

Ectopic pregnancy; risk factors and comparison of intervention success rates in tubal ectopic pregnancy

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Summary

Objective: The assessment of ectopic pregnancy, its risk factors and comparison of the treatment modalities. **Material and Design:** Between January 2002 and July 2009, 254 ectopic pregnancies were reviewed retrospectively at the Department of Obstetrics and Gynecology, Ege University. Complaints of patients, localizations of ectopic pregnancy and comparison of patients, whether they had medical therapy or surgery, were evaluated. Methotrexate (50 mg/m² IM) was used in hemodynamically stable patients (hCG concentrations of patients varied between 450 IU/l and 3660 IU/l). Patients with fetal cardiac activity and serum hCG concentrations higher than 5000 IU/l, were treated surgically. Serum hCG concentrations were measured until the hormone was undetectable (< 1 IU/l). **Results:** Tubal ectopic pregnancy consisted of 95% of ectopic pregnancies in this trial. The most frequently seen symptom was abdominopelvic pain (77%). Ectopic pregnancy occurred in patients including those with a history of pelvic surgery (12%), previous ectopic pregnancy (6%), usage of intrauterine devices (6%), history of infertility (5.5%) and history of pelvic inflammatory disease (4%). While hemodynamically stable, 83 patients were given single dose methotrexate (50 mg/m²), and 165 patients were treated surgically. Totally 93 salpingectomies and 54 salpingostomies were performed. Of 83 patients administered single dose methotrexate, 69 were successfully treated with one course, six patients needed a second course and surgical intervention was performed in eight patients. On the other hand, of patients that underwent surgery, seven of the salpingostomy group needed methotrexate for persistent trophoblasts and three of this group were reoperated. The tube was preserved in 49 patients in the salpingostomy group (90.7%) versus 75 (92.8%) in the methotrexate group (p : 0.916). When undetectable hCG levels following initial therapy were considered, no significant difference was found between the two treatment groups (p : 0.804). **Discussion:** In selected patients with low serum hCG concentrations systemic methotrexate is a good alternative. Early diagnosis of ectopic pregnancy improves medical therapy. Although salpingectomy solves the problem definitely, comprehensive studies are required concerning future fertility of salpingectomy patients compared with salpingostomy patients.

Key words: Tubal ectopic pregnancy; Methotrexate; Salpingostomy.

Introduction

Ectopic pregnancy occurs in 1-2% of pregnant women and may threaten women's health seriously [1]. The mortality rate declined from 72-90% in 1980 to 0.14% in 1990 [2]. Tubal ectopic pregnancy accounts for 95-99% of ectopic pregnancies [3]. Ovarian, abdominal, cornual and cervical ectopic pregnancy are rarely seen [4].

Although a proportion of women with ectopic pregnancy have no identifiable causal factors, the risk is increased by several factors: previous ectopic pregnancy, tubal damage from infection or surgery, a history of infertility, treatment for in vitro fertilization, advanced age, and smoking [5, 6].

History and physical examination alone do not reliably diagnose or exclude ectopic pregnancy, in that 97% of patients have abdominopelvic pain and vaginal bleeding. Quantitative hCG measurement and transvaginal ultrasonography are important for diagnosis and management of ectopic pregnancy. Expectant and medical management are possible, and should be considered in selected cases. Surgical treatments may be radical (salpingectomy) or conservative (usually salpingostomy), and they may be performed by laparoscopy or laparotomy.

In this study we considered the risk factors and the management of ectopic pregnancy and compared the treatment options (methotrexate vs salpingostomy).

Material and Method

Between January 2002 and July 2009, 254 ectopic pregnancies were reviewed retrospectively at the Department of Obstetrics and Gynecology, Ege University. Combining transvaginal ultrasonography and quantitative serum hCG levels were used for diagnosis. In this trial, suspicion of tubal pregnancy during ultrasonography was categorized as tubal although there was lack of any extra evidence. Endometrial biopsy was performed in some cases to see whether there is chorion villus or not.

Complaints of patients, localizations of ectopic pregnancy, and comparison of patients whether they had medical therapy or surgery, were evaluated. Methotrexate (50 mg/m² IM) was used in hemodynamically stable patients. Also methotrexate cases were eligible if hCG concentrations were below 5000 IU/l, adnexal mass was less than 3.5 cm in diameter and there was negative fetal heart activity. Traditionally, all patients at our institution were screened with a baseline hCG, Rh factor, complete blood count, aspartate aminotransferase, creatinine, and blood urea nitrogen (BUN). White cell counts < 1500 μ /l, abnormal renal function, or elevation in liver function values more than twice the upper limit of normal were contraindications to methotrexate. The day methotrexate was given was considered day 1 in our protocol. A repeat hCG was performed on days 4 and 7. If the hCG level declined < 15% between days 4 and 7, a second dose of methotrexate was given and the protocol was restarted on a new day. We also compared the success rates between salpingostomy and single dose methotrexate therapy for tubal pregnancy.

