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ORIGINAL RESEARCH ORIJINAL ARAŞTIRMA

Investigation of the Effect of Bilateral Salpingectomy on Serum Antimullerian Hormone Levels in Patients Undergoing Total Abdominal Hysterectomy for Benign Gynecologic Causes Article

Benign Jinekolojik Nedenlerle Total Abdominal Histerektomi Yapılan Hastalarda Operasyona Bilateral Salpenjektomi Eklenmesinin Serum Antimülleryan Hormon Seviyeleri Üzerine Etkisinin Araştırılması

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ABSTRACT

Objective: The goal of this research was to explore how intraoperative bilateral salpingectomy impacts ovarian reserve in individuals undergoing hysterectomy (TAHS due, to non cancerous reasons. Serum anti-Müllerian hormone (AMH) levels were used as the primary biomarker to evaluate ovarian reserve. Material and Methods: We selected 29 premenopausal patients aged 40-45 years who were scheduled for total abdominal hysterectomy for benign indications. Participants were allocated into two groups based on surgical preference: total abdominal hysterectomy only (TAH, n=15) and total abdominal hysterectomy with bilateral salpingectomy (TAH+BS, n=14). Serum AMH levels were measured in both groups preoperatively, on postoperative day 2 and at 1 month postoperatively. In addition, follicle-stimulating hormone (FSH), luteinizing hormone (LH), and estradiol (E2) levels were evaluated on day 3 of the menstrual cycle. Results: The mean age (TAH: 43.13±1.68, TAH+BS: 42.85±1.56, p=0.447) and BMI values (TAH: 29.22±4.03, TAH+BS: 27.35±5.60, p=0.280) of the groups were similar. Preoperative AMH levels were 1.14±0.78 ng/mL in the TAH group and 1.16±0.58 ng/mL in the TAH+BS group (p=0.906). Both groups demonstrated a significant decrease in AMH values during the postoperative period, with the nadir occurring on postoperative day 2. There was no significant difference between the groups in postoperative day 2 (TAH: 0.79±0.13, TAH+BS: 0.75±0.21, p=0.691) and 1-month (TAH: 0.94±0.78, TAH+BS: 0.92±0.58, p=0.377) measurements. Conclusion: The addition of bilateral salpingectomy during hysterectomy had no additional negative effect on ovarian reserve compared to hysterectomy alone. This indicates that having both fallopian tubes removed can be done safely at the time, as a hysterectomy to lower the chances of developing cancer.

Keywords: Anti-Mullerian hormone; total abdominal hysterectomy; bilateral salpingectomy; ovarian reserve; premenopause

ÖZET

Amaç: Bu çalışmanın amacı, benign sebeplerle total abdominal histerektomi (TAH) yapılan hastalarda, operasyon sırasında bilateral salpenjektomi eklemenin over rezervi üzerindeki etkisini serum anti-Müllerian hormon (AMH) seviyeleri ile incelemektir. Gereç ve Yöntemler: Çalışma kapsamında, benign nedenlerden dolayı total abdominal histerektomi planlanan 40-45 yaş arası 29 premenopozal hasta seçildi. Hastalar, yalnızca total abdominal histerektomi yapılanlar (TAH, n=15) ve histerektomi ile birlikte bilateral salpenjektomi uygulananlar (TAH+BS, n=14) olarak iki gruba ayrıldı. Her iki grupta preoperatif, postoperatif 2. gün ve 1. ayda serum AMH seviyeleri ölçüldü. Ek olarak, menstrüel döngünün 3. gününde FSH, LH ve E2 düzeyleri değerlendirildi. Bulgular: Grupların yaş ortalamaları (TAH: 43.13±1.68, TAH+BS: 42.85±1.56, p=0.447) ve VKİ değerleri (TAH: 29.22±4.03, TAH+BS: 27.35±5.60, p=0.280) benzerdi. Preoperatif AMH düzeyleri TAH grubunda 1.14±0.78 ng/mL, TAH+BS grubunda 1.16±0.58 ng/mL olarak kaydedildi (p=0.906). Her iki grupta da postoperatif dönemde AMH değerlerinde düşüş izlendi. Postoperatif 2. gün (TAH: 0.79±0.13, TAH+BS: 0.75±0.21, p=0.691) ve 1. ay (TAH: 0.94±0.78, TAH+BS: 0.92±0.58, p=0.377) ölçümlerinde, gruplar arası anlamlı bir fark saptanmadı. Sonuç: Histerektomi sırasında bilateral salpenjektomi eklemmesinin over rezervine ek bir olumsuz etkisi gözlenmemiştir. Bu durum, over kanseri riskini azaltmak amacıyla histerektomi esnasında bilateral salpenjektominin güvenle uygulanabileceğini göstermektedir

