

Second-Look Laparoscopy Assessment of Tubal Conditions for Previous Ectopic Pregnancy after Methotrexate Therapy or Laparoscopic Salpingotomy

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Citation: Yu X, Guan J (2015) Second-look laparoscopy assessment of tubal conditions for previous ectopic pregnancy after methotrexate therapy or laparoscopic salpingotomy. *Enliven: Gynecol Obstet* 2(4): 007.

Received Date: 13th June 2015

Accepted Date: 14th August 2015

Published Date: 20th August 2015

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Abstract

Objective

To evaluate the severity of fallopian tubal conditions in patients with previous EP after methotrexate or laparoscopic conservative treatment using the second-look laparoscopy (SLL).

Methods

This was a retrospective clinical study in a university hospital. After reviewing medical records, thirty-eight women with EP were divided into group I (methotrexate therapy) and II (laparoscopic salpingotomy) according to the conservative treatment options they previously received. Then, the second-look laparoscopy was carried out to evaluate the severity of the fallopian tubal conditions (including integrity, patency and adhesion).

Results

The integrity and patency rates of the treated tubes in group I were 94.12% (16/17) and 52.94% (9/17), higher than those in group II (with 57.69% and 7.69%), respectively. But no difference was found in the adhesion rate of peri homolateral tubes between groups I (41.18%) and II (57.69%).

Conclusion

Our results suggested that conservative medical treatment with MTX by SLL could protect the tubal conditions better than laparoscopic salpingotomy, confirming that methotrexate treatment would be a very good way to preserve the tubes and improve future fertility. The second-look laparoscopy could be recommended to the EP patients with a desire for pregnancy.

Keywords Second-look laparoscopy; Tubal ectopic pregnancy; Methotrexate; Laparoscopic salpingotomy

Synopsis Use of second-look laparoscopy in EP after MTX therapy and conservative surgery.

Introduction

A recent tendency for ectopic pregnancy (EP) to marked increase over the past several decades has been in associated with the excessive reliance on assisted reproductive techniques and the high incidence of sexually transmitted diseases (STD). Women with previous life-threatening EP would be fearful of future fertility or conception because its recurrence rate was about 10 to 20% [1,2]. Early EP diagnosis and management come into

reality due to the considerable progress in diagnosis, real-time monitoring and treatments, such as transvaginal ultrasonography, serial measurement of serum hCG and laparoscopic surgery. Due to the occurrence of operative trauma or complications to fallopian tubes, the optimization for EP management should include the initial recovery and further preservation of subsequent fertility.

Currently, the recommended and available treatment options include medical treatment mainly with methotrexate and laparoscopic salpingotomy or salpingectomy. In details, systemic methotrexate (MTX) and laparoscopic salpingostomy could successfully cure the majority of patients with unruptured tubal pregnancy in stable haemodynamical condition [3,4]. Especially, medical treatment with MTX is recommended and preferred for the early EP, because it would protect future fertility better with little or without complications compared with invasive measures such as laparoscopic salpingotomy or salpingectomy [5-7].

Ideally, an early second-look or postoperative laparoscopy for infertility makes adhesiolysis easier and less formation of thick and vascular adhesions [8,9]. However, limited reports about the fallopian tubal conditions had not been explored through second-look laparoscopy in patients with previous EP after MTX. Therefore, the present investigation was to compare the adhesion, integrity and patency conditions using second-look laparoscopy for previous EP.

Materials and Methods

Patients Selections

From Jan 2009 to Dec 2013, thirty-eight patients initially treated for EP were enrolled due to infertility or other gynecological diseases in the Peking People's Hospital. After reviewing medical records, patients who satisfied the selection criteria were prospectively randomized into two groups based on past conservative treatment options for EP: Group I was conservative MTX therapy (n=16) and Group II was laparoscopic salpingotomy group (linear salpingotomy without suturing) (n=22). Among them, one in Group I and four in Group II underwent the same treatment in bilateral tubes. So we would assess and compare 17 tubes in Group I and 26 in Group II. Specific informed written consent was obtained from each subject and the study was approved by the Local Ethics Committee approval. (Table 1) showed the clinical information of the patients.

