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ORIGINAL ARTICLE / ÖZGÜN ARAŞTIRMA

Tubal passage control after methotrexate treatment in ectopic pregnancies

Ektopik gebeliklerde metotreksat tedavisinden sonra tubal pasaj kontrolü

Neval Yaman Görük[1], Abdulkadir Turgut[2], Senem Yaman Tunç[3], Necdet Süer[4]

[1]Ümraniye Eğitim ve Araştırma Hastanesi, İstanbul, Türkiye
[2]Dicle Üniversitesi Tıp Fakültesi, Diyarbakır, Türkiye
[3]Batman Dünya Hastanesi, Batman, Türkiye
[4]Medeniyet Üniversitesi Göztepe Eğitim ve Araştırma Hastanesi, İstanbul, Türkiye

ABSTRACT

Objectives: In this study, it was aimed to evaluate the results of ipsilateral tubal passage control in the cases treated with methotrexate (MTX).

Materials and methods: Totally 30 patients aged between 21 and 40 years who have received single dose MTX treatment due to ectopic pregnancy was included. All patients were as hemodynamically stabile. Serum beta human chorionic gonadotropin (BhCG) levels and ultrasonographic findings prior to the MTX treatment were recorded. Patients were re-evaluated 6 months after serum BhCG levels became negative for the outcome of treatment.

Results: The mean age of the 30 cases was 30.6±4.4 years. The BhCG levels of the cases was changing between 160 and 10910, their average is 2387±2499 IU/L. The MTX dose was changing between 50 to 100 mg, with average of 67.7±13.5 mg. Four (13.3%) of the cases received additional dose of MTX. Laparotomy was performed in 3 (10%) cases due to tubal rupture developing during the treatment. Among 27 cases on whom the tubal passage control is made 6 months after the treatment, tubal passage was found to be open in 22 (81.5%) of the cases and closed in 5 (18.5%). There was no significant difference between the BhCG levels of cases with open and closed tubal passage ($p>0.05$).

Conclusion: The medical treatment to be applied on non-ruptured ectopic pregnancies has many advantages. Less tubal damage occurs by the medical treatment, it decreases the morbidity for anesthesia and surgery. *J Clin Exp Invest 2011; 2 (4): 400-403*

Key words: Ectopic pregnancy, methotrexate, tubal passage

ÖZET

Amaç: Bu çalışmada metotreksat (MTX) ile tedavi olmuş ektopik gebelik olgularında ipsilateral tubal pasaj kontrolü yapılarak sonuçların değerlendirilmesi amaçlandı.

Gereç ve yöntem: Çalışmaya ektopik gebelik nedeniyle tek doz MTX tedavisi almış yaşları 21 ile 40 arasında değişmekte olan 30 hasta dahil edildi. Hastaların tümü hemodinamik olarak stabildi. MTX tedavisine başlamadan önceki serum beta human chorionic gonadotropin (BhCG) seviyeleri, ultrasonografi bulguları kaydedildi. Serum BhCG düzeyleri negatif olduktan 6 ay sonra tubal pasaj kontrolü yapılan hastalar tedavi sonuçları ile tekrar değerlendirildi.

Bulgular: Çalışmaya alınan 30 olgunun yaş ortalaması 30.6±4.4 yıl idi. Olguların BhCG düzeyleri 160 ile 10910 IU/L arasında değişmekte olup, ortalaması 2387±2499 IU/L idi. Kullandıkları MTX dozları 50 mg ile 100 mg arasında değişmekte olup, ortalaması 67.7±13.5 mg idi. Olguların 4'üne (%13.3) ek doz MTX uygulandı. Olguların 3'üne (%10) tedavi sırasında gelişen tubal rüptür nedeniyle laparotomi yapıldı. Tedaviden 6 ay sonra tubal pasaj kontrolü yapılan 27 olgunun, 22'sinin (%81.5) tubal pasajı açık, 5'inin (%18.5) kapalı bulundu. Tubal pasajı açık olan olgular ile kapalı olan olguların BhCG düzeyleri arasında istatistiksel olarak anlamlı bir farklılık bulunmadı ($p>0.05$).

Sonuç: Rüptüre olmamış ektopik gebeliklerde uygulanacak medikal tedavi ile daha az tubal hasar meydana gelmekte, anesteziye ve cerrahiye ait morbidite azaltmaktadır.

Anahtar kelimeler: Ektopik gebelik, metotreksat, tubal pasaj

INTRODUCTION

The ectopic pregnancy is defined as the settlement of fertilized ovum outside the uterus, frequently at fallopian tubes.[1] Together with the fact that abnormal localization is at fallopian tube at 90%, more rarely abdominal, cervical, ovarian, interstitial, in-

Yazışma Adresi /Correspondence: Dr. Neval Yaman Görük
Ümraniye Eğit. ve Araş. Hast. Kadın Hast. ve Doğum Kliniği, Ümraniye, İstanbul E-mail: neval-yaman81@hotmail.com
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traligamentous, heterotopic, multiple ectopic pregnancies can be observed.[2] The ectopic pregnancy is an important reason for maternal mortality and morbidity. However, by early establishment of ectopic pregnancy diagnosis with the help of contemporary diagnostic methods, the treatment modalities which are more conservative than before can be applied.

