A Three-Year Audit of the Management of Ectopic Pregnancy

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Abstract

Objective: To audit the management of ectopic pregnancy over a three-year period.
Materials and Methods: The medical records of 40 women diagnosed and hospitalized with ectopic pregnancy from 1999 to 2002 at Fatih University Hospital were evaluated retrospectively.
Results: Mean age of women was 29.3 years. The most common presenting symptom was abdominal pain (67.5%) and most frequent physical finding was abdominal tenderness (97.5%). The prevalence of smoking was 60%. Past histories of laparotomy and previous ectopic pregnancy were 37.5% and 17.5% respectively. 52.5% of the patients were using a contraceptive method. The most common contraceptive methods were coitus interruptus (25%) and intrauterine device (20%). In 65% of the cases, the ectopic pregnancy was located in the right tuba uterina and in 35% was located in left tuba uterina. Ten women (25%) were followed-up with expectant management, 9 women (22.5%) received single-dose methotrexate. 21 women (52.5%) were treated surgically. The mean levels of β hCG in different groups were as follows: Expectant management group=921.2±648.4 mIU/L, methotrexate therapy group=1664±1571 mIU/L, radical surgery group=1327±1346 mIU/L, conservative surgery group=1955±1696 mIU/L. In two cases (22.2%) single-dose methotrexate therapy failed and required a second dose of methotrexate. 32.5% of the patients underwent laparotomy and 20% of the cases underwent laparoscopy. Conservative tubal surgery was performed in 28.5%. There was no complication and none required further surgery.
Conclusion: Although expectant management and methotrexate therapy are effective and safe options in patients with ectopic pregnancy, the majority of women still undergo surgical management as a result of late admission to hospital and delay in diagnosis.

Keywords: ectopic pregnancy, treatment options

Özet

Üç Yıllık Ektopik Gebelik Olguları Tedavilerinin Değerlendirilmesi

Amaç: Üç yıllık ektopik gebelik olgularının tedavilerini değerlendirmek.
Materyal ve Metot: 1999-2002 tarihlerinde Fatih Üniversitesi Hastanesi'nde ektopik gebelik tanısıyla tedavi gören 40 hasta retrospektif olarak araştırıldı.
Sonuçlar: Hastaların yaş ortalaması 29.3 idi. En sık başvuru şikâyeti karın ağrısı (%67.5), en sık muayene bulgusu ise abdominal hassasiyet idi (%97.5). Sigara içme oranı %60 idi. Laparotomi öyküsüne %37.5, önceden ektopik gebelik geçirme öyküsüne %17.5 oranında rastlandı. Hastaların %52.5'i bir kontraseptif yöntem kullanmaktaydı. En sık kullanılan yöntem geri çekme (%25) ve intrauterin araçtı (%20). Olguların %65'inde ektopik gebelik, sağ tubaya yerleşirken, %35'inde sol tubaya yerleştiği görüldü. Ortalama β hCG seviyeleri, gözlem ile takip edilen grupta 921.2±648.4 mIU/L, metotreksat uygulanan grupta 1664±1571 mIU/L, radikal cerrahi uygulanan grupta 1327±1346 mIU/L, konservatif cerrahi uygulanan grupta 1955±1696 mIU/L idi. On ektopik gebelik olgusu, (%25) gözlem altında takip edilirken, 11 olguya (%22.5) tek doz metotreksat uygulandı. Yirmi bir olgu (%52.5) cerrahi olarak tedavi edildi. İki olguda tek doz metotreksat başarısız oldu ve ikinci doz metotreksat uygulandı. Hastaların %32.5'ine laparotomi, %20'sine laparoskopi uygulandı. Konservatif tubal cerrahi olguların %28.5'ine uygulandı. Hiçbir olguda komplikasyon meydana gelmedi. Tekrar cerrahi gerekmedi.
Tartışma: Ektopik gebelik olgularında, bekleme tedavisi ve metotreksat kullanımının etkili ve güvenli olmasına rağmen, cerrahi tedavinin halen büyük bir oranda uygulanması, hastaların hastaneye geç başvurmalarına bağlanabilir.

Anahtar sözcükler: ektopik gebelik, tedavi yöntemleri

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Introduction

Ectopic pregnancy causes major maternal morbidity and mortality with pregnancy loss, and its incidence is increasing worldwide (1). In the United States, the annual incidence of ectopic pregnancy increased from 0.37% of pregnancies in 1948 to 1.97% in 1992. Despite the continued increase in in-

cidence, the rate of death from ectopic pregnancy declined almost 90% from 1979 to 1992. This decrease is primarily the result of earlier diagnosis, before tubal rupture (2). Alternatives of treatment are surgery, medical therapy and expectant management. In the present study we evaluated the treatment options of 40 women with ectopic pregnancy, retrospectively.

