

Therapeutic Curettage On Follow Up Human Chorionic Gonadotropin Levels in Ectopic Pregnancy

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ABSTRACT

In this study, we aimed to investigate the effect of therapeutic curettage and adjuvant methotrexate treatments on follow up human chorionic gonadotropin levels in ectopic pregnancy.

Twenty-five patients who received methotrexate treatment out of 57 patients with a diagnosis of ectopic pregnancy and who completed their treatment at the hospital between 2016-2017 were included in the study. With random grouping, curettage was performed in 14 patients and was not performed in 11 patients. The percentage of changes in serum human chorionic gonadotropin levels between days 1 and 4, days 4 and 7, and days 1 and 7 were compared.

Comparing two groups, there was no statistically significant difference between the percentages of changes in serum human chorionic gonadotropin levels.

Early diagnosis and treatment of ectopic pregnancy, an important cause of maternal mortality in the first trimester, is crucial. Regarding the surgical burden and no significant changes in serum levels of human chorionic gonadotropin in patients treated with therapeutic curettage and concurrent methotrexate treatment, curettage should be performed in selected patients or in patients with difficulty in diagnosis.

Key Words: Ectopic pregnancy, methotrexate, serum human chorionic gonadotropin, therapeutic curettage

Introduction

Ectopic pregnancy is one of the major causes of maternal mortality in the first trimester (1-3). Patients present with abdominal pain, missed period and vaginal bleeding. Diagnosis is based on (a) clinical symptoms at admission, (b) plateau serum human chorionic gonadotropin (hCG) levels, (c) transvaginal ultrasonography (TVU) showing no intrauterine gestational sac and/or presence of gestational sac outside the uterus and/or presence of intrauterine pseudo sac and (d) absence of intrauterine cytotrophoblast and syncytiotrophoblast activity in the therapeutic curettage material (4). Because of its fatal course, rapid diagnosis and early treatment are important (5,6). Therefore, it is not always possible to wait for the pathological examination of the curettage material. For this reason, patients are diagnosed and treatment is initiated considering clinical symptoms at admission, serum hCG levels and TVU. Treatment can be done in two ways, methotrexate (MTX) therapy or surgical treatment (7).

In this study, the effect of therapeutic curettage on percentage changes between day 1, 4 and 7 serum hCG levels used in the follow-up of patients treated with MTX was investigated.

Materials and Methods

Patient Selection: Patients who were admitted to our hospital between 2016-2017 with a diagnosis of ectopic pregnancy based on medical history, TVU and follow-up serum hCG levels, and who completed their treatment in our hospital with a single dose MTX (50 mg/m², I.M.) with no requirement for second dose MTX or surgery were included in this study. Exclusion criteria were as follows: (a) patients with serum hCG levels above 10.000 IU, (b) ectopic pregnancy mass greater than 4 cm on TVU, (c) hemodynamically unstable patients, and (d) ectopic pregnancy with fetal heart rate activity.

Study Groups and Laboratory tests: Written informed consent was obtained from all participants. All patients were randomized to receive MTX therapy with concurrent therapeutic

Table 1. The clinical and demographic features of the two groups

	Patients with concurrent therapeutic curettage	Patients without concurrent therapeutic curettage	P
Age (year), mean \pm SD	31.3 \pm 4.73	30.3 \pm 5.85	NS
Gravida, median (min.-max.)	3.0 (1-16)	2 (1-5)	NS
Parity, median (min.-max.)	1.0 (0-3)	1 (0-3)	NS
Abortion, n	5	3	NS
Endometrial thickness (mm), mean \pm SD	11.7 \pm 2.79	12.2 \pm 2.75	NS

SD: Standart deviation, mm: Millimeter, NS: Not significant

curettage or MTX therapy alone. The percentage changes between day 1,4 and 7 serum hCG levels were compared between two groups.

Statistical Analysis: SPSS version 22 (SPSS Inc., IL, USA) was used for statistical analysis. Histogram and Kolmogorov-Smirnov test were used for testing for normality of the distribution. Student's t-test and Mann-Whitney U tests were used for comparing differences between two groups, where appropriate. $p < 0.05$ was considered statistically significant.

Results

Clinical and Demographic Characteristics: Fifty-seven patients were diagnosed with ectopic pregnancy between 2016-2017 in our hospital and MTX treatment was administered to 25 (43.9%) patients. Of these patients, 14 (56%) underwent MTX therapy concurrent with therapeutic curettage (Group 1) and 11 patients (44%) underwent MTX therapy alone (Group 2).

The mean age of the patients was 30.8 ± 5.16 years, and the mean endometrial thickness was 11.9 ± 2.72 mm. The median values for gravida, parity, and abortion were 3 (min.-max. = 1-16), 1 (min.-max.=0-3), and 0 (min.-max. = 0-14), respectively. Out of a total of 14 endometrial analyses, a positive Arias-Stella reaction was found in 10 cases (71,4%), hypersecretory changes in 2 patients (14,3%), and proliferative changes in 2 patients (14,3%). The clinical and demographic features of the two groups were shown in Table 1.

