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Original Article

Serum antimullerian hormone before and after laparoscopic excision of ovarian endometrioma

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Abstract

Background

Surgery of ovarian endometrioma may have a detrimental effect on ovarian reserve. This study aims to evaluate the effect of laparoscopic cystectomy on serum antimullerian hormone (AMH) in patients with endometrioma.

Materials and methods

A prospective study was performed at El-Galaa Maternity Teaching Hospital where 60 women with endometriomas underwent laparoscopic cystectomy. Serum AMH, follicle-stimulating hormone (FSH), luteinizing hormone, estradiol, and antral follicle count (AFC) were measured preoperatively and at 3 months postoperatively.

Outcome measures

The ovarian reserve was measured based on the change of AMH level before and after surgery. Moreover, the secondary end point was to detect the changes in FSH, luteinizing hormone, estradiol, and AFC.

Results

Serum AMH decreased significantly from the baseline (4.12 ± 3.41) to 3 months postoperatively (2.62 ± 2.7). The AFC increased significantly from the baseline to 3 months after the operation.

Conclusion

Laparoscopic cystectomy of ovarian endometriomas causes a significant decline in serum AMH level and a significant increase in the level of FSH.

Keywords: Antimullerian hormone, cystectomy, endometrioma, ovarian reserve

Introduction

Endometriosis is a reproductive age disorder of women, characterized by the presence of endometrial glands and stroma outside the uterine cavity. It is a complex gynecological disease in its physiopathological aspects and clinical implications. Some women with endometriosis are asymptomatic, but for many, it has severe effects on their physical, mental, and social well-being.

The disease is usually manifested with pelvic pain, dysmenorrhea, and infertility. The prevalence is found to be 7–10% among the general female population. Nonetheless, high prevalence rates have been noted among women with subfertility (50%) [1]. Endometrioma is the formation of a cyst within the ovary with ectopic endometrium tissue lining and is found to be in 20% of patients with endometriosis [2]. It has been proposed that ovarian endometriomas, in most cases (90%), are formed by either invagination of the ovarian cortex after implantation of the endometrial foci on the ovarian surface or by coelomic metaplasia of the ovarian epithelium [3].

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The treatment of ovarian endometriomas has been a subject of controversy. Laparoscopic ovarian cystectomy seems to be the method of choice [4–6]. However, fertility doubtfully may be reduced by traumatic surgery. It removes not only the endometrioma but also the healthy ovarian cortex [7,8].

Several studies have demonstrated that the number of oocytes obtained after ovarian stimulation during in-vitro fertilization cycles was fewer oocytes from ovaries that had undergone cystectomy [9–12]. Moreover, several independent researchers have demonstrated decreased ovarian reserve markers, such as the serum antimullerian hormone (AMH) and inhibin B concentrations, after the surgical excision of ovarian endometriomas [13–18].

Nowadays, it is apparently evident that AMH is an excellent marker as it is unaffected by the use of hormonal drugs and is menstrual cycle independent. Therefore, it is the most reliable and reproducible tool [19].

In the present study, the aim was to assess the effect of laparoscopic endometrioma excision on the ovarian reserve tests. We measured basal serum levels of follicle-stimulating hormone (FSH), luteinizing hormone, estradiol (E2), and AMH before and 3 months after laparoscopic surgery. Antral follicle count (AFC) was also measured preoperatively and postoperatively.

Materials and Methods

A total of 60 patients were recruited in the study. They all underwent laparoscopic ovarian cystectomy at Al Galaa Maternity Teaching Hospital. Hospital ethical approval was obtained

The study included women with regular period cycles who had endometrioma, whether unilateral or bilateral, single or multiple, presenting with infertility or pelvic pain. Exclusion criteria include suspected ovarian malignancy, previous adnexal surgery, and evidence of postmenopausal FSH.

All patients had vaginal ultrasound examination for the diagnosis of the endometrioma and to check for the AFC. The ultrasound examination was performed by LOGIQ C5 Premium (Gereral Electric Medical System, China) with a transvaginal probe 7 MHz.

Preoperatively on day 2 of the cycle, FSH, luteinizing hormone, E2 were measured together with AMH. These measurements were repeated 3 months postoperatively.

