

Retrospective Analysis of Follow-up and Treatment of Patients with Ectopic Pregnancy and Our 6 Years of Clinical Experience

Ektopik Gebelik Ön Tanısı ile Başvuran Olguların Takip ve Tedavilerinin Retrospektif Analizi: 6 Yıllık Klinik Deneyimimiz

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Abstract:

Objective: In this study, we aimed to make a retrospective analysis of the follow-up and the treatment of the patients who were admitted to our clinic, which is a tertiary center, with the preliminary diagnosis of ectopic pregnancy between 2010-2016 to contribute to the data related to ectopic pregnancy in our country.

Materials and Methods: We retrospectively evaluated the follow-up and the treatment of 452 patients who were admitted to our clinic with a diagnosis of ectopic pregnancy between 2010-2016. We separated these cases into different groups according to their diagnosis, the way of treatment and results.

Results: The study was conducted in Bakırköy Dr. Sadi Konuk Training and Research Hospital, between 2010-2016 with 452 female cases. We did not visualize any ectopic mass in 12.6% of the cases (n = 57); 85% (n = 385) was tubal; 0.2% (n = 1) was cornual; 1.2% (n = 5) was ovarian, 0.2% (n = 1) was heterotopic; 0.4% (n = 2) was molar pregnancy, and 0.2% (n = 1) was scar pregnancy. Methotrexate (Mtx) treatment success rate was 72.7%. 17 % (n = 77) of the cases used Mtx; general rupture rate of the cases was 25.7% (n = 116); rupture rate after Mtx treatment was 27.2% (n = 21). In the Mtx group the rate of detecting an ectopic mass was significantly higher (p = 0.001; p <0.01). 74.1% (149 cases) of the cases we performed laparoscopy and 25.8% (53 patients) of the cases we performed laparotomy. 86% (173 patients) was performed salpingectomy, 10.9% (18 patients) salpingostomy, and 2.9% ovarian resection.

Conclusion: Looking at the data in our clinic, we use follow-up, surgical and medical treatment methods. The success rate of medical treatment was 72.7%, and laparoscopic surgery was performed in 74.1% of the cases.

Keywords: Ectopic Pregnancy, Laparoscopy, Methotrexate

Özet:

Amaç: Bu çalışmada, 2010-2016 yılları arasında ektopik gebelik ön tanısı ile üçüncü basamak bir merkez olan kliniğimize başvuran hastaların takibi ve tedavisinin retrospektif incelenmesi amaçlandı. Bu sayede ülkemizdeki ektopik gebelik ile ilgili verilere katkıda bulunulması hedeflendi.

Gereç ve Yöntem: 2010-2016 yılları arasında ektopik gebelik tanısı ile kliniğimize başvuran 452 hastanın takip ve tedavileri retrospektif olarak incelendi. Bu olgular; tanı, tedavi şekli ve sonuçlarına göre farklı gruplara ayrıldı.

Bulgular: Çalışma, 2010-2016 yılları arasında Sağlık Bilimleri Üniversitesi Bakırköy Dr. Sadi Konuk Eğitim ve Araştırma Hastanesi'nde 452 kadın olgu ile gerçekleştirildi. Hastaların yaşları 15-49 arasında değişmekte olup, ortalama 33.86 ± 6.50 yılıdır. Olguların %12,6'sında ektopik odak gözlenmedi (n = 57); %85 hastada (n = 385) tubal; %0,2 hastada (n = 1) kornual; %1,2 (n = 5) yumurtalık, %0,2 (n = 1) heterotopik; %0,4 (n = 2) molar gebelik, %0,2 (n = 1) skar gebelik idi. Mtx (Metotreksat) tedavisi başarı oranı %72,7 idi, olguların %17'si (n = 77) Mtx kullanıldı. Olguların genel rüptür oranı %25,7 (n = 116); Mtx tedavisinden sonra rüptür oranı %27,2 (n = 21) idi. Mtx grubunda ektopik kitle saptama oranı anlamlı derecede yüksekti (p = 0.001; p <0.01). Opere olan hastaların %74,1'i (149 olgu) laparoskopi %25,8'i (53 hasta) laparotomi ile tedavi edildi. %86'sına (173 hasta) salpingektomi, %10,9'una (18 hasta) salpingostomi ve %2,9'una over rezeksiyonu yapıldı.

