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AMH trend after laparoscopic cystectomy and ovarian suturing in patients with endometriomas

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Abstract
Purpose To evaluate the ovarian reserve after laparoscopic cystectomy with suturing in patients with endometriomas.
Methods A total of 80 women with unilateral or bilateral endometriomas underwent laparoscopic cystectomy using sutures for hemostasis after the excision of ovarian cysts. Serum levels of antimullerian hormone (AMH) and FSH were measured at the day 3 of menstrual cycles preoperatively, 6 and 12 months postoperatively.
Results In the bilateral endometrioma group, serum AMH level decreased significantly from the baseline (4.68 ± 2.87 ng/ml) to 6 months (3.05 ± 1.99 ng/ml) and 12 months (2.26 ± 1.88 ng/ml) postoperatively, whereas the FSH level increased significantly from baseline to 12 months postoperatively ($P < 0.05$). Those patients with unilateral endometriomas also had lower levels of AMH in 6 and 12 months after operation. When compared between unilateral and bilateral endometrioma group, the rate of AMH decline 6 and 12 months and the rate of FSH increase 12 months postoperatively reached statistical significance ($P < 0.05$).
Conclusions The changes of the AMH and FSH values suggest that the ovarian reserve is obviously reduced in spite of suturing technology used as a method of hemostasis after stripping ovarian endometriomas, especially in those with bilateral cysts. The protective effect of the ovarian suturing for ovarian reserve may be marginal.

Keywords Laparoscopic cystectomy · Endometrioma · Ovarian reserve

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Introduction

Endometriosis is a common disease in which the endometrial glands and stroma are found outside the uterine cavity, and endometrioma is defined as the presence of an ovarian cyst with ectopic endometriotic tissues. Laparoscopic ovarian cystectomy is currently the most valid approach in treatment of endometriomas [1, 2]. However, there are concerns about the ovarian reserve damage during surgery including the removal of healthy ovarian tissue adjacent to the cyst capsule and the thermal damage of ovarian follicles by use of bipolar coagulation for hemostasis purposes [3]. Some investigators propose that the ovarian reserve was less reduced in sutured ovaries than in those electrocoagulated, they suggest suturing technology can be a better choice after stripping ovarian endometriomas [4, 5].

To investigate the extent of ovarian reserve impairment, the antimullerian hormone (AMH) was recommended as the most reliable marker, and its production was reported to be stable throughout the menstrual cycle [6]. To the best of our knowledge, few studies have assessed the impairment on ovarian reserve induced by laparoscopic excision using serum AMH levels. The aim of this prospective study was to evaluate the impact of laparoscopic cystectomy with ovarian suturing for endometrioma on ovarian reserve as measured by serum AMH levels.

Materials and methods

Patients

Between January 2012 and December 2013, 80 patients aged between 21 and 35 years with ovarian endometriomas requiring surgical removal were enrolled in the study. The diagnoses of unilateral and bilateral cystectomy (at least 4 cm) were observed for two menstrual cycles by ultrasound on day 3 of each cycle. The treatment protocol was approved by the Ethics Committee of Jinhua Municipal Central Hospital, and informed consent was obtained from all patients. The exclusion criteria were as follows: patients with polycystic ovarian syndrome according to the Rotterdam criteria, previous ovarian surgery, premature ovarian failure, ovarian malignant diseases, intake of hormonal medications within 3 months before enrollment, and any other endocrine disorders such as hyperprolactinemia, congenital adrenal hyperplasia or Cushing's syndrome.

Laparoscopic cystectomy techniques

The laparoscopic cystectomy operations were performed under general anesthesia by the same team of experienced surgeons. After adhesiolysis and mobilization of the ovary, we identified the cleavage plane between the cyst capsule and the normal ovarian tissue. Then, two grasping forceps were used to gently strip the cyst wall from the ovary. Meticulous reconstruction and hemostasis were performed by using 3-0 polyglactin without bipolar forceps electrocoagulation. All endometrioma specimens obtained from operation were submitted for pathology examination.