For this aim, the more frequently used agent has become methotrexate (MTX). As the experiences obtained with the medical treatment flourish, single dose treatment regimens have appeared for simplifying the treatment, increasing the harmony, decreasing the side effects and costs.[3]

The reproductive result after the ectopic pregnancy is generally evaluated with the determination of tubal opening with histerosalpingography (HSG), future pregnancy and ectopic pregnancy's relapse rate. In this study, the ipsilateral tubal passage control has been done in cases treated with MTX, and their results have been evaluated.

MATERIALS AND METHODS

Totally 30 cases which have been given medical treatment due to ectopic pregnancy diagnosis in a Training and Research Hospital Clinic of Obstetrics and Gynecology have been included to study content. To the patients, the ectopic pregnancy diagnosis has been established by applying anamnesis, gynecological examination, physical examination, pregnancy test, ultrasonography (USG) and dilatation and curettage (D&C). All patients have been informed about their statuses, the risks that they have been told. To the patients in which findings in favors of rupture has not been determined and which have been stabile hemodynamically, the information on the treatment protocol has been given and their consents have been obtained and single dose MTX treatment has been started.

From all patients, before starting the treatment, serum BhCG, full blood count, kidney and liver function tests have been requested. The serum beta human chorionic gonadotropin values and USG findings have been recorded. Then, MTX 50 mg/ m^2 dose has been made as i.m. At the 4th day of the treatment, the serum BhCG values have been repeated. The increases in the serum BhCG concentration between the 1st and 4th days have been accepted as normal. Between the 4th and 7th day, in the patients in whose serum BhCG concentration there is 15% decrease, the single dose MTX treatment has been accepted as adequate. Then, till the levels have become indeterminable, the weekly BhCG follow-ups have been realized. However, to the patients in which any increase in the serum BhCG concentration after this or a decrease under 15% at the 7th day, the treatment protocol has been repeated.

The patients benefiting from the MTX treatment have been called for control after 6 months after their serum BhCG levels have reached to negative values. The gynaecological examination and transvaginal USG have been realized. Their USG findings have been recorded. The patients requesting the evaluation of the oviducts opening at the side where the ectopic pregnancy develops have been informed about this issue. In the direction of the patients' preferences, the ipsilateral tubal passage controls have been made in 18 of them with diagnostic laparoscopy and in 9 of them with HSG.

When HSG is imaged, 10ml iodine has been given inside from cervix with hysterography tool in a way not passing the pressure of 180 mm Hg to the patient in dorsolithotomy position in the sterile environment. Meanwhile, the patient has been brought to the neutral position, two units of spot film have been imaged, and the tubal opening has been controlled.

To the cases to which the diagnostic laparoscopy will be applied, information regarding the interventions to be applied and their complications have been given and their approvals have been obtained. The cases have been given the dorsolithotomy position under the general anaesthesia and the bladder has been emptied with sterile foley catheter. The venter dermis, vulva and vagina have been cleaned with povidone iodine. The uterus elevator has been placed to cervix. The verres injection has been entered while the patients have been at neutral position. After the confirmation of peritoneal entrance, the abdomen has been inflated with carbon dioxide gas till the pressure of 15 mmHg. After the trochar insertion, the patient has been brought to trendelenburg position and the operation has been started. Uterus, oviducts, ovaries has been panoramically evaluated. 50 ml methylene blue has been given inside from cervix with rubin tube placed as transvaginal and it has been observed whether transmission from oviducts is available or not.

The treatment results of these patients whose tubal opening control has been realized with diagnostic laparoscopy and HSG have been examined and evaluated prospectively.

Statistical analysis

For statistical analyses, NCSS (Number Cruncher Statistical System) 2007&PASS 2008 Statistical

Software (Utah, USA) program has been used. While evaluating the study data, in addition to the descriptive statistical methods (Mean, Standard deviation, frequency), Mann Whitney U test of the quantitative data has been used. In the comparison of the qualitative data, Fisher's Exact Chi-Square test has been used. The statistically significance has been accepted at the level of $p<0.05$.

RESULTS

The average age of the cases was 30.63±4.36 years. Twelve of the cases (40%) have experienced surgery previously. While 20 of the cases (66.7%) have not used contraception method, 6 of the cases (20%) use intrauterine device, 2 of the cases (6.7%) use tubal ligation and 1 of the cases (3.3%) uses depo-provera and oral contraceptives.

As the cases' BhCG levels change between 160 IU/L and 10910 IU/L, its average is 2387±2500 IU/L. As the MTX doses that they have used change between 50 mg and 100 mg, its average is 67.7±13.5 mg.