Operation technique

Operative laparoscopy was performed during the late proliferative phase of the cycle through the insertion of a 10-mm subumbilical trocar and three 5-mm trocars in the lower abdomen. In all patients, the preoperative diagnosis of endometrioma was confirmed through laparoscopy. The pelvic cavity was explored, and the surface of the cyst was assessed for possible evidence of malignancy. The ovary was then mobilized from any adhesions. Attempts were made to perform cystectomy without rupture of the cyst. However, the cyst was ruptured in almost all cases inevitably, the contents were aspirated, and the chocolate fluid was rinsed. Then the inner wall of the cyst was checked for possible vegetations, the cleavage plane was identified, and the cyst wall was stripped of the ovary by traction and counter-traction using two atraumatic grasping forceps. Bipolar electrocoagulation was occasionally used to secure hemostasis.

Results

A total of 60 patients were included in the study, with mean age of 28.24 ± 5.28 years. Among the patients, 41 (68.3%) had unilateral and 19 (31.7%) had bilateral endometriomas. The baseline characteristics of patients are showed in Table 1.

The serum levels of AMH decreased significantly 3 months ($P < 0.001$) postoperatively.

The serum levels of FSH increased significantly 3 months ($P = 0.041$) after the operation. Although the AFC increased significantly 3 months after the operation ($P = 0.008$), the serum level of E2 remained unchanged ($P = 0.320$). The changes in the ovarian reserve markers after the laparoscopic cystectomy are summarized in Table 2.

The role of age, cyst size, bilaterally, and multiplicity were compared with the changes of AMH level after laparoscopic cystectomy. The changes of AMH in these groups are summarized in Table 3. Patients older than 38 years had significantly lower baseline serum level of AMH when compared with those younger than 38 years (1.56 ± 2.49 vs. 4.12 ± 3.48 ng/ml; $P = 0.003$). Both groups had significantly lower AMH levels ($P < 0.001$) 3 months after the operation (Table 3).

Women with large and small cysts (3 cm as a cut-off value) had no significant difference regarding the baseline level of

Table 1: Baseline characteristics of the 60 patients with endometrioma undergoing laparoscopic cystectomy

Variables	Values ($n=60$) [n (%)]
Age groups (years)	26.54±34
<38	54 (90)
>38	6 (10)
Location	
Unilateral	41 (68.3)
Bilateral	19 (31.7)
Cyst size	
>3 cm	55 (91.6)
<3 cm	5 (8.4)
Number of cysts	
Single unilateral	31 (51.6)
Single bilateral	16 (26.6)
Multiple unilateral	7 (11.6)
Multiple bilateral	6 (10.2)
Main complain	
Infertility	24 (40)
Pain	36 (60)

Table 2: The mean levels of ovarian reserve markers before and after laparoscopic ovarian cystectomy in 60 patients with endometriomas

	Preoperative	Postoperative 3 months	*P*
AMH (ng/ml)	4.12±3.41	2.62±2.7	<0.001
FSH (mIU/ml)	7.01±4.10	7.89±4.29	0.041
LH (mIU/ml)	7.22±8.02	5.86±4.54	NS
E2 (pg/ml)	55.8±50.1	51.2±46.2	NS
AFC	7.1±2.8	10.60±2.8	<0.001

AFC, antral follicle counts; AMH, antimullerian hormone; E2, estradiol; FSH, follicle-stimulating hormone; LH, luteinizing hormone.

Table 3: The serum level of antimullerian hormone before and after laparoscopic ovarian cystectomy in 60 patients with endometriomas in different groups

	Preoperative	Postoperative 3 months	*P*
Age (years)			
<38	4.12±3.40	2.09±2.48[a]	<0.001
>38	1.56±2.48	0.41±0.36[a]	<0.001
Cyst size (cm)			
>3	4.01±3.55	2.23±2.58[a]	0.017
<3	2.86±2.58	1.29±1.07[a]	0.023
Bilaterality			
Unilateral	4.20±3.69	2.26±2.83[a]	<0.001
Bilateral	3.29±3.19	1.22±1.46[a]	<0.001
Number of cysts			
Single unilateral	4.21±3.80	2.55±2.82[a]	0.014
Single bilateral	2.59±1.89	1.06±0.99[a]	0.004
Multiple unilateral	3.42±2.55	2.88±1.06[a]	0.066
Multiple bilateral	4.49±4.78	1.14±1.39[a]	0.026

[a]*P*<005 for antimullerian hormone when compared with the baseline.

