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RESEARCH ARTICLE

Comparison of Hematological Parameters in Ectopic Pregnancies Receiving Surgical and Medical Treatment

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ABSTRACT

Objective: To observe the changes in laboratory parameters of patients who received medical treatment and underwent surgery for ectopic pregnancy (EP).

Materials and Methods: Demographic characteristics, pre- and post-treatment laboratory parameters of patients diagnosed with EP in our clinic between 2020 and 2022 were retrospectively scanned and compared. Eighty patients who received medical treatment and 68 patients who underwent surgery were screened, 8 patients were excluded due to insufficient data.

Results: The beta-human chorionic gonadotropin value in the surgery group was significantly higher than the methotrexate (MTX) group ($p<0.05$). The white blood cell (WBC) values before and after the treatment in the surgery group were significantly higher than the MTX group ($p<0.05$). WBC and platelet values were significantly lower after treatment in the surgery group than before treatment ($p<0.05$). Post-treatment WBC, thrombocyte reduction, and monocyte value were significantly higher in the surgery group than in the MTX group ($p<0.05$). Platelet value after treatment was significantly higher in the surgery group than in the MTX group ($p<0.05$). In the MTX group, monocytes and lymphocyte counts were significantly lower after treatment than before treatment ($p<0.05$).

Conclusion: Hematological parameters vary according to the type of treatment in ectopic pregnancies. Compared to the medical treatment group, the hemogram and hematocrit counts of the surgical group were lower; WBC, monocytes and lymphocyte counts were found to be higher.

Keywords: Ectopic pregnancy, hematocrit, hemogram, methotrexate

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INTRODUCTION

Ectopic pregnancy (EP) is when an embryo implants anywhere other than the uterus, most frequently in the fallopian tubes. Tubal ectopic pregnancies account for 96% of all EP.[1] The most frequent EP symptoms in the first trimester are vaginal bleeding and stomach pain.[2] EP typically presents with amenorrhea before vaginal bleeding. The timing, character, and severity of abdominal pain vary and there is no pathognomonic pain pattern for EP.[3] The treatment management of EP has changed over the years. The preferred management is usually pharmacological treatment with methotrexate (MTX) rather than surgical treatment. 4% of all maternal deaths in pregnancies are caused by EP, which is one of the major causes of maternal mortality in the first trimester despite advances in the diagnosis and treatment.[2,4,5] If intrauterine pregnancy cannot be proven despite a positive beta-human chorionic gonadotropin (β-hCG) value in the serum, EP is presumed.[6] With repeated β-hCG monitoring, the diagnosis is clarified in stable individuals.[7] The medicinal therapy with systemic MTX and surgical delivery of the pregnancy are the two most often used methods for the treatment of EP. Furthermore, it has been demonstrated that MTX therapy preserves future fertility and is more affordable than surgical management.[8] Surgical treatment; It is indicated in ruptured patients for whom medical treatment is contraindicated, with hemodynamic compromise,

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pain or signs of intra-abdominal bleeding. Various surgical approaches have been reported that result in a faster reduction of β-hCG levels compared to medical therapy.[9]

In our study, the pre- and post-treatment laboratory findings of patients who underwent medical and surgical treatment for EP were compared.

MATERIALS and METHODS

This study, which is cross-sectional in nature, was carried out by retrospectively assessing EP-diagnosed patients who applied to our institution between 2020 and 2022. The local ethics committee gave its clearance for the study (Date: 09.09.2022, Decision no. 2022/3946). The local committee gave its approval, and the study was conducted in line with the Declaration of Helsinki.

