Effect of laparoscopic excision of endometriomas on ovarian reserve: serial changes in the serum antimüllerian hormone levels

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Objective: To investigate the effect of laparoscopic endometrioma stripping on serum antimüllerian hormone (AMH) and the correlation between the clinicopathologic factors.
Design: Prospective study.
Setting: University hospital.
Patient(s): Sixty-five women with endometriomas.
Intervention(s): All patients underwent laparoscopic cystectomy. Serum AMH, FSH, LH, E_2, and antral follicle count (AFC) were measured preoperatively, at 6 weeks, and at 6 months postoperatively. Specimens were analyzed histopathologically.
Main Outcome Measure(s): The primary end point was to assess the ovarian reserve damage based on alterations of AMH and the secondary end point was to detect the changes in FSH, LH, E_2, and AFC.
Result(s): Serum AMH decreased significantly at the sixth month (61%) postoperatively. The FSH level increased significantly at the sixth week, but returned to normal at the sixth month. The AFC increased significantly at the sixth week and at the sixth month. The AMH level decrease was more evident in patients with the cyst <5 cm (65.7% vs. 41.3%). The AMH decrease was more in bilateral compared with unilateral endometriomas (67% versus 57%, respectively). No correlation was detected between the histopathologic analyses and tAMH level. Initially the AMH level was the only independent factor affecting the AMH decrease (odds ratio, 3.68; 95% confidence interval 1.66–8.14).
Conclusion(s): Laparoscopic cystectomy of ovarian endometriomas causes a significant and progressive decline in serum AMH levels. (Fertil Steril® 2012;97:1472–8. ©2012 by American Society for Reproductive Medicine.)
Key Words: Endometrioma, laparoscopy, ovarian reserve, antimüllerian hormone, antral follicle count

Endometriosis is the presence of endometrial glands and stroma outside the uterine cavity affecting mostly women of reproductive age. The disease is usually manifested with pelvic pain, dysmenorrhea, and infertility. The prevalence is found to be 7%–10%, but among infertile women it increases up to 50% (1).

Endometrioma is the formation of a cyst within the ovary with ectopic endometrium tissue lining and is found to be in 17%–44% of patients with endometriosis (2). It is hypothesized that endometriomas arise as a consequence of coelomic metaplasia of the ovarian epithelium or the invagination of the inverted ovarian cortex after implantation of the endometriotic foci on the ovarian surface (3). In either case the cyst has a pseudocapsule adjacent to the normal ovarian tissue.

The treatment of endometriosis must aim at the destruction of all lesions, adhesiolysis to ensure the normal anatomical structure, prevent recurrences, and increase conception rates in patients with subfertility. Although the most effective treatment modality of endometrioma is controversial, laparoscopic excision by the stripping technique is accepted to be the gold standard surgical approach. A recent meta-analysis showed that in comparison to drainage and ablative surgery, excision of endometriomas are better in terms of reduced pain, increased pregnancy, and decreased recurrence and reoperation rates (4).

One of the major concerns about excision of endometriomas is their negative effect on ovarian reserve because of follicle loss (5). Removal of endometriomas has been associated with poorer performances in IVF procedures, and decreased ovarian volumes have also been reported after surgery (6).

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Ovarian reserve describes the number and quality of the follicles in the ovaries at any given time. At present, there is no ideal test to measure ovarian reserve, but age, basal levels of FSH, LH, E_2, inhibin B, and recently antimüllerian hormone (AMH) have emerged as clinically useful markers (7). Sonographic measurements, like basal antral follicle count (AFC), ovarian volume, and stromal blood flow, are also being used for ovarian reserve testing (8). Among these markers AMH and AFC are accepted to be the most reliable markers. Antimüllerian hormone belongs to the transforming growth factor-β (TGF-β) family and is secreted by the granulosa cells (GC) of the recruited follicles until they become sensitive to FSH (9). Major advantages of AMH are that it is menstrual cycle independent and is also unaffected by the use of oral contraceptive (OC) pills and GnRH agonists (10).

In the present study, our purpose was to assess the effect of laparoscopic endometrioma excision on the ovarian reserve tests. We measured basal serum levels of FSH, LH, E_2, and AMH serially before and after laparoscopic surgery. Antral follicle count was also measured preoperatively and postoperatively. In addition we investigated the correlation between the changes in these ovarian reserve markers with the histopathologic analysis of follicle loss after the operation.