Treatment success was defined with undetectable hCG levels following initial therapy without the need for any extra medical or surgical intervention. The Student's t-test was used to

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Table 1. — *Symptoms of patients.*

Symptoms	Rates
Abdominopelvic pain	77%
Vaginal bleeding	14%
Vaginal bleeding and pelvic pain	7%
During check up	2%

Table 2. — *Localizations of ectopic pregnancies.*

Localizations	Number of patients (n: 254)
Tubal	n: 243 (95%)
Cornual	n: 3
Cervical	n: 3
Rudimentary horn	n: 3
Ovarian	n: 1
Abdominal	n: 1

Table 3. — *Baseline characteristics of the two treatment groups.*

Characteristics	Methotrexate group (n: 83)	Salpingostomy group (n: 54)
Mean age	26.4 (5.3)	27.9 (4.6)
Duration of gestation (days)	44.3 (15.3)	46.1 (16.0)
Previous risk factor (patients)	19	23
Pretreatment serum hCG (IU/L)	450-3660	1100-7310
Ectopic pregnancy visible on TVS	48	34
Hospitalization period	9.2 (5.3)	3.7 (3.2)

compare the groups. Differences were considered significant at the $p < 0.05$ level. Statistical analysis was undertaken using SPSS version 12.

Results

Tubal ectopic pregnancy accounted for 95% of ectopic pregnancies in this trial. The most frequently seen symptom was abdominopelvic pain (77%). Mostly seen complaints of patients and localizations of ectopic pregnancies are shown in Tables 1 and 2.

Various factors are known about the associations of ectopic pregnancy. Although history of pelvic surgery (12%), previous ectopic pregnancy (6%), usage of intrauterine devices (6%), history of infertility (5.5%) and history of pelvic inflammatory disease (4%) were established, unknown reasons (64%) still took first place in this trial (Figure 1).

While hCG concentrations of patients varied between 450 IU/l and 3660 IU/l in the methotrexate group, it varied between 1100 IU/l and 7310 IU/l in the salpingostomy group.

Hemodynamically stable patients (83 in total) were given single dose methotrexate (50 mg/m²) and 165 patients were treated surgically. Totally 93 salpingectomies and 54 salpingostomies were performed. Of 83 patients administered single dose methotrexate 69 (83%) were successfully treated with one course, eight patients needed a second course and at the end, surgical intervention was performed in six patients. On the other hand, patients that underwent surgery, seven (12%) of the salpingostomy group needed methotrexate for persistent trophoblasts and three of this group were reoperated (initial

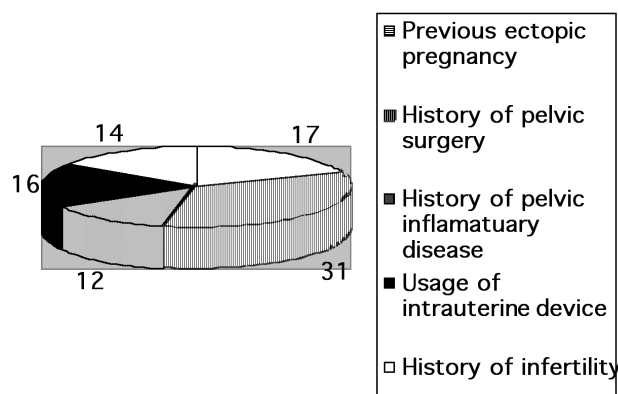


Figure 1. — Distribution of patients with risk factors for ectopic pregnancy in this trial.

therapy was laparoscopic salpingostomy for all). When we compared laparoscopic salpingostomy success rates with laparoscopy the difference was insignificant. The tube was preserved in 49 (90.7%) patients in the salpingostomy group versus 75 (92.8%) in the methotrexate group. When undetectable hCG levels following initial therapy were considered, no significant difference was found between the two treatment groups. Baseline characteristics of both treatment groups and trial profiles are shown in Figures 2 and 3 and Table 3.

Discussion

Pregnancy begins with a fertilized egg. Normally, the fertilized egg attaches itself to the lining of the uterus. With an ectopic pregnancy, the fertilized egg implants somewhere else. If it is undiagnosed it may lead to high mortality and morbidity rates.