Anahtar Kelimeler: Anti-Müllerian hormon; total abdominal histerektomi; bilateral salpenjektomi; over rezervi; premenopoz

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Ovarian cancer has one of the highest mortality rates among gynecologic cancers. Recent studies have revealed that most ovarian cancers, especially high-grade serous ovarian cancers, actually originate from the fimbrial end of the fallopian tube. 1,2 Unlike inflammatory processes such as acute pancreatitis, ovarian cancer is a more insidious disease and early diagnosis is vital. Therefore, the idea of simultaneous bilateral salpingectomy in patients scheduled for hysterectomy for benign reasons has come to the forefront. Since pathological conditions such as ischemia-reperfusion injury in the ovaries can affect ovarian reserve, evaluation of ovarian reserve is of great importance. 4

Serum Anti-Müllerian hormone (AMH), which is used to measure ovarian reserve, is known as an important biomarker secreted from the granulosa cells of small antral follicles and directly indicates ovarian reserve. ^{5,6} AMH remains fairly constant throughout the menstrual cycle and is secreted independently of gonadotropins. ⁷ Because of these characteristics, AMH levels are recognized as a reliable indicator of ovarian reserve.

Studies have shown that various surgical procedures, such as uterine artery embolization and ovarian cystectomy, may be effective on ovarian reserve.^{8,9} However, the number of studies examining the effect of bilateral salpingectomy performed during hysterectomy on ovarian reserve remains very limited.¹⁰

This study was conducted with the aim as to find out whether bilateral salpingectomy has any impact, if any, on the serum AMH levels in pre menopausal patients undergoing total abdominal hysterectomy solely for benign gynecological indications.

MATERIAL AND METHODS

STUDY OBJECTS, MATERIALS AND PARTICIPANTS

This prospective study included 29 premenopausal patients aged 40-45 years who were planned to undergo abdominal hysterectomy for benign reasons but had no indication for oophorectomy. The sample size was calculated to detect a difference of 0.5 ng/mL in AMH levels between groups with a 5% margin of error (α =0.05) and 80% power (β =0.20). The study

was conducted in accordance with the 1964 Declaration of Helsinki and was approved by the Ethics Committee of Ankara Numune Training and Research Hospital (Ethics Committee Approval No: 864/2014). All patients participating in the study were informed and their consent was obtained. All data has been anonymized, ensuring privacy and data security.

INCLUSION AND EXCLUSION CRITERIA

The study included premenopausal women aged 40-45 years who were scheduled for abdominal hysterectomy for benign reasons. Exclusion criteria included steroid or sex steroid use in the last 6 months, history of tubal surgery, lactation or pregnancy, and request for oophorectomy. These criteria were determined to minimize the effect of non-surgical factors on AMH levels (Figure 1).

PARTICIPANT PREPARATION AND SELECTION

Participants were selected among eligible patients who applied to the Gynecology and Obstetrics Outpatient Clinic of Ankara Numune Training and Research Hospital between February 2014 and February 2015. During the selection process, patients were informed about the study in detail and their consent was obtained. According to the criteria determined in line with the hypothesis and purpose of the study, meticulous preparation was made for preoperative and postoperative measurements.

STUDY DESIGN

This study was designed as a prospective observational study. Patients were divided into two groups as TAH (total abdominal hysterectomy, n=15) and TAH+BS (total abdominal hysterectomy + bilateral salpingectomy, n=14) according to surgical technique preference. The lack of randomization was considered as a limitation of the study and this was taken into account when evaluating the results (Figure 1).