The diagnosis of EP was made by the plateauing β-hCG values or by observing an extrauterine mass on ultrasound. A total of 148 patients with this diagnosis were screened; 8 of them were disqualified from the study due to insufficient information. Seventy-five patients who were administered 50 mg intramuscular MTX per square meter were included in the study in patients for whom medical treatment was decided due to EP. At the time of admission, 65 patients who underwent surgical procedure due to the inability to tolerate medical treatment or the contraindication of medical treatment were included in the study. Age, blood type, pregnancy information (gravida and parity), number and kind of surgeries, pelvic infection history, and EP history were among the demographic and medical histories of the patients that were retrospectively scanned from patient files. In patients treated with MTX, whole blood values obtained immediately before drug administration and on the 4th day of drug administration were obtained from the hospital information system. Whole blood values, which were routinely checked on the operation day, preoperatively and on the second postoperative day, were obtained from the hospital information system from the patients treated with surgery. β-hCG values measured before treatment were recorded in both patient groups. For whole blood analysis, samples were taken into tubes with EDTA (ethylenediaminetetraacetate) and studied with the Premier Hb9210 (Trinity Biotech, Ireland) device. Gel tubes containing β-hCG samples were used for the EL ×800 Absorbance Microplate Reader's analysis (Biotek, Winooski, VT, USA).

Statistical Analysis

The descriptive statistics of the data used mean, standard deviation, median minimum, maximum, frequency, and ratio values. The distribution of the variables was examined using the Kolmogorov–Smirnov test. In order to analyze quantitative independent data, Mann–Whitney U-test and independent sample t-test were used. The t-test was used to analyze the dependent quantitative data. The Chi-square test was employed to analyze qualitative independent data, and the Fischer test was applied when the Chi-square test conditions were not met. The study was conducted using the Statistical Package for the Social Sciences (Chicago, Illinois, USA) program version 28.0. P<0.05 was used to determine the results' statistical significance.

RESULTS

Age, body mass index, and the proportion of patients who were pregnant did not substantially differ between the MTX and surgical groups (p>0.05). The difference between the β-hCG values in the MTX and surgery groups was statistically significant (p<0.05). When the two groups were compared, there was no discernible difference in the prevalence of smoking, intrauterine devices, previous operations, or pelvic inflammatory illness (p>0.05) (Table 1).

Before and after therapy, hematocrit (HCT) and hemoglobin (HB) values were substantially lower in the surgery group than in the MTX group in both cases (p<0.05). After treatment, HB and HCT values in both groups were considerably lower than they were before treatment (p<0.05). In both groups, the change in HB and HCT after treatment did not differ significantly (p>0.05) (Table 2). In the surgery group, the pre- and post-treatment white blood cell (WBC) values were significantly higher than the MTX group (p<0.05). The post-treatment WBC value in the MTX group did not differ substantially from the pre-treatment value (p>0.05). The post-treatment WBC was considerably lower than the pre-treatment WBC in the surgery group (p<0.05). In the surgery group, the post-treatment WBC reduction was significantly higher than in the MTX group (p<0.05) (Table 2).

Neutrophil counts in the surgery group were considerably greater than in the MTX group both before and after the treatment (p<0.05). In the MTX group, post-treatment neutrophil value did not change significantly compared to pre-treatment (p>0.05). After surgery, the group's neutrophil counts were considerably lower than they were prior to surgery (p<0.05). Surgery patients experienced much more of a drop in neutrophils than MTX patients did after therapy (p<0.05) (Table 3).

There was no noticeable variation in platelet value between the two groups before medication (p>0.05). After treatment, the surgical group's platelet value was noticeably higher than the MTX group's (p<0.05). When compared to pretreatment, the platelet value in the MTX group did not significantly alter following therapy (p>0.05). Platelet value in the

Table 1. Demographic characteristics of patients who received medical treatment and underwent surgery

	MTX (n=75)				Surgery (n=65)				p
	Mean±SD	n	%	Median	Mean±SD	n	%	Median	
Age	31.6±6.2			30.0	30.2±6.1			31.0	0.196[t]
BMI	25.8±3.7			25.1	25.1±3.3			24.4	0.142[m]
Gravide	2.97±1.55			3.00	3.46±2.34			3.00	0.163[m]
Parite	1.43±1.38			1.00	1.78±1.23			2.00	0.054[m]
β-hCG	2256.1±3690.2			1166.0	9752.5±15217.7			3025.0	0.000[m]
Smoking									
No		69	92.0			61	93.8		0.672X^2
Yes		6	8.0			4	6.2		
Previous surgery									
No		45	60.0			40	61.5		0.853X^2
Yes		30	40.0			25	38.5		
Pelvic inflammatory disease									
No		66	88.0			56	86.2		0.745X^2
Yes		9	12.0			9	13.8		
Intrauterine device									
No		69	92.0			58	89.2		0.573X^2
Yes		6	8.0			7	10.8		

