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ORIGINAL ARTICLE

The role of anti-mullerian hormone in determining ovarian reserve in patients with endometrioma and benign cysts

[1]Ergül DEMİRÇİVİ
[2]Duygu VARDAĞLI
[3]Ali İsmet TEKİRDAĞ
[3]Özgür AKBAYIR
[3]Ahmet GÜLKILIK
[4]Beyhan ÖMER
[5]Sezai ŞAHMAY

[1]Department of Obstetrics and Gynecology, Istanbul Medeniyet University, Istanbul, Turkey

[2]Division of Health Service Vocational School, Istanbul Esenyurt University, Istanbul, Turkey

[3]Department of Obstetrics and Gynecology, Istanbul Kanuni Sultan Suleyman Training and Research Hospital, Istanbul, Turkey

[4]Department of Biochemistry, Istanbul Universitiy Faculty of Medicine, Istanbul, Turkey

[5]Department of Obstetrics and Gynecology, Istanbul Universitiy Cerrahpasa Faculty of Medicine, Istanbul, Turkey

ORCID ID

ED : 0000-0002-4448-3863
DV : 0000-0002-9022-1338
AİT : 0000-0002-0076-4815
ÖA : 0000-0002-2699-4969
AG : 0000-0002-9403-592X
BÖ : 0000-0001-7938-6281
SŞ : 0000-0001-9363-5360

ABSTRACT

Objective: Our aim was to determine the effects of endometrioma by itself and its surgery on ovarian reserve via pre- and postoperative serial measurements of Anti-Mullerian Hormone (AMH) in patients with endometrioma and benign cysts.

Material and Methods: Our study was conducted at an education and research hospital as a prospective controlled clinical trial. Participants were divided according to their diagnosis into endometrioma and non-endometrioma groups. Serial blood samples of the patients for serum AMH levels were collected preoperatively, and postoperatively at the first week, first month, and third month, respectively.

Results: A total of 46 patients (25 for the study and 21 for control groups) were included in the study. The mean age of our patients was 31.8±5.57 in the endometrioma group and 29.38±8.64 in the control group. The AMH value was lower in the endometrioma group, but the difference did not reach statistical significance ($p>0.05$). However, in the postoperative AMH levels measured at the 1st week, 1st month, and 1st year, the values were significantly higher in the non-endometrioma group compared to the endometrioma group ($p<0.05$).

Conclusion: According to our study, we can conclude that endometrioma surgery affects ovarian reserve significantly and more negatively than benign cystectomies.

Keywords: Anti-mullerian hormone (AMH), benign cyst, endometrioma, ovarian reserve, surgery.

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Correspondence: Ergül DEMİRÇİVİ, MD. İstanbul Medeniyet Üniversitesi, Kadın Hastalıkları ve Doğum Anabilim Dalı, İstanbul, Türkiye.
Tel: +90 216 566 40 00 **e-mail:** drergul@yahoo.com
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INTRODUCTION

Endometriosis affects approximately 10% of women of reproductive age.[1] It is most commonly found in pelvic organs such as the peritoneum, ovary, or recto-vaginal septum.[2] Ovarian endometrioma may originate from endometriotic peritoneal implants on the ovarian surface[3] or from metaplasia of ovarian surface epithelium invaginations.[4] Primordial follicles in the ovarian cortex constitute the ovarian reserve,[5] and endometrioma can affect the ovarian reserve either by itself or through the damage caused to the ovarian cortex during surgical treatment. Various clinical tests are available to estimate ovarian reserve. Serum follicle-stimulating hormone (FSH) and estradiol in the follicular phase have been used as markers for ovarian reserve, but their reliability is limited.[6] Recently, anti-Mullerian hormone (AMH), which is produced by granulosa cells of preantral and antral follicles in a gonadotropin-independent period, has started to be used for more precise determination of ovarian reserve.[7,8] In our study, we aimed to determine the effect of endometrioma and its surgery on ovarian reserve through pre- and postoperative serial measurements of anti-Mullerian hormone in patients with endometrioma and benign cysts.