Hormone measurements

Venous blood samples were drawn from the patients at day 3 of menstrual cycles preoperatively, 6 and 12 months postoperatively. Serum AMH level was analyzed with an enzyme-linked immunosorbent assay (ELISA) [Diagnostic Systems Laboratories (DSL), USA]. The intra-assay and inter-assay coefficients of variation for AMH was 9.4 and 7.2 %, respectively, with a detection limit of 0.006 ng/ml. Serum FSH level was measured using an Immulite 2000 immunoassay system (Diagnostic Products, Los Angeles, CA), with a detection limit of 0.1 mIU/ml.

Statistics

Statistical analysis was performed using SPSS version 13.0. Paired sample *t* test was used to compare the differences in AMH and FSH levels before and after the operation within the same group. Independent *t* test was used to compare the AMH and FSH levels between unilateral and bilateral endometriomas groups. Data were presented as mean ± SD and $P < 0.05$ was considered statistically significant.

Results

Initially, 80 women were included in this study. The mean age of our cohort was 29.1 years (rage 21–35 years). Eight women got pregnant and four lost to follow-up. Thus, 68 women formed the final study group, of whom 36 had unilateral and 32 had bilateral endometriomas.

The median level of baseline serum AMH was 5.02 ± 3.05 ng/ml in unilateral endometrioma group, which thereafter decreased to 4.43 ± 2.13 and 4.07 ± 2.06 ng/ml at 6 and 12 month postoperatively. However, the trend of decrease in AMH level was not statistically significant. While in the bilateral endometrioma group, the serum AMH level significant decreased in 6 and 12 postoperative month as compared to baseline serum AMH level ($P < 0.05$ and $P < 0.01$) (Table 1). The level of baseline serum FSH was 5.36 ± 1.81 mIU/ml, it remained approximately unchanged after 6 and 12 months postoperatively ($P > 0.05$) in unilateral endometrioma group. In the bilateral endometrioma group, the serum FSH level slightly decreased in the 6th postoperative month ($P > 0.05$), then significantly decreased in the 12th postoperative month (8.26 ± 1.88 mIU/ml, $P < 0.05$) compared to baseline samples (Table 2).

There was no difference in preoperative serum AMH and FSH levels between the unilateral and bilateral endometrioma group. Postoperatively, the serum AMH level in the bilateral endometrioma group was significantly lower than in the unilateral endometrioma group during 6 months (3.05 ± 1.99 vs 4.43 ± 2.13 ng/ml, $P < 0.05$) and 12 months (2.26 ± 1.88 vs 4.07 ± 2.06 ng/ml, $P < 0.05$) postoperatively. On the other hand, the serum FSH level in the bilateral endometrioma group was significantly higher than in the unilateral endometrioma group during the 12th postoperative month (8.26 ± 1.88 vs 5.49 ± 2.06 mIU/ml, $P < 0.05$), there was no significant difference in serum FSH levels between two groups during the 6th postoperative month.

Discussion

Laparoscopic cystectomy is considered the optimal treatment for endometriomas, because it allows a more complete removal of the lesion and is associated with lower incidence of recurrence compared with other methods. Nonetheless, it is still under debate whether the ovarian tissue is damaged during surgery. We performed the

Table 1 The serum AMH values before and after operation

AMH (ng/ml)	Unilateral cysts group (n=36)	Bilateral cysts group (n=32)
Preoperative	5.02 ± 3.05	4.68 ± 2.87
Postoperative 6th	4.43 ± 2.13[b]	3.05 ± 1.99[a]
Postoperative 12th	4.07 ± 2.06[b]	2.26 ± 1.88[aa]

[a] $P < 0.05$, [aa] $P < 0.01$, compared with baseline; [b] $P < 0.05$, compared with bilateral cysts group

Table 2 The serum FSH values before and after operation

FSH (mIU/ml)	Unilateral cysts group (n=36)	Bilateral cysts group (n=32)
Preoperative	5.36 ± 1.81	5.38 ± 1.94
Postoperative 6th	5.52 ± 1.73	6.05 ± 1.99
Postoperative 12th	5.49 ± 2.06[b]	8.26 ± 1.88[a]

[a] $P < 0.05$, compared with baseline

[b] $P < 0.05$, compared with bilateral cysts group

stripping technique by the same experienced laparoscopists with high cautiousness and used suture instead of bipolar electrocoagulation for hemostasis. The aim of the study was to observe whether the ovarian reserve could be maintained similar to the preoperative level.