Table 1: Clinical information of patients with previous EP

Age	31.3±4.7	31.8±4.5	
Past history of previous pregnancy (%)			
Gravidity (times)	2.2±1.7	2.7±1.3	
Parity (times)	0	0.1±0.3	
Uterine pregnancy (%)	13	14	
Abortion (%)	13	14	
Previous tubal surgery (number)	0.1±0.3	1.3±0.6	<i>P</i> <0.01**
PID, n (%)	7	7	

Note: PID= Pelvic inflammatory disease; ** compared with Group I, *P*<0.01

Pathologic Observations and Findings on the Basis of the Second-Look Laparoscopy

In case of infertility or other gynecological diseases, the second-look laparoscopy (SLL) was performed to assess the pelvic and fallopian tubal conditions of patients after medical MTX or laparoscopic treatment with previous EP. The severities of tubal integrate or fracture, affected tubal morphology and per tubal pelvic adhesions were evaluated via laparoscopy according to the re-AFS classification (Revised American Fertility Society classification of endometriosis, 1985). Tubal patency was diagnosed via laparoscopy using diluted methylene blue dye. All the SLL procedures were performed by a single experienced surgeon. The laparoscopic findings were reported using a standard method in the surgery reports.

Statistical Analysis

Continuous data were presented as mean and standard deviation. Student's t-test was carried out when appropriate. The χ^2 test was used for categorical data with usual correction for small samples when appropriate. The minimal required sample size is 40, so Pearson chi-square test was used when the

expected frequency (E) was above 5, and Fisher's exact test when E was less than 5. A *P*-value of 0.05 was considered statistically significant.

Results

The clinical information of patients with previous EP in Group I and II was shown in (Table 1). Specifically, Group II had underwent more surgery number (1.3 ± 0.6) than Group I (0.1 ± 0.3, *P*<0.01). In addition, no statistically significant differences were found between groups in the age and in most of the previous pregnancy history, including gravidity, parity, uterine pregnancy and pelvic inflammatory disease (PID) (Table 1, *P*>0.05).

The detailed indications or observations on the basis of the second-look laparoscopy in Group I and II were shown in (Table 2). The results of our direct evaluation of fallopian tubes were in accordance with the aforementioned clinical results. All of the them were found to be infertile under second-look laparoscopy, which could just clearly illuminate the pathological causes of their infertility. And no significant difference were found in the occurrence rate of infertility, repeat ectopic pregnancy, endometriosis, uterine septum and the intervals between the second-look laparoscopy and the last EP (*P*>0.05).

Table 2: The indications or observations on the basis of the second-look laparoscopy

Indications	Group I (n=16)	Group II (n=22)
Infertility	15	15
Repeat ectopic pregnancy avidity (times)	1	5
Endometriosis	0	1
Intervals between SLL and last treatment	2.8±2.2	4.0±3.8

Group I and II also showed no statically difference with respect to the distribution of anatomic location of EP (Table 3, $\chi^2=0.003$, $P= 0.95$). In details, the incidence rates of affected tube were 47.06% at the right and 52.94% at the left fallopian tube, while 46.15% and 53.85% in group II were observed, respectively. As shown in Table 3, the integrity rate of homolateral tube in Group I was higher than Group II (94.12% vs. 57.69%, $P<0.05$). In contrast, more fracture rate of the homolateral tubes was found in Group II than Group I (42.31% vs. 5.88%, $P<0.05$, Figure 1A). Also, the hydrosalpinx was found at the distal end of tube in Group II (Figure 1B). Figure 1C showed a integrate tube with normal morphology in Group I.

The tubal patency rate of the treated side was higher in group I than group II (52.94% vs. 7.69%, $P<0.01$). Figure 2 showed that the fallopian tube was patent as seen after injection of the methylene blue in patients from Group I. Conversely, the lower tubal occlusion rate was found in Group I than Group II ($\chi^2 =8.81$, $P<0.01$). There was no significant difference in the mean adhesion score by revised American Fertility Society stage points (re-AFS), indicating the adhesion was easy to happen after EP.

Table 3: Comparison of tubal conditions under second-look laparoscopy

Tubal Conditions	Group I (n=17)	Group I (n=26)	P- Value
Affected tube (%)			
Both sides	5.88 (1)	15.38 (4)	
Right	47.06 (8)	46.15 (12)	
Left	52.94 (9)	53.85 (14)	
Homolateral tubal integrity (%)			
Integrate	94.12 (16)	57.69 (15)	$P= 0.024^*$
Fracture	5.88 (1)	42.31 (11)	$P= 0.024^*$
Tubal patency (%)			
Patent	52.94 (9)	7.69 (2)	$P= 0.003^{**}$
Occlusion	47.06 (8)	92.31 (24)	$P= 0.003^{**}$
Peritubal adhesion (%)			
Adhesions	41.18 (7)	57.69 (15)	
No adhesions	58.82 (10)	42.31(11)	