MATERIAL AND METHODS

Our study was conducted at an education and research hospital between 2012 and 2014. A total of 46 patients were included in the study and they were divided into two groups: the endometrioma group (n=25) and the non-endometrioma group (n=21). All patients were symptomatic, complaining of pain due to their endometriomas and benign cysts, and needed surgery. Our inclusion criteria for the study groups were patients who had cysts >4 cm (study group as endometrioma and for the control group as a hemorrhagic or simple cyst) and who were aged between 18–40 years. The exclusion criteria were patients with polycystic ovary syndrome (PCOS), a history of ovarian surgery, a malignancy or borderline ovarian tumor diagnosis after histological examination, endocrinological disorders (thyroid dysfunction, pituitary or adrenal disorders), or oral contraceptive or gonadotropin analog usage in the 3 months prior to surgery.

First, we examined all patients with serial ultrasonography, then collected blood samples for CA125, FSH, luteinizing hormone (LH), estradiol (E2), prolactin (PRL), and AMH (AMH Gen II ELISA, Beckman Coulter Life Sciences, Indiana, USA) during the proliferative phase of the cycle. Additionally, to determine serial serum AMH levels of the patients, their blood samples were collected at the first week, first month, and third month postoperatively. All blood samples were stored at -80 °C until biochemical measurements. For all patients, the ovarian surgery (cystectomy) procedures were done by the same surgery team through laparoscopy or laparotomy (for patients who failed the laparoscopic approach). Every patient's tissue samples were sent for histopathologic examination, and all results were confirmed with the preoperative diagnosis (endometrioma or benign cyst such as serous, mucinous, or corpus luteum cyst).

Statistical analysis was conducted with NCSS (Number Cruncher Statistical System) 2007 Statistical Software (Utah, USA) program. Descriptive statistical methods, Friedman test for nonparametric variables, Mann-Whitney U test for the comparison of nonparametric double groups, Student's t-test for the comparison of parametric double groups, and Chi-square test with Fisher's exact test for the comparison of variables were used for statistical analysis. We considered p-values <0.05 as statistically significant.

Table 1: Clinical and ultrasonographic data and p values between groups

	Endometrioma group (n=25) (Mean±SD)	Non-endometrioma group (n=21) (Mean±SD)	p
Age	31.8±5.57	29.38±8.64	0.258
BMI	20.92±1.29	20.95±1.4	0.935
Cyst diameter (cm)	5.16±1.49	5.57±1.17	0.310

SD: Standard deviation; BMI: Body mass index.

Table 2: Obstetric data and p values between groups

	Endometrioma group (n=25)	Non-endometrioma group (n=21)	p
Gravidity			0.715
Mean±SD	1.35±1.34	1.53±1.81	
Median (IQR)	1 (0–2)	1 (0–3)	
Parity			0.659
Mean±SD	1±1	1.16±1.3	
Median (IQR)	1 (0–2)	1 (0–2)	
Abortus			0.806
Mean±SD	0.13±0.34	0.16±0.38	
Median (IQR)	0 (0–0)	0 (0–0)	
Ectopic pregnancy			0.370
Mean±SD	0.04±0.21	0±0	
Median (IQR)	0 (0–0)	0 (0–0)	

SD: Standard deviation; IQR: Interquartile range.

Ethical Aspects

The feasibility and suitability of the prospective controlled study were approved by the local ethics committee (approval date and number: 2011-84/2011-10-11) and registered on the clinical trial website (NCT01982526). The study was conducted in compliance with the Declaration of Helsinki, and written informed consent was obtained from all participating patients.

