ASSESSING OVARIAN RESERVE IN WOMEN AFTER LAPAROSCOPIC SURGERY FOR OVARIAN ENDOMETRIOSIS

Tzu-Wei Liao, Ming-Yang Chang*, Chi-Hsin Chiang, Chi-Shing Shiao, T’ang-T’ang Hsieh, Yung-Kwei Soong
Department of Obstetrics and Gynecology, Chang Gung Memorial Hospital, Taipei, Taiwan.

SUMMARY

Objective: A retrospective study to evaluate the ovarian reserve via antral follicle counts and basal hormone changes in infertile patients who had previously undergone laparoscopic surgery for ovarian endometriosis.

Materials and Methods: Infertile women who had undergone laparoscopy for ovarian endometriosis were enrolled and divided into four groups according to the ovarian surgical procedure, determined by the degree of the invading lesion: bipolar cauterization of the superficial ovarian endometriosis (group A), cystectomy of the endometrioma with a diameter of less than 5 cm (group B) or a diameter of at least 5 cm (group C), or unilateral oophorectomy (group D). Follow-up statistics included basal serum hormone levels and ovarian antral follicle counts, which were determined about 12 months after surgery.

Results: The study included 233 women. We found a significant difference in remaining antral follicle counts in groups A, B, C, and D: 11.1 ± 3.5, 9.4 ± 3.1, 7.5 ± 2.3, and 4.0 ± 2.0, respectively (p < 0.001). There was no difference in day 3 follicle-stimulating hormone (FSH) levels: 6.2 ± 2.0, 6.2 ± 2.8, 6.3 ± 2.2, and 7.8 ± 2.1 IU/L in groups A, B, C, and D, respectively. Significantly higher basal FSH levels were noted when comparing group D with groups A, B, and C (p < 0.05).

Conclusions: Ovarian endometrioma cystectomy or oophorectomy damages the ovarian reserve. Damage to the vascular system and the cortex of the ovary during surgery might accelerate depletion of the follicular pool. The FSH level is compromised significantly until the follicular pool is depleted below a certain threshold. This might be because of various components controlling FSH modulation, mainly inhibin but possibly other steroids and peptides influenced by extraovarian mechanisms or the aging of neuroendocrine tissues. [Taiwanese J Obstet Gynecol 2004;43(3):144–148]

Key Words: ovarian reserve, ovarian endometriosis, ovarian surgery, infertility

Introduction

Ovarian endometrioma is endometriosis in the form of a pseudocyst formed by an accumulation of menstrual debris from the shedding and bleeding of active implants located at the site of inversion, resulting in progressive invagination of the ovarian cortex [1]. The origin of the chocolate-colored fluid could be cyst-wall exudation, congested blood vessels in the cyst wall, or inflammation around persistent intracystic endometriosis. Women with endometrioma may present symptoms of pelvic pain, dysmenorrhea, infertility, and possibly decreasing ovarian reserve due to ovarian mass reduction by either direct invasion of endometriotic implants, compression effects, or surgical damage to the mass.

Although treatment for endometrioma is controversial, surgery is considered the treatment of choice, and only surgery can destroy it completely. Surgery results in lower recurrence rates and higher rates of symptom relief [2,3]. However, concern has been raised that the mechanical removal of the pseudocapsule of the endometrioma may remove some of the adja-
cent healthy ovarian stroma, and so impair the ovarian reserve and its response to gonadotropin stimulation [4].

Many methods have been used to predict ovarian response and to evaluate ovarian reserve [5–12]. Measurements of basal follicle-stimulating hormone (FSH) and estradiol (E2) levels and antral follicle counts are most widely applied because they are reliable, direct, and noninvasive. Women begin to have a subtle increase in serum FSH concentrations in their mid-30s, coinciding with the time at which fertility begins to decline [13]. Since this report, basal FSH has been used to predict ovarian reserve, and is more usefully regarded as a prognostic test for in vitro fertilization (IVF) outcomes. The number of small antral follicles in the ovaries, as measured by ultrasonography, is also clearly related to reproductive age and may reflect the size of the remaining primordial follicle pool, the ovarian reserve [14].