Note: $*P<0.05$; $**P<0.01$

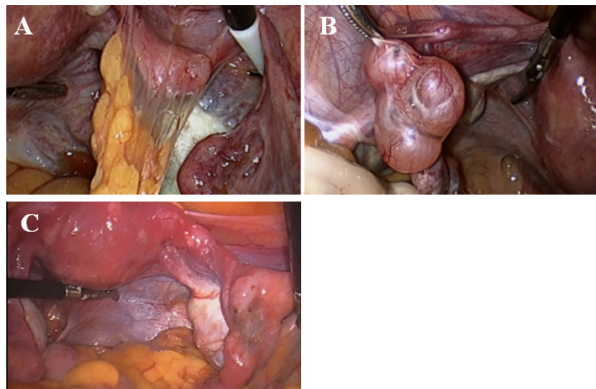


Figure 1: Images of tubal conditions or findings by SLL
 (A) Fracture in the right tube under laparoscopic salpingotomy
 (B) Hydrosalpinx at the distal end of left tube under laparoscopic salpingotomy
 (C) Tubal appearance after medical treatment with methotrexate



Figure 2: The fallopian tube with a medical treatment history was patent as seen in the methylene blue

Discussion

Clearly, future child bearing is one of the most concerns for women undergoing treatment for unruptured EP. Therefore, it would be reasonable to consider reproductive performance as an important variable when selecting the best treatment options. Then, does the treatment for resolution of EP affect subsequent spontaneous fertility following treatment for EP where an affected fallopian tube is conserved? Almost all of the data concluded that the outcomes of success and pregnancy rate were similar after medical treatment or laparoscopic salpingostomy [10-13]. For example, no significant difference was found from a multicentre, randomized and controlled trial (DEMETER, 2013), which showed that the two-year rates of intrauterine pregnancy were 67% after medical treatment and 71% after conservative surgery [14]. While existing studies are enough to evaluate the efficacy of intrauterine pregnancy, little is available to assess tubal conditions (patency and per tubal adhesion) after a conservative treatment for an EP. Medical therapy has an established place in the treatment of ectopic pregnancy, and in selected patients it appears to be as effective as surgery. Currently, many successful cases of EP with conservative treatment have led doctors or investigators to search more effective screening programs for EP, so as to realize the early detection of ectopic pregnancy for the first time and its recurrence. For example, real-time measurement on human chorionic gonadotropin (hCG), high-resolution transvaginal ultrasound (TVUS) and laparoscopic approach have allowed the early detection of EP, improving the chance of retaining tubal functions and further fertility for conservative treatment options [15,16]. Both the hysterosalpingography (HSG) and diagnostic laparoscopy are the effective tools for tubal patency assessment and HSG is the option most used in evaluating tubal patency after drug therapy for EP in published data. For example, the tubal patency rate could reach to 72.2% or 56.7%-83.9% in drug group, which were obtained from two individual groups [17,18]. When using salpingostomy, the tubal patency rate was 55% using HSG in laparoscopic salpingostomy verse 59% in MTX group, so no significant difference was found between the two treatments in the patency rate [19].

As all we know, the laparoscopy is largely accepted as the gold standard in diagnosing tubal occlusion. However, it is a more costly and invasive test than HSG. Therefore, it is usually reserved for women who could also benefit from laparoscopy in the assessment or treatment of another pelvic pathology. In addition, few data are available in assessing the tubal conditions by SLL after EP.

So we selected the SLL as our diagnostic tool in the study based on the above reasons. Fujishita had observed the tubal conditions by SLL or HSG in salpingotomy group (salpingotomy without suturing) [20] and he found that the tubal patency rate was 90% and per tubal adhesions rate was 33%, which were mostly comprised of filmy adhesion. In this

study, we described for the first time the assessment of tubal conditions using SLL in patients with previous EP, after MTX therapy or laparoscopic salpingotomy. Our data showed that the findings by SLL were different between Group I and II, in integrity, patency and peri-homolateral tubal adhesions. Our results highlighted that the medical treatment would better protect the affected tube and improve future fertility than the invasive laparoscopic salpingotomy. Therefore, the MTX treatment was less likely to influence tubal

conductance. On the other hand, the linear salpingotomy was more likely to affect or damage the whole tubal layer. Although the tubal appearance was complete and integrate, some tubes were still detected to be in occlusion.

Our results established a relationship between tubal conditions and MTX treatment in terms of SLL findings. For the early detection of unruptured tubal pregnancy, the combination of medical treatment and SLL monitoring would be preferred for predicting methotrexate failure and conserving future fertility. Because the first treatment of our patients were performed or done in different hospitals and or by different surgeon. Therefore, based factors indeed existed in the management protocol and surgical skills, so the tubal patency rate in our SLL was lower than that in the Fujishita's report [14]. Based on all of the above, it is necessary to regulate the principles of microsurgical for EP and improve the surgeon's technical.

Conflict of Interest

The authors declared no conflict of interest.

Author Contributions

XMY and JG Conceived and designed the experiments: XMY analyzed the data and wrote the paper.

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