AMH, a member of the transforming growth factor-β family, is secreted by granulose cells in preantral and early antral follicles [7]. It was first reported in 1981 by Donohoe [8], because the serum AMH level is considered an indication for the size of the growing follicle pool, the utility of AMH measurement as an ideal estimator of ovarian function has recently developed. Basal FSH level is the most widely used marker of ovarian reserve. With combined use of AMH and FSH evaluation, we prospectively investigated the ovarian reserve of 80 patients after the excision of endometriomas cysts.

Chang et al. [9] believed that a surgery-related ovarian impairment really exists, but it partially recovered up to 3 months postoperatively. As a result, some investigators suggest delaying the follow-up intervals to observe whether the decreased AMH levels could be fully recovered. In our study, the serum AMH level continuously decreased after 6 and 12 months postoperatively as compared to baseline samples in the unilateral endometrioma group, though this reduction was not statistically significant. On the other hand, this difference reached statistical difference during the similar time frame ($P < 0.05$ and $P < 0.01$) in the bilateral endometrioma group. Although there were no data about serum AMH level 3 months after surgery, our data showed that the decrease of the serum AMH level is not temporary but sustained over 6–12 months. The results indicate that laparoscopic cystectomy can lead to a irreversible damage to ovarian reserve especially in bilaterality group, which was also supported by the increase trend of FSH in the bilateral endometrioma group 12 months postoperatively ($P < 0.05$) in our study. The findings of the current data are in line with the study by Raffi and Ferrero [10, 11]. Hwu et al. [12] also demonstrated that the serum AMH level in endometrioma patients with previous cystectomy was significantly lower than those without previous cystectomy. In our study, the difference between the postoperative and preoperative groups did not reach statistical significance in patients operated for a unilateral endometriomas, which could be explained by the normal contralateral ovary compensating for the ovarian function [13] and was not the case in bilateral endometrioma group as evident from the results of our study (Table 2).

Two studies that reported ovarian reserve was not affected by laparoscopic cystectomy [14, 15]. However, we found both articles had the common characteristic about short-term follow-up intervals (1 month postoperatively), limited number of patients, and relatively small sample of bilateral endometrioma patients. As a matter of fact, Alper et al. [15] showed that the serum AMH level deceased 1 month postoperatively. Unfortunately, the difference did not reach statistical significance. In his study, a total of 16 patients were included, of which only one had bilateral endometriomas. Therefore, their conclusions need to be further investigated empirically. Recent study [16] showed that, even when performed by experienced laparoscopists with every effort to be atraumatic, the laparoscopic cystectomy reduced the ovarian reserve. The causes of the decrease serum AMH level postoperatively might as follows: sutures elevate intraovarian pressure with ischemic regions produce additional damage of healthy tissue, although the thermal destruction to ovarian stroma and vascularization induced by bipolar electrocoagulation is more extensive. The presence of ovarian tissue adjacent to the lesion has been documented in many pathologic specimens indicating the inevitable removal of healthy tissue during laparoscopic stripping technique [14, 17]. A difficult striping procedure due to severe adhesion and multiple

endometrioma cysts aggravates ovarian impairment. The inflammation-mediated injury following operation may cause ovarian damage resulting in decreased ovarian reserve. Thus, several techniques had been proposed for preserving ovarian reserve during surgery such as the combined cystectomy plus ablation of the remaining 10–20 % close to ovarian hilus [18], a three-step approach [19], injection of vasopressin around the cyst wall [20], and the ultrasound-guided puncture with methotrexate [21], or alcohol [22]. Further clinical trials are mandatory to evaluate the effect of these suggestions.

Current data suggest a progressive decline in ovarian reserve following cystectomy surgery in spite of suturing technology used as a method of hemostasis. In patients with a unilateral endometrioma, the impact of surgery on future fertility may be minimal, while excision of bilateral endometrioma can be great. The negative impact of this procedure on ovarian reserve should be fully considered before operation.

Compliance with ethical standards

Conflict of interest The authors have no conflicts of interest.

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