Sonuç: Kliniğimizdeki verilere baktığımızda tedavi yöntemleri olarak takip, cerrahi tedavi ve medikal tedaviyi kullanıyoruz. Tıbbi tedavinin başarı oranı %72,7 idi. Cerrahi yöntemin laparoskopik olarak uygulanması ise %74,1 olarak görüldü.

Anahtar Kelimeler: Ektopik Gebelik, Laparoskopi, Metotreksat

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1. INTRODUCTION

Ectopic pregnancy is defined as the implantation of a fertilized ovum outside the uterus in the blastocyst stage, often in the fallopian tube (98%). It also may be cervical, interstitial, abdominal, ovarian, intraligamentary and on the scar. In rare cases, heterotopic pregnancy (both intra-uterine and extrauterine) can be seen (1). In recent years, an increase in ectopic pregnancy is noticed. The prevalence of ectopic pregnancy was calculated as approximately 2% of all conception in the mid-20th century (2). The ratio is increasing to %2-5 in patients who utilized assisted reproductive technology (3). The risk of recurrence is 10% in women with one previous ectopic pregnancy, and it increases to 25% in women with two or more previous ectopic pregnancies (4). The prevalence of ectopic pregnancy among pregnant women admitted to the emergency department with vaginal bleeding, and abdominal pain varies between 6-16%. Increased frequency of pelvic infections, increased use of intrauterine devices, and widespread use of surgical methods in infertility treatment are the main causes of this increase (5,6). The factors that increased the diagnosis include; the measurement of susceptible human chorionic gonadotropin (β hcg), increased use of transvaginal ultrasonography and laparoscopy for definitive diagnosis and increased use of assisted reproductive techniques with reconstructive tubal surgical procedures (7). There are studies in process researching the accurate diagnosis of ectopic pregnancy or pregnancies of unknown location (8). By increasing early diagnosis, we see a decrease in mortality rates; however, an ectopic pregnancy is still considered the most often cause of maternal death in early pregnancy (9,10). Treatment options can be conservative follow-up, medical or surgical. All methods can be effective. It depends on the clinical situation, the localization of ectopic pregnancy and the available facilities (11).

Although operative treatment of ectopic pregnancy is still the primary treatment modality worldwide, methotrexate (Mtx) treatment is appropriate in an unruptured ectopic pregnancy (12). Medical treatment has many advantages compared to surgical treatment, such as less tubal damage, lower cost, and controversial but higher fertility potential (13). On the other hand, it can only be applied to selected patients in follow-up treatment. When we look at the data, one-third of ectopic pregnancies are appropriate for the treatment of methotrexate (14). Methotrexate treatment has a success rate of between 68 and 98% (15,16).

2. MATERIAL AND METHOD

The study was conducted with 452 female patients in Bakırköy Dr. Sadi Konuk Training and Research Hospital between 2010-2016. A detailed anamnesis was obtained including age, parity, additional health issues and ectopic pregnancy history. We performed an ultrasound examination and took a blood sample to evaluate the β hcg level. The cases were separated into groups according to treatment, Methotrexate use or rupture. The distribution of demographic characteristics and clinical data are presented in Table 1.

Ethical Declaration

This study was prepared by rearrangement of the speciality thesis by the first author. The ethical consent was obtained from the Clinical Ethical Committee of The Dr. Sadi Konuk Research and Education Hospital (No: 2020-484) and Helsinki Declaration rules were followed to conduct this study.

3. RESULTS

The ages of the cases ranged from 15 to 49, and the mean age was 33.86 ± 6.50 years. The presence of rupture according to the mean age, parity numbers, the existence of prior ectopic pregnancy, and the presence of fetal cardiac activity did not show a statistically significant difference ($p > 0.05$), as presented in Table 2. The rate of ruptured ectopic pregnancy was higher in the group with β hcg levels more than 2000; it was found to be statistically significant. Also, in the patients WHO had ruptured ectopic pregnancy, the presence of ectopic mass and the fetal node, was to be significantly higher ($p = 0.001$; $p < 0.01$). In 17% ($n = 77$) of the cases Mtx was used. The success rate of Mtx was 72.7%. In 25.7% ($n = 116$) cases, we observed rupture. Post-Mtx rupture was observed in 27.2% ($n = 21$) of the patients.