Table 3: Group division by cyst laterality and operation type, p values between groups

	Endometrioma group		Non-endometrioma group		p
Laterality					
Bilateral	6	24.00%	2	9.52%	0.268
Right	9	36.00%	12	57.14%	
Left	10	40.00%	7	33.33%	
Operation type					
Laparatomy	13	52.00%	5	23.81%	0.072
Laparoscopy	12	48.00%	16	76.19%	

Table 4: Preoperative hormone profile and Ca 125 levels of groups and p values between groups

	Endometrioma group (n=25)	Non-endometrioma group (n=21)	p
FSH			0.429
Mean±SD	6.87±2.35	6.21±2.59	
Median (IQR)	6.9 (4.79–8.25)	6.5 (3.7–8.4)	
LH			0.635
Mean±SD	6.06±3.45	5.32±2.69	
Median (IQR)	5.33 (3.55–8.8)	5.2 (3.1–6.8)	
E2			0.501
Mean±SD	100.44±87.7	107.27±78.34	
Median (IQR)	68 (54.5–97.5)	75 (61–150)	
PRL			0.258
Mean±SD	13.86±3.6	16.73±6.37	
Median (IQR)	13 (11–15.75)	15 (12–22)	
CA125			**0.0001**
Mean±SD	56.76±38.35	22.56±28.36	
Median (IQR)	44 (28–79)	14.5 (7.5–22.5)	

FSH: Follicle-stimulating hormone; LH: Luteinizing hormone; E2: Estradiol; PRL: Prolactin; SD: Standard deviation; IQR: Interquartile range.

Table 5: P values for AMH results between groups

AMH	Endometrioma group	Non–endometrioma group	p
Preop			0.213
Patient numbers	25	21	
Mean±SD	1.45±1.55	2.12±1.72	
Median (IQR)	0.91 (0.59–1.62)	1.5 (0.57–3.88)	
Postop 1st week			**0.013**
Patient numbers	18	17	
Mean±SD	0.93±0.86	2.03±1.64	
Median (IQR)	0.79 (0.29–0.99)	1.12 (0.93–3.69)	
Postop 1st month			**0.020**
Patient numbers	9	11	
Mean±SD	0.87±0.16	2.09±1.83	
Median (IQR)	0.85 (0.76–0.93)	1.19 (1–4.5)	
Postop 3rd month			**0.022**
Patient numbers	6	7	
Mean±SD	0.87±0.13	3.03±2.62	
Median (IQR)	0.84 (0.75–1)	1.18 (0.98–6.3)	

AMH: Anti-mullerian hormone; SD: Standard deviation; IQR: Interquartile range.

RESULTS

The total number of patients included in our study, comprising the study group (patients with endometrioma) and the control group (patients with other benign cysts), was 46. However, during the postoperative period, we were unable to follow up with some patients from both the study and control groups due to difficulties in contacting them.

Clinical and ultrasonographic findings, as well as obstetric data, were reported in Tables 1 and 2. Cyst laterality and operation type were also investigated between the two groups (Table 3). There was no statistical significance between the two groups.

In Table 4, preoperative hormone profiles and CA125 median values were compared between groups, and only the CA125 value of the endometrioma group was significantly higher than that of the non-endometrioma group (p=0.0001).

When investigating AMH values between the study and control groups, we found no significant difference in preoperative values. However, postoperative AMH values were significantly higher in the non-endometrioma group than in the endometrioma group at the 1st week (p=0.013), 1st month (p=0.02), and 3rd month (p=0.02) (Table 5). Preoperatively, the mean AMH value of the endometrioma group was lower than that of the non-endometrioma group.

In other words, when analyzing AMH measurements over time within each group, we found no difference (Table 6).

Table 6: P values between each AMH measurement time matchs for both groups

	NEG	EG
AMH postop 1st week - AMH preop	0.332	0.102
AMH postop 1st month - AMH preop	0.213	0.441
AMH postop 3rd month - AMH preop	0.612	0.249
AMH postop 1st month - AMH postop 1st week	0.859	0.139
AMH postop 3rd month - AMH postop 1st week	0.998	0.173
AMH postop 3rd month - AMH postop 1st week	0.998	0.686

AMH: Anti-mullerian hormone; NEG: Non-endometrioma group; EG: Endometrioma group.