AMH (4.01 ± 3.55 vs. 2.86 ± 2.58 ng/ml; $P = 0.149$). The decrease in AMH after the operation was similar between the two study groups (Table 3). However, regarding AMH level between those with large and small cysts 3 months after the operation ($P = 0.366$), there was no significant difference.

There were 19 (31.7%) patients with bilateral and 41 (68.3%) patients with unilateral endometriomas. The baseline AMH level was comparable between these two groups (3.29 ± 3.10 vs. 4.21 ± 3.71 ng/ml; $P = 0.074$). The AMH level decreased significantly 3 months after the operation in those with unilateral ($P < 0.001$) and bilateral ($P < 0.001$) endometriomas (Table 3).

Those with single unilateral cysts had significantly higher baseline levels of AMH when compared with those with single bilateral cysts (4.21 ± 3.82 vs. 2.59 ± 1.89 ng/ml; $P = 0.006$). Moreover, in those with multiple bilateral cysts, the baseline serum levels of AMH were significantly higher compared with those with single bilateral ones (4.49 ± 4.78 vs. 2.59 ± 1.98 ng/ml; $P = 0.026$). The trend of reduction of AMH levels after the operation was similar in all groups (Table 3).

Discussion

Laparoscopic ovarian cystectomy has been considered the treatment of choice for endometriomas [4]. However, the best and most efficient conservative laparoscopic technique remains a controversial issue in the literature [20–27]. The debate is between excision and ablation of the capsule.

The reported benefits in favors of surgery include a decrease in the recurrence of symptoms and signs and a reduction in the recurrence of the endometrioma. There are also some reports that show an increase in responsiveness to ovarian stimulation and cumulative pregnancy rate (PR) in randomized controlled trials [4,5].

Concern has been expressed over the risk of damaging ovarian reserve owing to excision of the capsule or to the use of electrocautery in surgically treating ovarian endometriomas. Ablation may have a higher risk of recurrence, but excision may result in more significant damage to ovarian follicular reserve, which could compromise future ovarian response during in-vitro fertilization [28].

This study showed a reduction in ovarian reserve after laparoscopic cystectomy for ovarian endometriomas as measured by serum AMH levels. This is consistent with other studies with follow-up periods of 1 month [13,29], 3 months [15,29,30], and 9 months [31]. Two studies showed no statistically significant decline in serum AMH level 3 months after the surgery [29,32].

According to age (>38 years), the baseline serum AMH level was lower in older patients. However, it did not reach a statistically significant level. Three months after surgery, there is a significant reduction in AMH level in both age groups. Hirokawa *et al*. [33] demonstrated no significant correlation between the rate of decline in serum AMH level and patients' age. Celik *et al*. [34] found a weakly negative correlation between age and preoperative AMH level, with no independent age effect on postoperative AMH level.

Comparison of two different cyst sizes (<3 cm and >3 cm) revealed that there was no significant difference in the baseline AMH level. However, after 3 months of surgery, there was a significant reduction in the levels of AMH. The size of endometrioma did not correlate with baseline and postoperative AMH level in two other studies [29]. Exacoustos *et al*. [35] demonstrated that there was an adverse effect of surgery in large and also in small cysts on ultrasonographic results. Ovarian stripping had a significant decrease in residual ovarian volume regardless of the size of the endometrioma, which may result in diminished ovarian reserve and function.

In this study, patient with bilateral endometriomas, compared with unilateral cysts, had a lower baseline AMH level, which remained lower at the end of the follow-up period, although there was no statistically significant difference. However, 3 months after surgery, the level of AMH was

significantly lower in all patients with unilateral and bilateral endometriomas.

There is no consistent report on the effect of bilaterality on the AMH level. In the study by Hirokawa *et al*. [33], bilaterality was the unique factor correlating with the rate of postoperative decline, which was not shown by Celik *et al*. [34]. Hwu *et al*. [36] showed a significantly lower baseline level in bilateral endometriomas and reported a more profound effect of bilaterality on the ovarian reserve, regardless of either conservative or surgical intervention.