In the group that used Mtx, the mean age, parity numbers, history of ectopic pregnancy, β hcg level and the presence of fetal cardiac activity did not show a statistically significant difference ($p > 0.05$). We observed that ectopic mass was seen more in the Mtx group ($p = 0.001$; $p < 0.01$) however, fetal node was visualized more in the non-Mtx group ($p = 0.028$; $p < 0.05$) as presented in Table 3.

As presented in Table 4, according to treatment modalities, there was no statistically significant difference between the groups according to their age, parity numbers and ectopic history ($p > 0.05$). The proportion of the patients with higher β hcg measurements was significantly higher in the groups which had an operation, medical treatment + operation and follow-up+ RC ($p =$

0.001; $p < 0.01$). The rate of detecting an ectopic mass was significantly higher in the groups that had medical treatment, medical treatment + operation and directly operation ($p = 0.001$; $p < 0.01$). Presence of fetal node ratio

was significantly higher in operation and medical treatment + operation groups ($p = 0.001$; $p < 0.01$). There was no statistically significant difference between the groups on fetal cardiac activity ($p > 0$).

Table 1. Distribution of Demographic Characteristics and Clinical Data

		Min-Max (Median)	Average±SD
Age (year)		15-49 (34)	33.86±6.50
Parity		0-6 (1)	1.52±1.15
βhcg		22-100000 (1735)	3798.35±8363.15
Type of ectopic pregnancy		N	%
	Unknown	57	12.6
	Tubal	385	85
	Cornual	1	0.2
	Ovarian	5	1.2
	Heterotopic	1	0.2
	Molar pregnancy	2	0.4
	Scar pregnancy	1	0.2
Previous delivery	Nulliparous	81	17.9
	Multiparous	371	82
	Vaginal delivery	173	38.3
	C-section	198	43.8
Parity	Nulliparous	81	17.9
	Multiparous	371	82.1
History of Ectopic Pregnancy	(-)	412	91.2
	(+)	40	8.8
βhcg	<2000	250	55.3
	>2000	202	44.7
Presence of ectopic mass	(-)	57	12.6
	(+)	395	87.4
Fetal node	(-)	363	91.9
	(+)	32	8.1
Fetal cardiac activity	(-)	5	15.6
	(+)	27	84.4
Treatment method	Follow	128	28.3
	Medical treatment	77	17.0
	Direct operation	180	39.8
	Medical treatment+operation	21	4.6
	Curettage+Follow up	46	10.2
Operation	(-)	251	55.5
	(+)	201	44.4
	Salpingectomy	173	38.3
	Salpingostomy	22	4.8
	Ovarian resection	6	1.3
Operation Method	Laparoscopy	149	33.0
	Laparotomy	52	11.7

βhcg: Beta-human chorionic gonadotropin

Table 2. Evaluation According to Rupture Rate

n (%)		Total	Rupture (-) (n=336)	Rupture (+) (n=116)	p
		n (%)	n (%)		
History of Ectopic Pregnancy	(+)	40 (8.8)	26 (7.7)	14 (12.1)	^a 0.220
	(-)	412 (91.2)	310 (92.3)	102 (87.9)	
βhcg	<2000	250 (55.3)	203 (60.4)	47 (40.5)	^b 0.001**
	>2000	202 (44.7)	133 (39.6)	69 (59.5)	
Presence of ectopic mass	(-)	57 (12.6)	56 (16.7)	1 (0.9)	^a 0.001**
	(+)	395 (87.4)	280 (83.3)	115 (99.1)	
Fetal node	(-)	363 (91.9)	269 (96.1)	94 (81.7)	^a 0.001**
	(+)	32 (8.1)	11 (3.9)	21 (18.3)	
Fetal Cardiac Activity	(-)	5 (15.6)	1 (9.1)	4 (19.0)	^c 0.637
	(+)	27 (84.4)	10 (90.9)	17 (81.0)	

^aYates' Continuity Correction Test^bPearson Chi-Square Test^cFisher's Exact Test