Numerous studies have assessed IVF outcome in women with endometriosis [15], but little information is available in the literature on ovarian reserve in treated ovarian endometriosis. This retrospective study was designed to evaluate and compare the ovarian reserve of infertile patients who had previously undergone laparoscopic surgery for ovarian endometriosis.

Materials and Methods

All women who visited our infertility clinic and completed the standard evaluation between September 1996 and August 2002 were analyzed. Patients who had previously undergone laparoscopic surgery for ovarian endometriosis were considered eligible for the study. Diagnosis of endometriosis, based on sonographic measurements, surgical findings confirmed at laparoscopy, and/or microscopic pathologic examination, was determined from medical records. In patients with more than one endometrioma, we added together the diameters of each endometrioma. Women were included in the study if they were aged between 20 and 40 years but had not conceived within 1 year after surgery. Patients who had received steroids or estrogen-suppressing medication within 3 months before evaluation were excluded.

At surgical laparoscopy, pelvic and peritoneal lesions and adhesions were inspected. Adhesions were lysed using sharp dissection to fully mobilize the ovaries. Endometriotic lesions involving peritoneal and ovarian surfaces were cauterized using bipolar coagulation. In cases of ovarian endometrioma, we punctured, drained, and washed the cavity of the endometrioma of all its “chocolate” content. The inner lining of the cyst was stripped from the normal ovarian tissue using two grasping forceps pulled slowly in opposite directions, followed by selective cauterization of the bleeding vessels to achieve hemostasis, allowing secondary closure of the defect. Ovaries were removed only if the lesion had destroyed the whole ovarian stroma and surgery could not preserve any of the remaining ovarian tissue. The specimens were removed from the abdominal cavity using a bag. All the procedures were performed by the same surgeon (MYC).

Patients were classified into four groups according to the degree of invasion and the surgical procedure. In group A, there was only superficial endometriosis in both ovaries, and these were treated using superficial electrocauterization. In group B, with ovarian endometrioma of less than 5 cm in diameter, treatment was ovarian cystectomy. In group C, cystectomy was performed for endometriomas of at least 5 cm, while in group D, unilateral oophorectomy was performed.

Follow-up measurements after surgery included serum hormone levels (day 3 FSH and E2), as well as ovarian antral follicle counts. Vaginal ultrasound was performed on cycle day 3, using an Aloka Sonography SSD-1400 with a 5.5 MHz transvaginal probe (UST-984-5; Mitakashi, Aloka, Japan), to determine the number of antral follicles with diameters of more than 2 mm and less than 12 mm in both ovaries. All patients had a follow-up period of more than 1 year.

Statistical analysis was performed using Student’s t test and one-way analysis of variance (ANOVA), as appropriate. A p value of less than 0.05 was considered statistically significant.

Results

A total of 233 patients who had been treated with laparoscopic surgery and who met the eligibility criteria were enrolled. There were 117, 61, 41, and 14 patients in groups A, B, C, and D, respectively. The mean age was 34.4 ± 4.2 years, and the mean duration of infertility was 3.5 ± 2.2 years. There was no significant difference in mean age or mean duration of infertility among the four groups.

Clinical characteristics and ovarian parameters are presented in the Table. The average basal FSH level before surgery was 6.1 ± 3.2 IU/L, with no significant difference among the four groups. After surgery, there was a significant difference in antral follicle counts among the four groups (p < 0.001, one-way ANOVA). There was no significant difference among the four groups in day 3 FSH levels after surgery. Significantly higher basal FSH levels were only noted between group...
D and groups A, B, and C after surgery (p < 0.05, Student’s t test). There was no significant difference in E2 level among the four groups.

