Also, tubal surgery and sexually transmitted infections were responsible for the majority of cases of tubal damage leading to ectopic pregnancies. Postabortal sepsis or puerperal infection, endometriosis, and appendicitis were additional causes of tubal pathology. One attack of salpingitis resulted in a subsequent EP in up to 9% of patients.[17]

Conducting further researches studying the effect of size and site of tubal EP on the prognosis of tubal patency after MTX therapy is recommended. A prospective evaluation of the impact of methotrexate therapy on future fertility is warranted. Although the research has reached its objectives, there were some limitations: a) the small sample size, b) conducting the research on patients who were attending the SCU hospital clinic limiting generalizability of results, c) no comparative group, as it is a descriptive study, d) the HSG gives a radiological picture to assess the patency but does not determine the actual tubal function, e) the history of the patients' tubal patency was not known, and f) the fertility of the patients' could not be assessed as the study was a short prospective study, with a follow up for three months only.

Citation: Aboelroose AA, Eldein AMF, Ahmed WAS, et al. Hysterosalpingography for tubal patency after methotrexate therapy for ectopic pregnancy. *Int J Pregn & Chi Birth.* 2020;6(3):76–79. DOI: 10.15406/ipcb.2020.06.00201

Conclusion

Tubal patency after methotrexate therapy for the management of unruptured tubal ectopic pregnancy was high. However, this may lead to tubal block and hydrosalpinx in some patients.

Acknowledgments

None.

Conflicts of interest

Author declare that there is no conflict of interest.

Funding

None.

References

1. Varma R, Gupta J. Tubal ectopic pregnancy. *BMJ Clinical Evidence*. 2009;1406.
2. Autry A. Medical Treatment of Ectopic Pregnancy. *Obstetrics & Gynecology.* 2013;122(4):733–734.
3. Goyaux N, Leke R, Keita N, et al. Ectopic pregnancy in African developing countries. *Acta obstetricia et gynecologica Scandinavica*. 2003;82(4):305–312.
4. Barnhart K, van Mello NM, Bourne T, et al. Pregnancy of unknown location: a consensus statement of nomenclature, definitions, and outcome. *Fertility and sterility*. 2011;95(3):857–866.
5. Mol F, Mol BW, Ankum WM, et al. Current evidence on surgery, systemic methotrexate and expectant management in the treatment of tubal ectopic pregnancy: a systematic review and meta-analysis. *Human reproduction update*. 2008;14(4):309–319.
6. Farquhar CM. Ectopic pregnancy. *The Lancet*. 2005;366(9485):583–591.
7. National Institute for Health and Care Excellence. Ectopic pregnancy and miscarriage; diagnosis and initial management. 2019.
8. Elson CJ, Salim R, Potdar N, et al. Diagnosis and management of ectopic pregnancy. *BJOG.* 2016;123:e15–e55.
9. Elito J, Han KK, Camano L. Tubal patency after clinical treatment of unruptured ectopic pregnancy. *International Journal of Gynecology & Obstetrics*. 2005;88(3):309–313.
10. Elito Junior J, Han KK, Camano L. Tubal patency following surgical and clinical treatment of ectopic pregnancy. *Sao Paulo Medical Journal*. 2006;124(5):264–266.
11. Soliman AT, Salem HA. Unruptured tubal ectopic pregnancy: conservative laparoscopy or methotrexate?. *Journal of Evidence-Based Women's Health Journal Society*. 2014;4(4):179–183.
12. Debby A, Golan A, Sadan O, et al. Fertility outcome following combined methotrexate treatment of unruptured extrauterine pregnancy. *BJOG*: *An International Journal of Obstetrics & Gynaecology*. 2000;107(5):626–630.
13. Eschenbach DA, Wölner-Hanssen P, Hawes SE, et al. Acute pelvic inflammatory disease: associations of clinical and laboratory findings with laparoscopic findings. *Obstetrics & Gynecology*. 1997;89(2):184–192.
14. Mårdh PA. Tubal factor infertility, with special regard to chlamydial salpingitis. *Current opinion in infectious diseases*. 2004;17(1):49–52.
15. Garcia Grau E, Checa Vizcaíno MÁ, Oliveira M, et al. The value of hysterosalpingography following medical treatment with methotrexate for ectopic pregnancy. *Obstetrics and gynecology international*. 2011.
16. Abd el-kader LM, Salim HTh, Yousif AA, et al. Study on the Management of Ectopic Pregnancy in Women's Health Center-Assiut University Hospitals. *Med J Cairo Univ*. 2014;82(1):815–819.
17. Juneau C, Bates G W. Reproductive outcomes after medical and Surgical Management of Ectopic Pregnancy. *Clinical Obstetrics and Gynecology*. 2012;55(2):455–460.