[t]: Independent sample t-test; [m]: Mann–whitney u-test; X^2: Chi-square test (Fischer test). MTX: Methotrexate; SD: Standard deviation; BMI: Body mass index; β-hCG: Beta-human chorionic gonadotropin

Table 2. Hemogram, hematocrit and white blood cell changes in patients who received medical treatment and underwent surgery

	MTX (n=75)		Surgery (n=65)		p
	Mean±SD/n-%	Median	Mean±SD/n-%	Median	
HB					
Pre-treatment	12.1±1.8	12.3	11.4±1.8	11.7	0.016[m]
Post treatment	11.8±1.3	11.9	10.7±1.5	10.6	0.000[m]
Pre-post treatment change	-0.24±1.56	-0.30	−0.711.73±	-0.80	0.087[m]
Intra-group change p	0.002[w]		0.002[w]		
HCT					
Pre-treatment	38.0±3.7	38.4	34.3±5.3	35.1	0.000[m]
Post treatment	36.1±5.6	36.5	31.6±4.4	31.5	0.000[m]
Pre-post treatment change	−1.91±5.11	−1.40	−2.72±4.98	−3.50	0.062[m]
Intra-group change p	0.000[w]		0.000[w]		
WBC					
Pre-treatment	8.3±2.1	8.1	10.8±4.0	10.5	0.000[m]
Post treatment	8.5±3.3	8.1	9.5±3.1	8.9	0.014[m]
Pre-post treatment change	0.19±3.01	−0.21	−1.27±3.64	−1.57	0.020[m]
Intra-group change p	0.509[w]		0.010[w]		

[m]: Mann-whitney u-test; [w]: Wilcoxon test. MTX: Methotrexate; SD: Standard deviation; HB: Hemoglobin; HCT: Hematocrit; WBC: White blood cell

surgery group was substantially lower after therapy than it was before treatment (p<0.05). After therapy, platelet decrease was noticeably greater in the surgery group than in the MTX group (p<0.05) (Table 3).

Table 3. Changes in neutrophils, platelets, monocytes, and lymphocytes in patients who received medical treatment and underwent surgery

	MTX (n=75)		Surgery (n=65)		p
	Mean±SD/n-%	Median	Mean±SD/n-%	Median	
Neutrophil					
Pre-treatment	5.10±1.94	4.77	8.01±4.47	6.84	0.000[m]
Post treatment	6.52±9.10	4.93	7.81±10.92	5.50	0.016[m]
Pre-Post treatment change	1.42±9.11	−0.13	−0.20±11.80	−1.53	0.014[m]
Intra-group change p	0.887[w]		0.020[w]		
Platelet					
Pre-treatment	274.3±55.4	265.0	272.5±73.5	269.0	0.918[m]
Post treatment	269.5±68.4	254.0	244.6±88.0	230.0	0.009[m]
Pre-post treatment change	−4.81±50.93	−7.00	−27.91±72.30	−33.00	0.011[m]
Intra-group change p	0.119[w]		0.001[w]		
Monocytes					
Pre-treatment	0.65±0.62	0.55	0.61±0.22	0.59	0.520[m]
Post treatment	0.51±0.21	0.48	0.62±0.26	0.58	0.005[m]
Pre-post treatment change	−0.14±0.61	−0.07	0.01±0.29	0.04	0.031[m]
Intra-group change p	0.006[w]		0.608[w]		
Lymphocytes					
Pre-treatment	2.48±0.76	2.46	2.17±0.94	1.89	0.026[m]
Post treatment	2.28±0.79	2.27	2.08±0.98	1.95	0.044[m]
Pre-post treatment change	−0.20±0.75	−0.14	−0.09±1.23	−0.13	0.818[m]
Intra-group change p	0.043[w]		0.201[w]		