INTERVENTION AND PROCEDURES

Before the operation, venous blood samples were taken for the measurement of FSH, LH and E2 levels after 8-12 hours of fasting on the 3rd day of the menstrual cycle and sent to the biochemistry laboratory. Hormone levels were analyzed using the chemilumi-

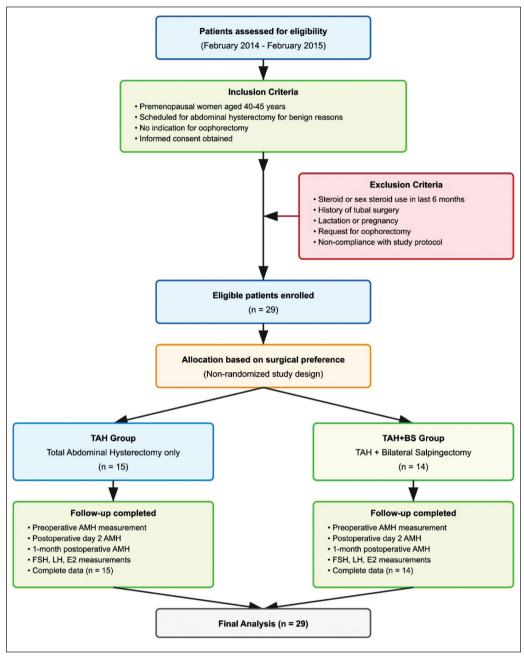


FIGURE 1: Patient flow diagram

nescent enzyme immune assay method. Blood samples taken for AMH measurement were placed in redcapped tubes, centrifuged and stored at -80°C. After all samples were collected, they were thawed and AMH levels were measured with 'Human Mullerian Inhibiting Substance/Anti-Mullerian hormone, MIS/AMH ELISA Kit' (CK-E11351i China). AMH levels were measured again on postoperative day 2 and 1 month postoperatively by the same method.

MEASUREMENT AND CALCULATION METHODS

FSH, LH and E2 hormones were measured by Chemiluminesan enzyme immune assay and AMH was measured by ELISA method. Measurements were performed preoperatively, postoperative day 2 and postoperative month 1 according to standard protocols. Measuring instruments were calibrated according to laboratory standards to ensure accuracy.

STATISTICAL ANALYSIS

Data analysis was performed with the Statistical Package for Social Sciences (SPSS) Windows 19.0 program. Descriptive statistics (mean, median, standard deviation) were evaluated for conformity to normal distribution by Kolmogorov-Smirnov test. Student t-test in independent groups and ANOVA for repeated measures were used for normally distributed data. In all analyzes, significance was tested with a 5% margin of error (p=0.05).

RESULTS

A total of 29 premenopausal patients were divided into two groups: those who underwent total abdominal hysterectomy (TAH) only and those who underwent TAH with bilateral salpingectomy (TAH+BS). The mean ages of the patients in the groups were very close to each other and did not show statistical significance in terms of age (p=0.447). Similarly, body mass index (BMI) values did not reveal a significant difference between the two groups (p=0.280). The most common reason for operation in both groups was myoma uteri. Other reasons for surgery included abnormal uterine bleeding, adenomyosis and chronic pelvic pain. Regarding the operation time, the operation time in the TAH+BS group was statistically significantly longer than in the TAH group (p=0.042). There was no significant difference in the presence of comorbidities such as hypertension, diabetes mellitus and thyroid disease (Table 1).

When preoperative hormone levels of the patients in both groups were analyzed, no significant difference was found in follicle stimulating hormone (FSH), luteinizing hormone (LH), estradiol (E2) and anti-Müllerian hormone (AMH) levels. FSH levels showed no significant difference between groups (p=0.801), LH levels were comparable (p=0.072), and E2 levels were similar (p=0.663). Although FSH, LH and E2 averages in the TAH group showed slight differences compared to the TAH+BS group, these differences were not statistically significant. Similarly, AMH levels did not show a significant difference between the two groups (p=0.906). Hormone measurements were performed between days 1-4 of

TABLE 1: Demographic and clinical characteristics of patients

Characteristics	TAH Group (n=15)	TAH+BS Group (n=14)	p value
Age (years)	43.13±1.68	42.85±1.56	0.447
BMI (kg/m²)	29.22±4.03	27.35±5.60	0.280
Gravida	3 (2-4)	3 (2-4)	0.856
Parity	2 (1-3)	2 (1-3)	0.924
Surgical Indications			
Myoma uteri	8 (53.3%)	7 (50.0%)	0.845
Abnormal uterine bleeding	4 (26.7%)	4 (28.6%)	0.912
Adenomyosis	2 (13.3%)	2 (14.3%)	0.942
Chronic pelvic pain	1 (6.7%)	1 (7.1%)	0.962
Duration of surgery (min)	95.3±15.4	110.2±18.6	0.042
Comorbidities			
Hypertension	3 (20.0%)	2 (14.3%)	0.678
Diabetes mellitus	2 (13.3%)	2 (14.3%)	0.942
Thyroid disease	1 (6.7%)	1 (7.1%)	0.962