**p<0,01

βhcg: Beta-human chorionic gonadotropin

Table 3. Evaluation according to Mtx Use

n (%)		Total	Mtx (-) (n=375)	Mtx (+) (n=77)	p
		n (%)	n (%)		
History of Ectopic Pregnancy	(+)	40 (8.8)	27 (5.9)	13 (2.8)	^a 0.321
	(-)	412 (91.2)	348 (76.9)	64 (14)	
βhcg	<2000	250 (55.3)	223 (49.3)	27 (5.9)	^b 0.278
	>2000	202 (44.7)	147 (32.5)	55 (12.1)	
Presence of ectopic focus	(-)	57 (12.6)	54 (11.9)	3 (0.7)	^a 0.001**
	(+)	395 (87.4)	321 (71.1)	74 (16.3)	
Fetal node	(-)	363 (80.3)	289 (63.9)	74 (16.3)	^a 0.028*
	(+)	32 (8.1)	29 (10.1)	3 (2.8)	
Fetal Cardiac Activity	(-)	5 (15.6)	5 (15.6)	0 (0)	^c 1.000
	(+)	27 (84.4)	24 (82.8)	3 (2.8)	

^aYates' Continuity Correction Test^bPearson Chi-Square Test^cFisher's Exact Test

*p<0,05

**p<0,01

βhcg: Beta-human chorionic gonadotropin Mtx: Methotrexate

Table 4 Evaluations according to treatment modalities

		Follow (n=128)	Medical Treatment (n=77)	Operation (n=180)	Medical+operation (n=21)	Curettage+ Follow (n=46)	p
		n (%)	n (%)	n (%)	n (%)		
History of Ectopic Pregnancy	(+)	7 (5,5)	8 (10,5)	15 (8,3)	4 (19,0)	6 (13,0)	^a 0,171
	(-)	121 (94,5)	69 (89,6)	165 (91,7)	18 (81,0)	40 (87,0)	
βhcg	<2000	98 (76,6)	49 (63,6)	76 (42,2)	7 (33,3)	20 (43,5)	^a 0,001*
	>2000	30 (23,4)	28 (36,4)	104 (57,8) *	14 (66,7) *	26 (56,5) *	
Presence of ectopic focus	(-)	26 (20,3)	3 (3,9)	5 (2,8)	0	23 (50,0)	^a 0,001*
	(+)	102 (79,7)	74 (96,1) *	175 (97,2) *	21 (100) *	23 (50,0)	
Fetal node	(-)	102 (100)	74 (100)	146 (83,4)	19 (90,5)	22 (95,7)	^a 0,001*
	(+)	0	0	29 (16,6) *	2 (9,5) *	1 (4,3)	
Fetal Cardiac Activity	(-)	0 (0)	0 (0)	5 (17,2)	0 (0)	0 (0)	^b 1,000
	(+)	0 (0)	0 (0)	24 (82,8)	2 (100)	1 (100)	

βhcg: Beta-human chorionic gonadotropin ^aPearson Chi-Square Test ^bFisher Freeman Halton Test
*p<0,01

For statistical analysis, the NCSS (Number Cruncher Statistical System) 2007 (Kaysville, Utah, USA) program was used. In the evaluation of the data, in addition to using descriptive statistical methods (Mean, Standard Deviation, Median, Frequency, Ratio, Minimum, Maximum) comparison of two groups showing normal distribution Student's t-test, was used. Comparison of the two groups of the parameters that did not show normal distribution. Mann-Whitney U test was used. Oneway Anova test was used for comparison of the three groups with normal distribution, and the Kruskal Wallis test was used for comparison of the groups with three or more normal distribution. Pearson's Chi-Square test, Fisher-Freeman-Halton test, Fisheracts Exact test and Yates-Corrected Chi-square test were used to compare qualitative data. Significance was evaluated as $p < 0.05$.

4. DISCUSSION

The diagnosis of ectopic pregnancy starts with suspicion. Careful anamnesis, a proper pelvic and physical examination are required. It is followed by necessary ancillary diagnostic methods. After diagnosis, a treatment applied according to the available methods can be

lifesaving. In our study, we studied 452 cases retrospectively to contribute to ectopic pregnancy data in our country and present the current treatment modalities and activities. When we evaluate the data, there was no significant difference between the patients who had cesarean and vaginal delivery. Some of the previous studies show that cesarean delivery increases the risk of ectopic pregnancy. However, some argue that there is no meaningful difference (17-20). We could not detect the pregnancy localization in 12.6% of the cases. Ectopic mass was localized in 87.4% of patients by ultrasound similar to the studies of by Dialani et al. in 2004 and Dogra et al. in 2005(21,22). 85% of these localizations were tubal; 0.2% cornual, 1.2% was ovarian, 0.2% was heterotropic and 0.2% was scar pregnancy. According to the literature, most of the ectopic pregnancies are seen in the fallopian tube (98%), the second place is ovarian (1.1%) (1), which was compatible with the tubal pregnancy rates (85%) found in our study.