The endometrioma by itself can affect the ovarian reserve negatively. Goldberg *et al*. [37] showed that, in women with advanced ovarian endometrioma, preoperative serum AMH values tend to be lower than those for age- and BMI-matched controls. These results suggest that even before the operation, the ovarian reserve could be minimal secondary to advanced endometriosis.

In our study, there was an increase in the FSH level in all patients 3 months after operation, which was significant, whereas there was no associated change in the level of E2 after the operation.

For the ovarian reserve, ultrasonographic AFC has been adopted as the most reliable marker beside AMH [35]. The reported data on changes in AFC after laparoscopic cystectomy of endometriomas have been conflicting. These data are not in line with the changes in the serum AMH level. In this study, there was a significant increase in AFC 3 months after surgery. Celik *et al*. [34] found a significant increase in AFC at the sixth week and sixth month postoperatively. Biacchiardi *et al*. [30] reported a nonsignificant increase in AFC 3 months postoperatively, whereas Ercan *et al.* [32] found a decrease in AFC along with a nonsignificant decline in AMH level. This discrepancy might be explained by the difficulty in the visualization of the antral follicles in ovaries affected by endometrioma. Thus, it is less reproducible than AMH and less reliable to assess ovarian reserve with this variable marker.

Several surgical techniques have been tried to minimize the risk of possible damage to healthy ovarian tissue and thereby decrease the risk of reduced ovarian reserve following surgery for endometriomas. Tsolakidis *et al.* [38] compared the laparoscopic stripping technique and a three-step approach (which is laparoscopic drainage, gonadotropin-releasing hormone analogs for 3 months, and laparoscopic laser vaporization) in a randomized clinical trial and documented no decrease in the serum AMH level with the ablation approach. Pados *et al.* [39], in a similar randomized study, reported a significant increase in AFC of the operated ovary after 6 months with the three-step procedure, although two recurrences (of 10 patients) occurred 1 year later. Donnez *et al.* [40], in a combined technique, first excised a large part of endometrioma wall according to the cystectomy technique, and then vaporized the remaining 10–20% of endometrioma wall close to the hilus with a CO_2 laser. This was done to achieve a low risk of recurrence by removing a large part of the endometrioma wall and the ablation causing a less harmfull effect on the ovarian tissue. They claim that with this combined method, ovarian volume and AFC are unaffected, with a high PR (40% at 8 months) and a low recurrence rate (<2%). Vaporization with CO_2 laser may be more tissue protective than coagulation, as the depth of vaporization is shallow. In the study by Roman *et al*. [41], another source of ablation, plasma energy, was compared with tissue-sparing cystectomy. This study reported that there was a significant decrease in the ovarian volume and reduction in AFC in the patients undergoing cystectomy.

Li *et al*. [42] treated 191 patients with benign ovarian cysts using three different methods: bipolar electrocoagulation, harmonic scalpel at laparoscopy, or simple suturing at laparotomy. Basal FSH and AMH levels were measured serially postoperatively. They reported that in patients with bilateral cysts at 12 months postoperatively, basal FSH levels were increased and AMH levels were decreased significantly more in the bipolar and harmonic scalpel group when compared with the suturing group. This study also supports the idea that damage to the ovarian vascular system by the energy modalities is an additional factor for the decreased ovarian reserve.

In conclusion, in patients with endometrioma who undergo laparoscopic cystectomy, the serum level of AMH decreased after the surgery. This was observed in all groups of patients according to age, cyst size, bilaterality, and multiplicity. There was also increase in FSH level after surgery. Preoperative assessment is of utmost importance, especially for those who are still have not yet completed their family.

Surgery has a fundamental role to play in the management of endometriomas. Despite concerns about the effect of this surgery on the ovarian reserve, the benefits regarding pain relief and spontaneous PRs favor this approach. All we are concerned about is what is the ideal surgical technique? There is a significant lack of well-conducted comparative studies. So, there is a need for more studies to compare excisional, laser ablation, and combined techniques and to evaluate the utility of gonadotropin-releasing hormone and two-step surgery. It is clear that considerable surgical expertise is required to decrease ovarian damage and to avoid incomplete surgery [43].

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Conflicts of interest

There are no conflicts of interest.

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