Values are presented as mean ± standard deviation or median (interquartile range) for continuous variables and n (%) for categorical variables. Abbreviations: BMI, body mass index; TAH, total abdominal hysterectomy; TAH+BS, total abdominal hysterectomy with bilateral salpingo-oophorectomy. Abbreviations: BMI, body mass index; TAH, total abdominal hysterectomy; TAH+BS, total abdominal hysterectomy with bilateral salpingo-oophorectomy.

the menstrual cycle and these values were similar in both groups (Table 2).

Preoperative AMH levels were similar in both groups (p=0.906). While the preoperative mean AMH level was 1.14 ng/mL in the TAH group, this value was 1.16 ng/mL in the TAH+BS group. By postoperative day 2, there was a significant decrease in AMH levels in both groups and the averages decreased to 0.79 ng/mL and 0.75 ng/mL, respectively. This decrease was statistically significant for both groups $(TAH \ group: p=0.036; TAH+BS \ group: p=0.042)$; however, no significant difference was observed between the groups in terms of postoperative day 2 AMH levels (p=0.691) (Table 3).

In the postoperative 1st month, a slight increase in AMH levels was observed in both groups, but this increase did not reach the preoperative values. In the TAH group, the postoperative 1st month AMH level was 0.94 ng/mL, while in the TAH+BS group it reached 0.92 ng/mL. There was no statistically significant difference between the groups in this measurement (p=0.377). These data indicate that TAH and TAH+BS procedures have a similar effect on AMH levels (Figure 2).

TABLE 2: Preoperative hormone levels of the groups				
Hormone Parameters	TAH Group (n=15)	TAH+BS Group (n=14)	p-value	
FSH (mIU/mL)*	7.35±1.11	7.24±1.16	0.801	
LH (mIU/mL)*	6.54±0.85	7.28±1.23	0.072	
E2 (pg/mL)*	62.07±10.20	63.79±10.76	0.663	
Preoperative AMH (ng/mL)*	1.14±0.78	1.16±0.58	0.906	

Values are presented as mean ± standard deviation. Hormone levels were measured on days 1–4 of the menstrual cycle. Abbreviations: TAH, total abdominal hysterectomy; TAH+BS, total abdominal hysterectomy with bilateral salpingectomy; FSH, follicle-stimulating hormone; LH, luteinizing hormone; E2, estradiol; AMH, anti-Müllerian hormone. Abbreviations: TAH, total abdominal hysterectomy; TAH+BS, total abdominal hysterectomy with bilateral salpingectomy; FSH, follicle-stimulating hormone; LH, luteinizing hormone; E2, estradiol; AMH, anti-Müllerian hormone.

TABLE 3: Changes in AMH levels over time				
AMH measurement time	TAH Group (n=15)	TAH+BS Group (n=14)	Between-Group p-value ¹	
Preoperative AMH (ng/mL)*	1.14±0.78	1.16±0.58	0.906	
Postoperative Day 2 AMH (ng/mL)*	0.79±0.13	0.75±0.21	0.691	
Postoperative Month 1 AMH (ng/mL)*	0.94±0.02	0.92±0.69	0.377	
Within-Group p-value ²	0.036	0.042		

Values are presented as mean ± standard deviation. ¹Independent samples t-test was used to compare the two groups. ²One-way repeated measures ANOVA was used for within-group comparisons. Abbreviations: TAH, total abdominal hysterectomy, TAH+BS, total abdominal hysterectomy with bilateral salpingectomy, AMH, anti-Müllerian hormone. Abbreviations: TAH, total abdominal hysterectomy, TAH+BS, total abdominal hysterectomy with bilateral salpingectomy; AMH, anti-Müllerian hormone.

In conclusion, a significant downward trend in AMH levels was observed in both groups postopera-

tively and the lowest level was reached especially on postoperative day 2. However, despite a partial recovery at 1 month postoperatively, AMH levels did not return to preoperative values. This suggests that surgical procedures may have a permanent decreasing effect on AMH (Figure 3).