Materials and Methods

In this retrospective study, 40 women were hospitalized with the diagnosis of ectopic pregnancy at the Department of Obstetrics and Gynecology of Fatih University Hospital from July 1999 to October 2002. Percentage, history and characteristics of 40 women with risk factors of ectopic pregnancy is shown in Table 1. Medical therapy or expectant management was performed in hemodynamically stable patients. Criteria for receiving methotrexate were as follows: patient who was hemodynamically stable without active bleeding or without signs of hemoperitoneum, patient who had no contraindication for receiving methotrexate, and unruptured mass <3.5 cm in greatest dimension (3). Radical surgical management was performed in patients with ruptured ectopic pregnancy. Comparison of continuous variables was made using Student's *t*-test or Mann-Whitney-U test, and categoric data using the χ^2 test with Yates' correction, or Fisher's exact probability test.

Results

Over a three-year period a total of 40 women had been diagnosed and hospitalized with ectopic pregnancy. Characteristics of women were as follows: Mean age: 29.3 years, gravidity-(n)=3, parity-(n)=1. Percentage of presenting signs and physical findings with ectopic pregnancy and the relation between these signs, findings and managements are shown in Table 2 and Table 3. Vaginal bleeding and adnexal tenderness were the most frequent presenting signs in expectant management group ($p < 0.05$) and radical surgery group ($p< 0.001$) group respectively. 52.5% of the patients were using a contraceptive method. The most common contraceptive methods were coitus interruptus (25%) and intrauterine device (20%). In 65% of the cases, the ectopic pregnancy was located in the right tuba uterina and in 35% was located in left tuba uterina. The laboratory and ultrasonography findings and managements are shown in Table 4.

Table 1. Characteristics of women and risk factors (n=40)

	%
Smoking	60
History of laparotomy	37.5
Previous ectopic pregnancy	17.5
Intrauterine device	20
≥35-years	22.5

Table 2. Presenting signs and physical findings of the patients

Signs and physical findings	%
Abdominal pain	67.5
Vaginal bleeding	32.5
Abdominal pain and vaginal bleeding	52.5
Delay of menstruation	77.5
Abdominal tenderness	97.5
Adnexal tenderness	47.5

Nine women (22.5%) received single-dose methotrexate. In two cases (22.2%) single-dose methotrexate therapy failed and required a second dose of methotrexate. Thus the success rate of single-dose methotrexate therapy was 77.7%. In two of the methotrexate therapy cases the fetal heart was positive. There was no need for further surgery after methotrexate therapy.

Twenty one women (52.5%) were treated surgically. 32.5% of the patients underwent laparotomy and 20% of the cases underwent laparoscopy. Conservative tubal surgery was performed in 28.5%. There was no complication and none required further surgery.

Discussion

Technological advances allow diagnosis of ectopic pregnancy before severe clinical symptoms arise. Early diagnosis has also contributed to a decline in morbidity, deaths and treatment costs. Timely and early diagnosis has made this disorder amenable to medical therapy, with success rates similar to those of traditional surgical treatment. This study supported that early admission to hospital and diagnosis allow to receive medical treatment or to follow-up with expectant management for ectopic pregnancy. Surgery was preferred when there were tubal rupture or a high potential for rupture, hypotension, anaemia or ectopic pregnancy mass which is larger than 3 cm in diameter (4).

The presence of fetal cardiac activity is often considered a relative contraindication for receiving methotrexate therapy (3,5). Generally methotrexate therapy in ectopic pregnancies with positive fetal cardiac activity is an unusual method. In a study Lipscomb et al (5) noted that positive fetal cardiac activity or free peritoneal fluid is relative contraindication to methotrexate therapy, but most of these restrictions are based on limited or anecdotal evidence. In this study, Lipscomb et al (5) evaluated the predictors of success of methotrexate treatment in 350 women with tubal ectopic pregnancies who were treated with methotrexate intramuscularly according to a single-dose protocol. The overall success rate was 91%. There was no relation between the women's age or parity, the size or volume of the conceptus or the presence of fluid in the peritoneal cavity and efficacy of treatment. But the mean serum chorionic gonadotropin and progesterone concentrations and the frequency of fetal cardiac activity were

Table 3. Presenting signs, physical findings and management

	Expectant management (n=10)	Methotrexate therapy (n=9)	Radical surgery (n=13)	Conservative surgery (n=8)
Abdominal pain	1	0	2	3
Vaginal bleeding	7*	4	1	1
Abdominal pain and vaginal bleeding	2	5	10**	4
Delay of menstruation	9	7	7	8
Abdominal tenderness	10	8	13	8
Adnexal tenderness	1	2	12***	5

* $p < 0.05$ Expectant management vs radical surgery and conservative surgery.