DISCUSSION

The aim of our study was to address the question: Does endometrioma affect ovarian reserve independently? We can affirmatively respond 'Yes,' as AMH levels were lower among patients in the endometrioma group compared to the control group, although the difference was not significant, possibly due to the small number of patients in each group. The second question was: Does endometrioma surgery affect ovarian reserve? Here, we confidently say 'YES,' as we demonstrated a significant decline in AMH levels after endometrioma surgery compared to the decline observed after surgeries in the control group.

The age-related decrease in AMH, as reported in a recent paper by Yu Wang et al.,[9] is already well-documented. Moreover, cyst size and laterality did not affect the AMH levels of endometrioma patients in the same study. However, a study by Karadağ et al.[10] showed that AMH levels were negatively correlated with cyst size. On the other hand, AMH levels were not affected by the laterality of the endometrioma in the study by Salihoğlu et al.,[11] but Nieweglowska et al.[12] found significantly decreased AMH levels in the bilateral endometrioma group compared to the unilateral group. In our study, we used age-matched groups to control for the effect of age on AMH levels and found no significant difference in size or laterality between the endometrioma and control (non-endometrioma) groups.

According to a recent meta-analysis, preoperative AMH levels were noticeably lower in the endometrioma group compared to the control group (including both healthy ovarian tissue and benign cyst groups).[13] We also observed a decline in AMH levels in the endometrioma group compared to the non-endometrioma group, but the difference was not statistically significant between groups, possibly due to the small number of patients in each group.

Surgical excision of endometriomas (cystectomy) is currently considered the standard treatment for pain relief.[14] However, cystectomy for endometrioma has a detrimental effect on ovarian reserve, which is reflected by a decline in AMH levels following the operation.[15,16]

The postoperative decline of AMH levels in endometrioma was proven by considering the pre- and postoperative results of only endometrioma groups in most studies. There are few studies that also include control (non-endometrioma) group results for pre- and postoperative AMH levels and assess if there are significant differences in or between groups.

In our study, we found significant differences between the endometrioma and non-endometrioma groups for postoperative AMH levels at the 1st week, 1st month, and 3rd month. However, within each group, we could not find any significant change in AMH measurements at different times. The non-significant AMH change between pre- and postoperative periods for both groups was surprising for us, given the literature consensus about postoperative AMH decline after ovarian surgery, especially for endometrioma. Nonetheless, we observed a postoperative AMH decline in both groups. We believe the small group sizes were a limitation of our study for statistically significant findings. However, our results strongly suggest that endometrioma surgery affects the ovaries more negatively than surgeries for other benign cysts. In the study by Chun et al.,[17] there was a significant postoperative AMH decrease in the endometrioma group when compared with the benign cyst group, as in our study, but there was no significant difference between the endometrioma and mature cystic teratoma groups. Also, in the same study, there was no significant preoperative difference in AMH levels between groups. Conversely, another study mentioned that the decline in AMH levels after surgery was similar between the endometrioma and benign ovarian cyst groups.[18]

This study contributes to the literature by suggesting that ovarian surgery for endometrioma may negatively affect ovarian reserve. However, as mentioned, the limitation of our study was the small group sizes.

CONCLUSION

Numerous studies have examined endometrioma and its surgical treatment, with most comparing AMH levels in the same patients before and after ovarian surgery. However, our investigation focused on the impact of surgery for both endometrioma and other cysts on ovarian reserve. In conclusion, there is a need for meta-analyses or reviews comparing pre- and postoperative AMH changes between endometrioma and other ovarian cyst groups to clarify the conflicting results of existing studies.

Statement

Ethics Committee Approval: The Bakırköy Sadi Konuk Training and Research Hospital Clinical Research Ethics Committee granted approval for this study (date: 26.09.2011, number: 2011-10-11).

Author Contributions: Concept – ED, AG; Design – ED, SŞ; Supervision – ED, ÖA, AİT; Resource – ED; Materials – ED, DV; Data Collection and/or Processing – ED, BÖ; Analysis and/or Interpretation – ED, AİT; Literature Search – ED, SŞ; Writing – ED, DV, AİT, ÖA, AG, BÖ, SŞ; Critical Reviews – ED, DV, AİT, ÖA, AG, BÖ, SŞ.

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