While the bulk dimension of 6 of the cases (20%) is below 4 cm, 24 of them (80%) is between 4 cm and 5.5 cm. Four of the cases (13.3%) received additional dose MTX. No significant difference was found in BhCG levels of the cases who received additional dose MTX and who not received ($p>0.05$). Also no significant relationship was found between additional MTX treatment and bulk dimension ($p>0.05$) (Table1).

Table 1. Dilatation and curettage, bulk size, additional treatment, laparotomy and tubal passage control

		n	%
D&C	Executed	21	70.0
	Not executed	9	30.0
Bulk size	<4 cm	6	20.0
	≥4-5.5 cm	24	80.0
Additional treatment	Available	4	13.3
	NA	26	86.7
Laparotomy	Available	3	10.0
	NA	27	90.0
Tubal passage control	open	22	81.5
	close	5	18.5

D&C: Dilatation and curettage

It has been found that tubal passage of 22 of 27 cases (81.5%) was open while tubal passage control was performed and 5 of them (18.5%) were closed. No significant difference was found in BhCG levels of the cases with open or closed tubal passage ($p>0.05$). Also, there was no significant relationship between tubal passage opening and bulk dimension ($p>0.05$) (Table 2).

Table 2. The evaluation of tubal passage control

		Tubal passage control		P
		Open	Close	
hCG, Mean±SD	(Median)	1555±1464 (922)	4589±4117 (4354)	0.151
Bulk size, n (%)	<4 cm	3 (%13.6)	2 (%40.0)	0.221
	≥4-5.5 cm	19 (%86.4)	3 (%60.0)	

DISCUSSION

In the past ten years, the ectopic pregnancy incidence has increased dramatically. The increase in the sexual inherited disease risk, ovulation induction, assisted reproductive techniques, tubal sterilization and more accurate diagnosis methods used in the diagnosis make think that the ectopic pregnancy incidence increases in fact.[4]

The anamnesis and physical examination determine the patients under risk and increase the possibility of determining the non-ruptured ectopic pregnancies. In the normal pregnancies, when Transvaginal USG and b-HCG levels go over 1000-1500 IU/L, gestational sac can be observed.[5] In 90% of the ectopic pregnancies, the evidences regarding the extrauterine pregnancy can be determined. The determination of yolk salk, embryo, cardiac activity together with a gestational sac outside uterus make the establishment of ectopic pregnancy diagnosis and require emergency action.[6]

Stovall et al. have published the results of MTX treatment in 100 patients and 50 of the 100 cases had diagnosis with laparoscopy and 50 of them with non- laparoscopy algorithm. Full resolution has realized in 96 patients between 14- 92 days. In four patients, due to tubal rupture, laparotomy has been required; in one case, at a late period such as 23rd day of the MTX application, a rupture has occurred. In five patients, fetal cardiac activity has been observed and in all of these, the treatment has become successful. In 49 of 58 patients (84%) to

whom the HSG is applied in the advanced follow-up, it has been shown that the ipsilateral oviducts are open.[7]

In study of Hajenius et al. have reported single sided tubal opening rate after the medical treatment of the ectopic pregnancy has been compared with the conservative laparoscopic treatment. The tubal opening rate at the ipsilateral side after medical treatment has been similar to the conservative laparoscopic treatment (linear salpingotomy) and between 60%-85%.[8]

Elito et al. have evaluated tubal transmission prospectively with HSG in the ectopic pregnancy cases to which conservative method has been applied as a follow-up or methotrexate treatment in 2005. It has been found that the cases having starting BhCG value>5000 IU/L have 12 times more risk for oviducts obstruction. However, no relation has been determined between the obstruction and ectopic pregnancy bulk size.[9]

In this study, 6 months after the medical treatment, in 27 cases, tubal opening control has been made. It has been researched whether ipsilateral oviducts are open or not with HSG. In a similar way to the rates in the literature, it has been found that 22 of the cases (81.5%) has open similar sided oviducts and 5 of them (18.5%) has been closed. Between serum BhCG levels of the cases with open tubal passage and the cases with closed ones when they get diagnosis, a statistically significant difference was not found (Table 2). However, while the average BhCG value of the cases whose ipsilateral tubal passages are observed open is 922 IU/ ml, the average BhCG value has been found as 4354 IU/ ml in the cases whose similar sided tubal passages are closed. We think, if the patient number being increased, a statistically significant difference can be obtained.

In conclusion, it has been suggested that, the aim at the ectopic pregnancy treatment is to protect the fertility rather than saving life. With this aim, MTX has been researched very commonly and it is at the first rank among the methods, which are alternative to the surgery treatment. The medical treatment decreases the morbidity belonging to the anaesthesia and surgery. The success rate and the future reproduction performance are similar to the ones to whom the surgery treatment has been applied.

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