Up to an estimated 20 in every 1,000 pregnancies are ectopic. Various factors are associated with ectopic pregnancy, including contraceptive choice, structural problems, fertility problems, inflammation or infection, and previous ectopic pregnancy.

If the ectopic pregnancy is detected early, an injection of the drug methotrexate may be used to stop cell growth and dissolve existing cells. If the ectopic pregnancy does not respond to medication, laparoscopy may be performed. Laparotomy may be needed for emergency surgery like heavy bleeding or tubal rupture. Mol *et al.* [7] reported that in selected patients with low serum hCG concentrations systemic methotrexate is a good alternative and added laparoscopy is the most effective one.

Complications of methotrexate are divided as minor (10%) such as adverse effects and major (7%) such as ruptured ectopic or persistent trophoblasts [8].

Studies that compare salpingostomy and salpingectomy could not demonstrate the fertility advantage because of the lack of supportive evidence [9, 10]. Although disadvantages of salpingostomy are known as the occurrence of persistent trophoblasts, monitoring hCG and recurrent ectopic pregnancy, an advantage of this operation over salpingectomy is the possibility of improved fertility.

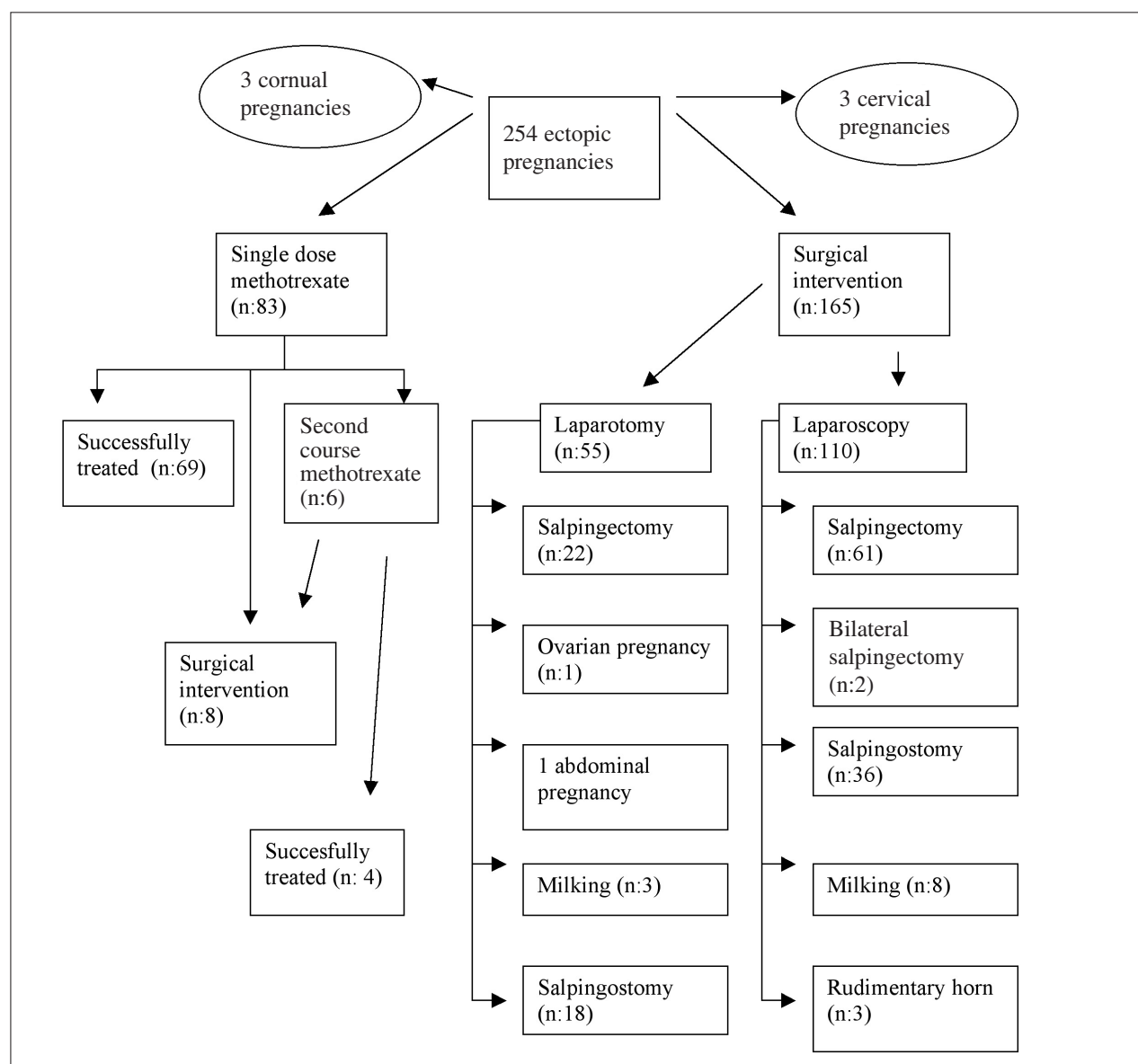


Figure 2. — Trial treatment profile.