[m]: Mann–Whitney U-test; [w]: Wilcoxon test. MTX: Methotrexate; SD: Standard deviation

In the two groups, there were no discernible differences in the pre-treatment monocyte value (p>0.05). In comparison to the MTX group, the post-treatment monocyte value was considerably greater in the surgery group (p<0.05). The monocyte value in the MTX group was substantially lower post-treatment than before treatment (p<0.05). The post-treatment monocyte value in the surgery group did not differ substantially from the pre-treatment (p>0.05). After therapy, monocyte decrease in the MTX group was noticeably higher than in the surgical group (p<0.05) (Table 3).

Before and after therapy, lymphocyte levels in the surgery group were considerably lower than in the MTX group (p<0.05). In the MTX group, the lymphocyte value after treatment was significantly lower than before treatment (p<0.05). In the surgery group, post-treatment lymphocyte value did not change significantly compared to pre-treatment (p>0.05). After treatment, there were no discernible differences in the groups' lymphocyte counts (p>0.05) (Table 3).

DISCUSSION

Because assisted reproductive technologies are now widely used, there has been a rise in EP rates in recent years.[10,11] In addition, *Neisseria gonorrhoeae*, Mycoplasma and schistosomiasis infections also pose a risk for EP.[12] Surgical interventions to the tube such as tubal reanastomosis, salpingostomy, tuboplasty increase the risk of EP.[13,14] In the patients included in our study, the rate of smoking (MTX: 8%, surgical group: 6.2%), previous pelvic infection (MTX: 12%, surgical group: 13.8%) was low, while previous abdominal surgery (MTX:%) 40, surgical group: 38.5% were found to be high. The initial serum β-hCG level is recognized as the single best predictive indication of effective follow-up and therapy for a single dosage of MTX, and hCG is now the only biomarker utilized in clinical practice.[15] Higher β-hCG levels are associated with increased failure rates.[15] According to the literature and our investigation, the surgical group's β-hCG value was higher than the group receiving MTX.

According to Deveci et al.,[16] patients who received emergency EG surgery had considerably lower HB values than those who underwent elective surgery. In a different study, patients who received MTX and those who underwent surgery had their HB and WBC values compared. There was no discernible difference between the groups in terms of HB and WBC values.[17] In our study, HB and HCT values before and after treatment were significantly lower in the surgical group than in the MTX group ($p<0.05$). In addition, post-treatment HB and HCT decrease was higher and WBC was lower in the surgical EP group. Most of the patients who underwent surgery for EP had low HB values and signs of intra-abdominal bleeding. This causes patients to be clinically unstable and medical treatment intolerable.

According to Aktün et al.,[18] no difference was found in terms of HB and HCT values in ruptured ectopic pregnancies who underwent surgery compared to non-ruptured ectopic pregnancies. No statistically significant difference in HB and HCT changes between patients who had surgery and received MTX treatment was seen in our study ($p>0.05$).

It has been shown that monocyte activation may disrupt the microenvironment in EP and have an effect on tubal motility and impairment of tubal motility causes the embryo to remain in the tuba and ruptures from there, leading to deterioration of the patient's hemodynamics.[19] Monocyte levels were found to be greater in the surgical group in our study.

CONCLUSION

EP is an important cause of first trimester maternal deaths, and early diagnosis and treatment are vital. In the evaluation of EP cases, careful examination of hematological parameters such as HB, HCT, WBC, as well as standard criteria, will guide the choice of treatment.

Disclosures

Ethics Committee Approval: The study was approved by the Necmettin Erbakan University Non-Pharmaceutical and Medical Device Research Ethics Committee (No: 2022/3946, Date: 09/09/2022).

Informed Consent: Written informed consent was obtained from all patients.

Peer-review: Externally peer reviewed.

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