In 8,8% (n = 40) of the cases, there was an ectopic pregnancy history. Similarly, Yao et al. had conducted a series of studies that showed women with an ectopic history had a recurrence rate of 8% and 9.8% after

methotrexate and salpingectomy, respectively (23). Our ectopic pregnancy rate among patients admitted to the emergency department was 0.8%. The rate in 2010 was 1.3%; this low rate was attributed to the inadequacy of records. The mean ectopic pregnancy rate varies between 12-20% over the years, and the distribution of years shows a significant decrease in the rates of ectopic pregnancy in our hospital in the last five years. This shift can be attributed to the improvement of the first and second step hospitals, consequently a decrease in the referral rates to third step hospitals like ours.

When the data about the treatment methods are analyzed; 39.8% case (180 patients) were directly operated; 74.1% (149 patients) with laparoscopy and 25.8% (53 patients) with laparotomy, 28.3% (128 patients) of the cases were followed conservatively, 17% (77 patients) methotrexate was applied, but 4.6% of them (21 patients) had to be operated after medical treatment because of rupture. In addition, 86% of the patients (173 patients) underwent salpingectomy, 8.9% (18 patients) had salpingostomy, and 1.3% had an ovarian resection. Forty-six patients underwent curettage following the conservative follow-up resulting in a decrease in β hcg levels. In our center, the experience in laparoscopy is sufficient; therefore, it can be performed in emergency conditions. The high rate of laparoscopy is attributed to the technical infrastructure and clinical experience. The high rate of salpingectomy was attributed to detecting a tubal rupture in the majority of the patients who were admitted to the emergency service. Similar to the literature published by Anderson et al. in 2004 and as expected, the risk of rupture was increased in patients who had visible ectopic mass, visible ectopic fetal node or β hcg over 2000 (24).

The Mtx treatment success rate was 78.7%, consistent with the literature (15,16). Only in 4.6% (21 patients) of patients who had methotrexate treatment, we observed a post-treatment rupture and performed an operation. The risk of rupture was increased by detecting an ectopic mass, ectopic fetal node and β hcg >2000, also consistent with the literature (16,24,25). In 2000, Lipscomp and colleagues published a cohort study with a single dose of Mtx-treated patients. In this study, 287 (92.9%) of 315 patients were successfully treated with Mtx (26). McCord ML published a further review of the successful treatment of ectopic pregnancy with a single dose of methotrexate. In this study, logistic regression analysis revealed that pretreatment serum β hcg levels were the only factor affecting failure. The size and volume of the mass, the volume of the hematoma and the presence of free peritoneal fluid in the pelvis were not significant risk factors for the failure of the treatment (27).

When the treatment modalities were considered, the ratio of β hcg measurements over 2000 was significantly higher in operation, medical treatment + operation and follow-up + RC groups. The higher values of β hcg in the operative group was expected; the high value of β hcg in the follow-up and RC group was attributed to the change of the diagnosis with missed pregnancies and incomplete abortion. These findings were compatible with a study by Inal and Mol et al. (28,29). In our study, the presence of ectopic mass was found significantly higher in the groups who had an operation, medical treatment, medical + operation. The fetal node presence was significantly higher in operation, and medical + operation groups and the detection of the fetal node is related to the operation. Again, these data are consistent with the literature, as found in the study conducted by Bixby et al. in 2005 (29,30). The limitation of our study was the retrospective nature and the small number of cases. In order to determine the actual ectopic pregnancy rates and demonstrate the success of treatment modalities in our country, more extensive studies and compilation of national data are needed. In conclusion, larger-scale studies must be done to determine the accurate rate of ectopic pregnancy distribution in our country. In our clinic, similar to the approach in the world, if ectopic pregnancy requires surgical treatment, it is treated with the laparoscopic method, and if it requires medical treatment, it is successfully treated with Mtx, and no death due to ectopic pregnancy has been observed.

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