MATERIALS AND METHODS

This prospective cohort study was conducted on 65 patients, who underwent laparoscopic ovarian endometrioma excision in the Department of Obstetrics and Gynecology at Dokuz Eylul University between January 2009 and March 2010. Inclusion criteria were: 1) presence of endometrioma with a diameter of at least 3 cm, 2) absence of previous ovarian surgery, 3) 18–45 years of age with regular menstrual cycles, and 4) absence of any endocrine disease. Exclusion criteria were as follows: 1) evidence of postmenopausal FSH levels, and 2) any suspicion of malignant ovarian disease and OC use or any other hormone therapy (HT) during past 3 months. This study was approved by the Institutional Review Board of Dokuz Eylul University Medical School and informed consent was obtained from all patients.

Endometrioma was diagnosed mainly by transvaginal ultrasonography or any other imaging techniques like computed tomography (CT) or magnetic resonance imaging (MRI). Age, gravidity and parity, tobacco use, menstrual regularity, drug use, and operation history of patients were recorded. Ultrasonographic examination for AFC was performed by Medison SonoAceX6 with a transvaginal 7-MHz probe. Antral follicle was considered as cysts measuring 2–10 mm in diameter within the ovary. Mean endometrioma diameter was measured in two dimensions.

Definitive diagnosis of endometrioma was done by observation of endometriotic foci during laparoscopy and histopathologic examination of these samples. All blue-black powder burn lesions or atypical white and opaque, red or vesicular lesions, and all ovarian cysts containing dense brown chocolate-like fluid were excised and examined histopathologically. During laparoscopy, patients were scored according to the revised American Fertility Society (AFS) for Reproductive Medicine Classification of Endometriosis and staged as minimal, mild, moderate, or severe endometriosis (11).

Hormonal Measurements

Preoperatively on the third day of the menstrual cycle FSH, LH, E_2, and AMH were measured and the FSH:LH ratio was calculated. The AFC in both ovaries and dimensions of endometrioma were assessed by transvaginal ultrasonography. On the day of ultrasonography, blood samples were obtained by venipuncture. The patient's sera were obtained from blood samples by centrifuge at $3{,}000 \times g$ for 10 minutes to separate cellular contents and debris. The serum was stored at -80°C until assayed. Serum FSH, LH, and E_2 levels were measured by the chemiluminescence method with original Abbott assays. The intra-assay and interassay coefficient of variations (CV) were 5.4% and 4.2% for FSH, 3.8% and 4.6% for LH, and 7.5% and 3.7% for E_2, respectively. Serum AMH levels were measured by ELISA (Diagnostic Systems Laboratories). For AMH, intra-assay CV was 4.57% with a detection limit of 0.006 ng/mL.

Operation Technique

All the laparoscopic cystectomies were performed under general anesthesia by one of the experienced surgeons. The surgery was done as follows. After establishment of pneumoperitoneum with the Verres needle through a 10-mm subumbilical vertical incision, a 10-mm laparoscope was introduced. Then, two to three additional 5-mm trocars were placed suprapubically for the introduction of ancillary instruments. At entrance to the abdomen pelvis, abdomen, and the surface of the cyst was assessed for possible evidence of malignancy. If no sign of malignancy was present, the ovary was mobilized from its adhesions, if there were any. The cyst was ruptured almost in all cases inevitably, and the contents were aspirated and the chocolate fluid content was rinsed and the inner wall of the cyst was checked for possible vegetations. If there were no vegetations present, the cleavage plane was identified and the cyst wall was stripped off the ovary by traction and countertraction exerted by using two atraumatic grasping forceps. In addition, sharp dissection with scissors was necessary when the cyst capsule was adherent to the surrounding ovarian tissue. Bipolar electrocoagulation was applied occasionally for hemostasis on the ovarian parenchyma with caution not to damage ovarian hilus and vascularity. The cyst wall was removed from the abdomen by means of an endobag. No major intraoperative or postoperative complication occurred in any patient and all were discharged 24 hours after the surgery.

Histopathologic Analysis

The pathologist evaluated the presence or absence of the ovarian tissue adjacent to the cyst wall and graded the morphological characteristics of this tissue on a semiquantitative scale of 0–4 (0 = complete absence of follicles; 1 = primordial follicles only; 2 = primordial and primary follicles; 3 = secondary follicles; and 4 = pattern of primary and secondary