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CLINICAL ARTICLE

Ovarian response to gonadotropins after laparoscopic salpingectomy for ectopic pregnancy

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ABSTRACT

Objective: To evaluate whether laparoscopic salpingectomy compromises ovarian response in women undergoing controlled ovarian hyperstimulation in vitro fertilization (IVF). *Methods:* In a retrospective study in Changsha, China, data from 76 women who underwent ovarian stimulation before and after laparoscopic salpingectomy for ectopic pregnancy were compared with those from 80 women who underwent 2 IVF cycles without surgical intervention between 2004 and 2009. *Results:* There were no differences in basal serum follicle-stimulating hormone (FSH) or estradiol (E_2); length of stimulation; or numbers of follicles, retrieved and fertilized oocytes, or high-quality embryos between the cycles before and after salpingectomy; however, initial and total doses of gonadotropins were significantly increased after surgery ($P<0.05$). IVF parameters were also comparable between the 2 cycles among women without surgical intervention, except for a significant increase in initial and total doses of gonadotropins at the second cycle ($P<0.05$). IVF parameters did not differ between the cycle subsequent to salpingectomy and the second cycle in women without surgical intervention. There were no significant differences between patients with unilateral and those with bilateral salpingectomy, nor between the operated and non-operated ovary in the same individual. *Conclusion:* Laparoscopic salpingectomy had no detrimental effect on ovarian response during IVF–embryo transfer treatment.
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1. Introduction

Ectopic pregnancy (EP) occurs more frequently in women who have undergone in vitro fertilization (IVF) treatment than in the normal population owing to tubal pathology, high steroid hormone levels that impair tubal function, and the increased number of embryos transferred [1,2]. Surgery is the common treatment of choice for EP. Clinicians often prefer salpingectomy over salpingostomy because of both the low risk of needing further treatment for persistent trophoblast and the possibility of a repeat EP after a more radical procedure [3]. In addition, studies have shown that the presence of hydrosalpinx may have a deleterious effect on the chances of successful pregnancy after IVF treatment [4], and that prophylactic salpingectomy may enhance the success of IVF [5–7]. Thus, some investigators have recommended that salpingectomy should be considered in patients before IVF is carried out [8].

A concern with salpingectomy is the possibility of impaired ovarian function after surgery [9]. Indeed, fewer ovulatory cycles have been noted after surgical division of the anastomotic blood vessels between the ovary and fimbria in rabbit [10]. Clinically, it has been reported that salpingectomy impairs ovarian blood flow and reduces antral follicle count [11], although no other studies have supported these findings. Thus, it seems important to determine whether or not salpingectomy does impair ovarian function.

In an attempt to aid both fertility specialists and their patients in the decision-making process, the aim of the present study was to evaluate the influence of laparoscopic salpingectomy for treatment of EP on ovarian stimulation parameters during the subsequent IVF cycle.

2. Materials and methods

In a retrospective study, the database of the Assisted Reproductive Technologies Center of CITIC–Xiangya Reproductive and Genetic Hospital, Changsha, China, was searched, and 76 women were identified who underwent an identical IVF and intracytoplasmic sperm injection (IVF/ICSI) cycle before and after salpingectomy for EP (surgical group) between January 1, 2004, and December 31, 2009. The study was approved by the Ethics Committee of the CITIC–Xiangya Reproductive and Genetic Hospital.

The study inclusion criteria were as follows: age younger than 40 years at second IVF cycle; a follicle-stimulating hormone (FSH) level on day 3 of the menstrual cycle of 10 mIU/mL or less, and an estradiol (E_2) level of 80 pg/mL or less; a period of less than 3 years between IVF cycles; use of an identical IVF/ICSI protocol at 2 cycles; no history of ovarian or other tubal surgery; and ovarian stimulation started at least 3 months after salpingectomy. Six women had 2 IVF

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cycles after salpingectomy, but only data from the first cycle after surgery were analyzed in the study.

To examine the effect of salpingectomy on ovarian function, 80 women who had no history of gynecologic surgery but had undergone 2 IVF treatment cycles as controls were also identified from the database (control group). The control women were matched with those in the surgical group by age at first IVF cycle, duration between cycles, etiology of infertility, and IVF protocol.

In the surgical group, bilateral salpingectomy was performed in 32 women, and unilateral salpingectomy in 44 women. Of these 44, an alternate procedure of proximal ligation was performed on the contralateral side in 23 women because of worries about recurrent EP; the 21 remaining women had unilateral non-operated tubes.

The long agonist protocol for controlled ovarian hyperstimulation was used. Controlled ovarian hyperstimulation was performed by administration of recombinant FSH (Gonal-F; Serono, Geneva, Switzerland) after pituitary suppression with 1.875 mg of triptorelin acetate injected intramuscularly during the midluteal phase of the preceding menstrual cycle. The initial FSH dose was 150–300 IU daily, which was individualized according to transvaginal ultrasonic measurements (GE Medical Systems Kretztechnik, Zipf, Austria) of the follicles and/or previous response to ovarian stimulation. Ovulation was induced by the administration of 5000–10 000 IU of human chorionic gonadotropin (hCG) when at least 3 follicles had reached a diameter of 18 mm. Transvaginal ultrasound-guided follicular aspiration was performed 34–36 hours later.

According to the routine procedure, 2 or 3 embryos were transferred on day 3 after oocyte retrieval. The luteal phase was supported by 600 mg per day of vaginal micronized progesterone (Utrogestan; Laboratoires Besins International, Montrouge, France) or by 80 mg per day of intramuscular progesterone (Gestone; Zhejiang Xianju, Zhejiang, China), starting from the day of oocyte retrieval.