When the relationship between AMH levels and age and BMI was analyzed by Pearson correlation analysis, no significant relationship was found between age and AMH (r=-0.142, p=0.461). A moderate negative correlation was found between BMI and AMH, indicating that AMH levels decreased as BMI increased (r=-0.384, p=0.040). This relationship was similar for both groups (TAH group: r=-0.392, p=0.043; TAH+BS group: r=-0.376, p=0.037) (Figure 4).

DISCUSSION

The main aim of this research was to investigate whether adding bilateral salpingectomy during total abdominal hysterectomy for benign gynecological conditions would adversely affect ovarian reserve as measured by serum Anti-Müllerian hormone (AMH) levels. The research shows that performing bilateral salpingectomy at the same time as hysterectomy does not reduce ovarian reserve more than performing hysterectomy alone. The postoperative AMH decline patterns were identical between surgical approaches

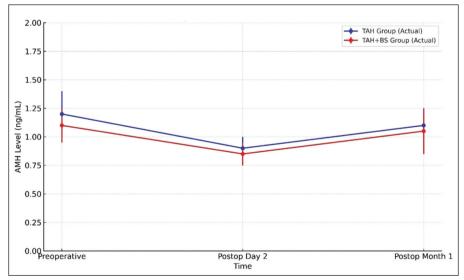


FIGURE 2: Changes in AMH levels over time (Adjusted to Thesis Data)

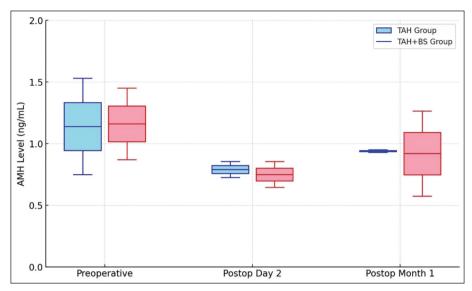


FIGURE 3: Distribution of AMH levels over time

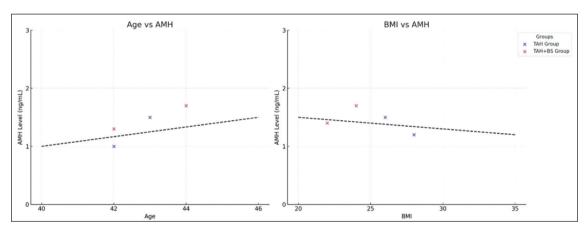


FIGURE 4: Correlation of AMH Levels with Age and BMI

and no significant differences emerged between groups at any measurement point. The study results confirm that performing bilateral salpingectomy during hysterectomy procedures for ovarian cancer prevention does not cause further damage to ovarian reserve.

Our findings revealed that both groups experienced a significant decline in AMH levels postoperatively, with the nadir occurring on postoperative day 2. The AMH levels showed partial recovery at one month follow-up but remained below preoperative values in both groups indicating that the surgical procedure itself rather than the addition of salpingectomy is the primary factor affecting ovarian reserve. Im-

portantly, there was no significant statistical difference between the groups at any measurement time point (p>0.05 for all comparisons). The study results show that bilateral salpingectomy during hysterectomy procedures does not negatively affect ovarian reserve according to AMH measurements. The discovery provides essential clinical guidance to premenopausal women who need hysterectomy because bilateral salpingectomy can be performed for ovarian cancer prevention without causing premature ovarian aging.

In this study, a significant decrease in serum AMH levels was observed in the postoperative period in both TAH and TAH+BS groups; however, no

significant difference was found between the two groups. These findings seem to be consistent with previous studies in the literature. For example, Tehranian et al. reported that the decrease in AMH levels after salpingectomy added to hysterectomy occurred at similar rates, but there was no significant difference between the groups. Similarly, Tavana et al. found that the combination of hysterectomy and bilateral salpingectomy did not affect ovarian reserve more than hysterectomy alone.

Some studies suggest that salpingectomy does not lead to a permanent decrease in AMH levels, thus does not have a long-term negative effect on ovarian reserve. Vahedpour et al. emphasized that salpingectomy added to hysterectomy had no long-term negative effect on serum AMH levels. However, Yuan et al. reported that the combination of hysterectomy and salpingectomy may lead to a more pronounced AMH decrease, especially in younger age groups, and this may be related to the interruption of the vascular connection between the uterus and ovary. 14

Furthermore, the study by Ye et al. showed that reductions in ovarian blood flow may contribute to the decrease in AMH levels and that this effect was more pronounced after bilateral salpingectomy. ¹⁵ Such studies shed light on new research to further investigate the effects of salpingectomy procedures added to hysterectomy on ovarian function.