Laboratory Results: The mean percent change in serum hCG levels was 24.1 ± 41.37 between days 1-7, 43.9 ± 23.04 between days 4-7 and 51.5 ± 37.78 between days 1-7. No statistically significant difference was found between Group 1 and Group 2 regarding percent changes between days 1-4, days 4-7 and days 1-7 ($p = 0.443$, $p = 0.614$, $p = 0.908$, respectively) (Table 2).

Discussion

In this study, the effect of concurrent therapeutic curettage on percentage changes in serum hCG levels between the first, fourth and seventh days of MTX therapy in patients receiving MTX therapy was found to be statistically insignificant compared with patients receiving MTX therapy alone.

Ectopic pregnancy is the most common life-threatening emergency in early pregnancy and remains an important cause of maternal mortality due to tubal rupture and catastrophic hemorrhage (8). Thus, rapid diagnosis and early treatment are important in the management. Ectopic pregnancy is usually diagnosed in the first trimester of pregnancy, mostly at 6-10 weeks of gestational age. Although investigating risk factors may help asymptomatic patients benefit from routine early imaging (9), patients without known risk factors were also found to be at risk (10). The physical findings of patients are variable and studies on the predictive value of specific risk factors and physical findings alone or in combination found that no combination correctly and consistently ruled out ectopic pregnancy (11).

In the clinical practice, pregnancy is mostly diagnosed by determining the urine or serum concentration of hCG. This hormone is detectable in urine and blood as early as 1 week before an expected menstrual period. In a normal pregnancy, the first-trimester hCG concentration rapidly increases, doubling about every 2 days (12). Patients with an ectopic pregnancy tend to have lower hCG levels than those with an intrauterine pregnancy (13). In our study, the mean hCG value was 1666 IU/l. However, a single serum hCG measurement cannot exclude ectopic pregnancy or predict the risk of rupture as demonstrated by several studies (5, 14). Serial hCG measurement is often used for ectopic pregnancy and ectopic pregnancy may present with rising, falling or plateau hCG levels.

Table 2. Percentage change in serum hCG levels in patients with and without concurrent therapeutic curettage

	Patients with concurrent therapeutic curettage	Patients without concurrent therapeutic curettage	P
hCG percent changes between days 1-4	18.1 ± 37.89	31.6 ± 46.16	0.443
hCG percent changes between days 4-7	46 ± 22.7	41.2 ± 24.25	0.614
hCG percent changes between days 1-7	50.7 ± 34.20	52.6 ± 43.63	0.908

hCG: human chorionic gonadotropin

However, as hCG has no use in the determination of the location of the gestational sac, TVU is useful in the assessment of women with problematic early pregnancy. In our study, all the patients were prediagnosed through TVU.

Although ectopic pregnancy can resolve spontaneously through regression or tubal abortion, about 90% of women with ectopic pregnancy and serum hCG levels greater than 2000 IU/L require operative intervention owing to increasing symptoms or tubal rupture (8). Being safe and effective, as well as ensuring the rapid return of uterine functions should be taken into consideration for the comfort of the patient while planning the ideal treatment. MTX is a chemotherapeutic agent that prevents the growth of trophoblasts by inhibiting cell division and DNA synthesis (15). Previous studies have shown that systemic MTX treatment achieves 90-100% success in tubal ectopic pregnancies in properly selected patients (16, 17). A meta-analysis of data for 1327 women with ectopic pregnancy treated with MTX showed that increasing hCG levels were significantly correlated with treatment failure (18), thus patients treated with MTX should be followed closely for hCG concentration. Surgical management should be reserved for patients who refuse or have contraindications to medical treatment, those in whom medical treatment has failed and those who are hemodynamically unstable. Several randomized studies found that MTX treatment in selected patients was as effective as surgical treatment (19, 20). The 2 treatments were also equally effective in tubal preservation; however, the hCG concentration declined more quickly after surgery (20). Since therapeutic curettage is an invasive procedure, it is believed that only MTX treatment should be preferred instead of MTX therapy with concurrent therapeutic curettage. However, there is no study in the literature on the effect of concurrent therapeutic curettage on treatment response. Common sense includes the initiation of MTX therapy following the diagnosis of ectopic pregnancy with the aforementioned diagnostic

criteria and not performing an invasive procedure such as curettage. In this respect, our study supports this approach.

In conclusion, it should be kept in mind that curettage performed in localized ectopic pregnancies might cause an additional surgical burden and anesthesia related problems if performed under anesthesia. Based on the data obtained in this study, it can be postulated that therapeutic curettage should be used as an adjunctive method in the diagnosis of ectopic pregnancy in pregnancies without localization.

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