** $p < 0.05$ Radical surgery vs expectant management.

*** $p < 0.001$ Radical surgery vs expectant management and methotrexate therapy.

lower in the successfully treated women (5). They concluded that the initial serum chorionic gonadotropin concentration is the best prognostic indicator of treatment success in women with ectopic pregnancies who are treated according to a single-dose methotrexate protocol (5). In another study, Lipscomb et al (6) reviewed a large single series of 315 patients with unruptured ectopic pregnancies treated with single dose methotrexate. They resulted in an overall success rate of 91.1 %. In 44 patients who had positive ectopic cardiac activity, the success rate was 87.5%. In 1999 Tzafettas et al (7) treated the unruptured ectopic pregnancies that had positive fetal cardiac activity with local methotrexate. Treatment was successful in 88.9% of the patients. In a recent study Halperin et al (8) evaluated efficacy of conservative management of ectopic pregnancy with fetal cardiac activity by combined local sonographically guided and systemic injection of methotrexate. They found the success rate 91.6% in the group of patients with ectopic pregnancy with fetal cardiac activity and 90.5% in the group of patients with ectopic pregnancy without fetal cardiac activity. In our study, nine of the patients received single dose methotrexate. In two cases fetal cardiac activity was positive. One of them required a second dose of methotrexate. Although methotrexate is an unusual therapy method in ectopic pregnancies with positive fetal cardiac activity, it can be applied in appropriate cases under careful monitorization.

Although there is evidence that methotrexate is an effective and safe option for a proportion of women with ectopic pregnancy, the majority of women still undergo surgical management (9). Rates of success of systemic methotrexate in studies were 96% with a multiple-dose protocol and 91.5% with a single dose protocol (2). The early use of plasma β hCG, ultrasonography and laparoscopy decreases the morbidity and mortality associated with ectopic pregnancy, allowing conservative tubal surgery when indicated (10). In the present study, when there was no evidence of tubal rupture or a high potential for rupture and vital signs were stable, either expectant management, methotrexate therapy or conservative tubal surgery was performed. In our study, the success rate of single-dose methotrexate was 77.7% which was similar to Ferrero's study (4). In two cases methotrexate therapy failed and required a second dose of methotrexate but there was no need for surgery. Expectant management was effective when there was no pain and when serum hCG levels were constantly low or were decreasing.

Table 4. Laboratory and ultrasonography findings and management

	Expectant management	Methotrexate therapy	Radical surgery	Conservative surgery
β hCG - mIU/L	921.2 ± 648.4*	1664 ± 1571	1327 ± 1346	1955 ± 1696
Mean Hb (gr/dl)	12.5	12.8	11.8	12.4
Mean CRL (mm)	6 ± 3.8	6.9 ± 2.7	3.5 ± 0.7	11.5 ± 7**
Mean gestational sac (mm)	15.2 ± 8.6	25.8 ± 8.3	32.5 ± 17.5*	22.5 ± 15.7
Fetal heart (positive/negative)		2		2

*$p < 0.05$

**$p < 0.02$

In this present study, vaginal bleeding and adnexal tenderness were the most frequent presenting signs in expectant management and radical surgery group respectively. These most frequent presenting signs could be attributed to early admission to hospital in expectant management group and late admission to hospital in radical surgery group.

In a study Zhu, et al (11) compared the surgical managements for ectopic pregnancy. They found that the success rates of salpingostomy and salpingectomy under laparoscopy or laparotomy were 100%. The operation time and length of hospital stay for laparoscopic salpingostomy were shorter than those for laparotomy with salpingostomy. They concluded that laparoscopic salpingostomy and laparoscopic salpingectomy are better than laparotomy in the treatment of ectopic pregnancy. In this retrospective audit of management of ectopic pregnancy, surgery was the most frequently used method (52.5%). 32.5% of the patients underwent laparotomy and this high incidence could be attributed to late admission to hospital that resulted with ruptured ectopic pregnancy, hemorrhage and unstable hemodynamics. Conservative tubal surgery was performed in 28.5%. There was no complication and none required further surgery. In similar studies Cooray et al (9) and Ferrero et al (4) reported that rate of surgery still higher than the rate previously reported in other studies.

There are some studies about the of predictive value of preoperative serum β hCG for failure of laparoscopic salpingostomy in ectopic pregnancies. Milad et al (12) examined various risk factors in women with ectopic pregnancies for conservative laparoscopic management. In this retrospective cohort study, they found that preoperative serum β hCG level was the only significant determinant of failure of laparoscopic linear salpingostomy for ectopic pregnancy. Tews et al (13) evaluated the association between preoperative β hCG and progesteron levels and success of linear salpingostomy in treatment of tubal pregnancy. They found that preoperative β hCG and progesteron levels are of no significance with regard to success of linear salpingostomy for treatment of tubal pregnancy. In our study the mean value of β hCG for conservative management was 1955 mIU/L. There was no complication and none required further surgery.

To conclude, timely and early diagnosis of ectopic pregnancy declines the mortality, morbidity and treatment costs and increases the success rates of methotrexate therapy, expectant management and conservative surgery. Although expectant management and methotrexate therapy are effective and safe options for women with ectopic pregnancy, the majority of women still undergo surgical management as a result of late admission to hospital and delay in diagnosis.

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