The long-term reduction of ovarian reserve with the addition of bilateral salpingectomy to total abdominal hysterectomy (TAH) is supported by the fact that serum anti-Müllerian hormone (AMH) levels in particular do not fully return to preoperative levels. This suggests that salpingectomy may affect ovarian blood flow, thereby accelerating the process of follicular atresia and bringing the menopausal transition earlier. In the study by Suneja et al. in 2020, only a limited change in AMH levels was observed in patients undergoing TAH+BS; however, it was stated that decreases in blood flow may have a long-term effect on ovarian function. In

On the other hand, some studies suggest that salpingectomy may lead to more pronounced AMH decreases by limiting ovarian blood supply, especially in younger age groups, thus negatively affecting ovarian reserve in the long term.¹⁸ These results indicate that women with low AMH levels might face such clinical ramifications as early menopause, increased osteoporotic changes and higher incidence of cardiovascular disease.¹⁹

In our study, although a negative correlation was observed between age and AMH (r=-0.142, p=0.461), this relationship did not reach statistical significance. On the other hand, a negative, moderately significant correlation was found between BMI and AMH (r=-0.384, p=0.040).

This finding is in line with the study published by Wang et al. in 2021. Wang et al. reported that there was a significant decrease in AMH levels as BMI increased and that this decrease was especially evident in women with high BMI.²⁰ Similar results were obtained in the multicenter study conducted by Jaswa et al. in 2020; it was suggested that BMI decreased AMH levels and this effect may occur directly through granulosa cells, independent of the dilution effect.²¹ In another study, it was reported that obesity and high BMI decreased AMH production by negatively affecting ovarian function and this effect was more pronounced especially in women over 32 years of age.²²

Taking these relationships into account, it appears that increases in age and BMI have the potential to reduce ovarian reserve by leading to a decrease in AMH levels. This becomes clinically relevant by increasing the risk of early menopause, especially for older women and women with high BMI.

The effect of prolonged surgery on hormone levels in the TAH+BS group is thought to be related to changes in the hypothalamic-pituitary-adrenal axis caused by surgical stress. This stress response may complicate postoperative hormone regulation. The increase in cortisol and other stress hormones with prolonged surgical time may negatively affect the healing process.²³

The main limitations of this study include the limited sample size (n=29) and the inability to observe long-term changes in AMH levels because the postoperative follow-up period was limited to a short period of only 1 month. In addition, the significantly longer operation time in the TAH+BS group

(110.2±18.6 vs 95.3±15.4 min, p=0.042) made it difficult to evaluate the effect of surgical stress on hormone levels.

Another limitation is that ovarian blood flow was not measured; therefore, we could not determine the effect of postoperative vascular changes on AMH levels. In addition, since the patients studied were within a narrow age category of ages 40-45 it contributed to the fact that the correlation of age and Anti mullerian hormone levels was not statistically relevant (r=-0.142 p=0.461) and differences in the effects in different age groups were ruled out. These limitations are important since they affect the external validity of the findings of this study and require that the same findings be tested in a broader age and sample population.

CONCLUSIONS

It has been concluded that the inclusion of bilateral salpingectomy with the primary operation does not have any adverse impacts on the AMH levels in premenopausal women who are undergoing total abdominal hysterectomy due to benign gynecological conditions. Our research showed a remarkable drop in AMH levels in both the groups during the postop-

erative period, however, in case of the groups no such significant difference was observed. Considering that especially high-grade ovarian cancers may originate from the fimbrial end of the salpinges, bilateral salpingectomy can be safely performed during hysterectomy without affecting ovarian reserve.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: Mustafa Erkan Sarı; Design: Mustafa Erkan Sarı; Control/Supervision: Özhan Özdemir; Data Collection and/or Processing: Vefa Şakar; Analysis and/or Interpretation: Vefa Şakar; Literature Review: Vefa Şakar; Writing the Article: Vefa Şakar; Critical Review: Özhan Özdemir; Materials: Vefa Şakar.

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