Hajenius *et al.* [11] compared laparoscopic salpingostomy versus single dose systemic methotrexate. A hundred patients were included in this study and 51 of them were allocated methotrexate. While 82% of patients were successfully treated with one course, of the 49 patients where laparoscopy was performed, 72% were successfully treated. In the same study tube preservation was above 90% for each group.

Sowter [12] *et al.* found that the treatment with single dose methotrexate had a 65% success rate which was significantly lower than laparoscopic salpingostomy (93%). During the follow-up period three women in the methotrexate group experienced tubal rupture.

One retrospective cohort study found that 7-year cumulative intrauterine pregnancy rate was lower in women

who had undergone salpingectomy rather than salpingostomy [13]. Contrary to that some studies found limited evidence on this [14, 15]. Oelsner *et al.* [16] compared laparoscopy with laparotomy and found no significant difference on future fertility between the two techniques.

Conclusion

In our study women who required more than one dose of methotrexate or surgical intervention had significantly higher initial serum hCG concentrations than those women who were treated successfully with only one dose. Selection criteria of methotrexate and close follow-up of hCG appear to be the most important factors for high success rates. No difference was found between

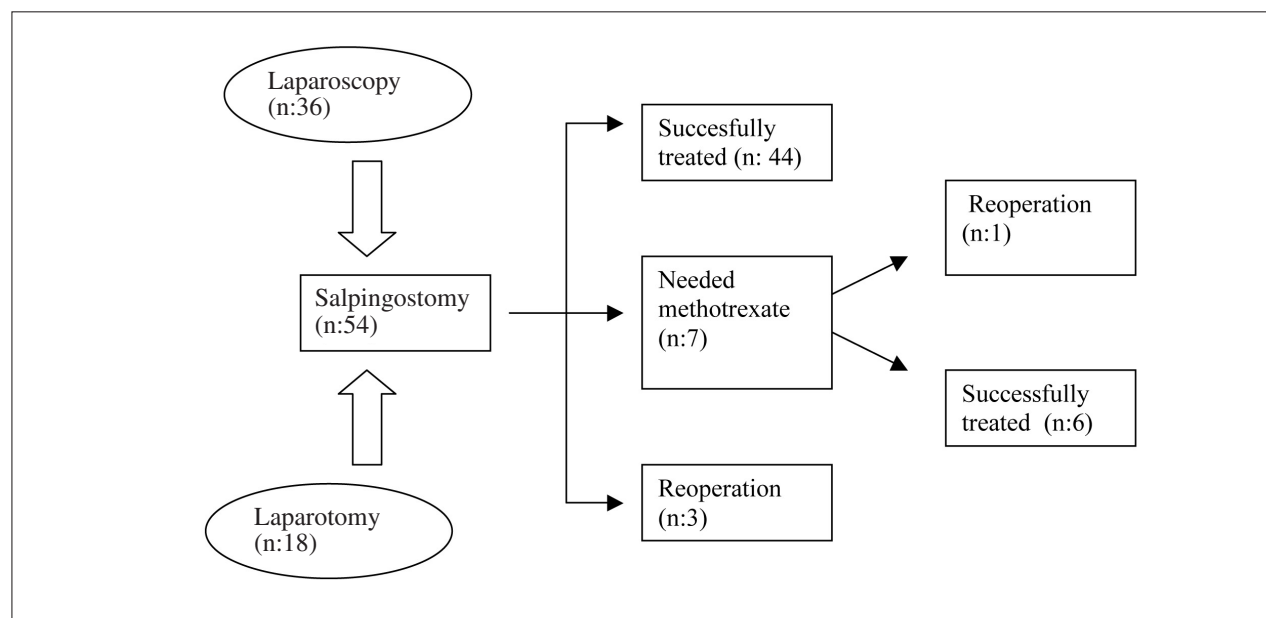


Figure 3. — Profile of the salpingostomy group.

success rates of laparotomy and laparoscopy but advantages of laparoscopy such as short hospitalization, less pain or cosmetic results make this technique better.

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