Discussion

Medical treatment has been ineffective for ovarian endometriotic cysts, and surgery is considered the procedure of choice. Cystectomy for ovarian endometrioma is widely performed because of its efficacy in decreasing the recurrence of symptoms and signs when compared to cyst content aspiration, fenestration, and coagulation [15,16]. However, cystectomy can provoke loss of normal ovarian tissue either by removal of ovarian stroma with oocytes together with the capsule or by thermal damage due to coagulation [3]. The reproductive results have been well demonstrated in women who have previously had ovarian surgery. One study demonstrated that postcystectomy ovaries had reduced follicular response in natural and clomiphene citrate-stimulated cycles, but produced a comparable number of follicles to normal ovaries when stimulated with gonadotropins and had a similar reproductive outcome [17]. Another study in Taiwanese women reported that ovarian surgery resulted in poor ovarian response and increased cancellation rates during controlled ovarian hyperstimulation [18]. However, the actual ovarian reserve parameters have not been well demonstrated. We thus analyzed ovarian reserve in women who had undergone surgery for endometriosis.

In the normal aging process, decreased numbers of human follicles and elevations in FSH and E2 levels represent the most clinically significant alterations in older reproductive-aged women. They are the most useful predictors of reproductive capacity. In this study, patients were of similar age and had various degrees of endometriosis surgery. We found a significant decrease in antral follicle counts but not in FSH and E2 levels in the four groups. Significantly higher basal FSH levels were only noted when the number of antral follicles diminished to a certain number. We previously found that a decrease in the ovarian cohort of antral follicles increases serum FSH level [9]. A recent study also reported that basal FSH is a good predictor of the size of the remaining follicle pool [19]. However, in this study, the measurement of ovarian reserve parameters show that basal hormone levels do not decay as the number of antral follicles decreases.

Basal hormones related to the hypothalamus-pituitary-ovary axis have a significant correlation with patient age and antral follicle count [19]. The size of the follicle pool is determined by age and the vascular system. It is not clear how hormones react when the follicle pool is decreased by iatrogenic vascular damage rather than by the normal aging process. Increasing understanding of the synthesis and secretion of somatotropins and their potential endocrine role in the regulation of FSH suggests that antral follicles are the main secretors of inhibin, which decreases the ovarian cohort of antral follicles and increases serum FSH level. Evidence is accumulating that a selective increase in FSH is due to diminished negative feedback by inhibin B secreted by granulosa cells of developing antral follicles during the early follicular phase and by inhibin A synthesized by the dominant follicle and the corpus luteum during the preceding luteal phase of the cycle [20]. However, to presume that a single deficiency in inhibin activity could account for postsurgical FSH levels fails to consider the extensive structural and functional overlap of the other components known to mediate FSH regulation. On the contrary, the monotropic rise in FSH is more likely to be dictated by the sum effect of inhibitory inputs from inhibins and follistatins, as well as E2, and the stimulatory inputs from gonadotropin-releasing hormone and activin [21].

Another hypothesis is that the hypothalamic-pituitary changes in premenopausal, middle-aged women (increases in FSH level and interpulse interval) may rep-
resent an intrinsic effect of aging on neuroendocrine tissues rather than a secondary event mediated by follicular decline [22]. A number of hormones and factors modulate ovarian-cell apoptosis. FSH has a suppressive effect on ovarian cell loss in cultures of rat granulosa cells [23]. This indicates that FSH may spare ovarian follicles from the atretic process. Unfortunately, much of this data is derived from studies performed in rodents, and relatively little is known about the extraovarian mechanisms regulating ovarian senescence in humans. In our study, FSH levels rose significantly until the antral follicle pool was depleted to a certain number. We presume that this was because of various components controlling FSH modulation. It is mainly controlled by inhibin synthesized by detectable antral follicles and primordial follicles undetectable by ultrasonography. It may also be modulated by other steroids and peptides influenced by extraovarian mechanisms or the aging of neuroendocrine tissues. When the follicle number is depleted below a certain threshold, fertility as well as the FSH level is compromised. This threshold is variable among women.

In conclusion, ovarian endometrioma cystectomy or oophorectomy may damage the ovarian reserve. Damage to the vascular system and the cortex of the ovary during surgery might accelerate the depletion of the follicular pool. The FSH level is compromised significantly until the follicular pool is depleted below a certain threshold. We presume that this is because of various components in FSH modulation. Gynecologists are most concerned about the adverse effects of endometriosis on infertility. A better understanding of these issues is a prerequisite to the development of clinical therapies that may, some day, enable the clinician to promote ovarian reserve and prolong the reproductive lifespan of the fertile and infertile patient.

References


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