The outcome measure of the study was ovarian response to gonadotropins. Ovarian response was assessed by calculating the total dose of gonadotropins administered; the duration of ovarian stimulation; the number of follicles (>12 mm and >17 mm in mean diameter) developing in both ovaries; the number of oocytes retrieved and fertilized; the number of high-quality embryos; and serum E_2 concentrations on the day of hCG administration.

For all women, baseline serum FSH and E_2 concentrations were measured before surgery and at 3 months after surgery but before ovarian stimulation commenced. An electrochemiluminescence immunoassay (Roche Diagnostics GmbH, Mannheim, Germany) was used to measure serum FSH and E_2.

Data are given as mean ± SD. Data that were normally distributed were analyzed by Student paired *t*-test and *t*-test when appropriate, whereas data that were not normally distributed were compared by Mann–Whitney U test. All statistical analyses were performed via SPSS version 11.0 (SPSS, Chicago, IL, USA). A *P* value of less than 0.05 was considered statistically significant.

3. Results

The mean ± SD age of women was 31.5 ± 4.2 years before salpingectomy and 32.1 ± 4.0 years after salpingectomy ($P<0.05$), and the mean duration between the 2 cycles was 12.8 ± 6.7 months. The main indications before the pre-salpingectomy IVF/ICSI cycle was tubal factors (n = 54), male factors (n = 7), and endometriosis (n = 5). Table 1 shows parameters at the pre- and post-salpingectomy IVF cycles among women in the surgical group, and at the 2 IVF cycles among women in the control group.

First, ovarian performance before and after salpingectomy was analyzed. No significant difference was observed in basal serum FSH and E_2 concentrations, number of days required for ovarian stimulation, number of follicles, number of retrieved and fertilized oocytes, or number of high-quality embryos in IVF cycles performed before and after salpingectomy. By contrast, the total and initial doses of FSH required were significantly increased by 239 and 31 units, respectively, after salpingectomy ($P<0.05$).

Second, a similar analysis was conducted between the 2 IVF cycles among women without surgical intervention. In line with the surgical group, ovarian response was comparable between the 2 cycles except that the total and initial doses of FSH required were 252 and 35 units higher, respectively, at the second cycle than at the first ($P<0.05$).

Last, data from women with and without salpingectomy were compared. IVF parameters in the cycle preceding salpingectomy were comparable to those in the first cycle in the control group. Similarly, the cycle subsequent to salpingectomy was compared with the second cycle in the control group, and no significant differences were found.

Table 2 shows the analysis of subgroups of patients who underwent bilateral and unilateral salpingectomy. In the comparison of bilateral versus unilateral salpingectomy, there was no significant difference in ovarian response over time.

Table 3 shows the difference in the number of developed follicles between the operated and non-operated ovary among individuals who underwent unilateral salpingectomy. No difference was found between the number of follicles developed from the operated ovary and the number developed from the intact adnexa.

4. Discussion

Various studies have attempted to evaluate the impact of salpingectomy on ovarian function; however, the results are not entirely

Table 1
Serum FSH and E_2 levels and ovarian response to stimulation in the surgical and control groups.[a,b,c]

Variable	Surgical group (n = 76)			Control group (n = 80)		
	Pre-salpingectomy	Post-salpingectomy	*P* value	First cycle	Second cycle	*P* value
Day 3 FSH, IU/L	6.9 ± 1.5	7.2 ± 1.6	$P>0.05$	7.2 ± 1.8	7.0 ± 1.6	$P>0.05$
Day 3 E_2, pg/ml	41.1 ± 11.5	39.2 ± 13.0	$P>0.05$	40.8 ± 10.5	42.0 ± 13.9	$P>0.05$
E_2 on day of hCG, pg/ml	2663.5 ± 1246	2783.3 ± 1281.3	$P>0.05$	2934.8 ± 1234.9	2882.5 ± 1167.3	$P>0.05$
Initial dose of FSH, IU	193.2 ± 52.7	221.7 ± 60.4	$P<0.05$	195 ± 51.2	226.7 ± 49.3	$P<0.05$
Total dose of FSH, IU	2124.5 ± 590.3	2370.8 ± 614.5	$P<0.05$	2149.5 ± 604.9	2376.0 ± 620.6	$P<0.05$
Length of FSH stimulation, days	10.7 ± 1.5	11.1 ± 1.8	$P>0.05$	11.1 ± 1.8	10.9 ± 1.7	$P>0.05$
No. of follicles >12 mm	11.9 ± 4.7	12.1 ± 4.6	$P>0.05$	12.1 ± 4.6	12.4 ± 4.4	$P>0.05$
No. of follicles >17 mm	6.4 ± 2.8	6.8 ± 3.5	$P>0.05$	7.0 ± 2.1	7.2 ± 2.5	$P>0.05$
No. of oocytes retrieved	11.1 ± 5.4	11.6 ± 4.1	$P>0.05$	11.5 ± 4.4	12.1 ± 4.8	$P>0.05$
No. of oocytes fertilized	8.3 ± 4.4	8.4 ± 3.9	$P>0.05$	8.0 ± 3.1	8.2 ± 4.2	$P>0.05$
No. of high-quality embryos	5.1 ± 3.3	5.3 ± 3.3	$P>0.05$	5.0 ± 3.2	5.0 ± 3.1	$P>0.05$

Abbreviations: FSH, follicle-stimulating hormone; E_2, estradiol; hCG, human chorionic gonadotropin.

[a] Values are given as mean ± SD.

[b] Pre-salpingectomy in surgical group versus the first cycle in control group, $P>0.05$.

[c] Post-salpingectomy in surgical group versus the second cycle in control group, $P>0.05$.

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