

The evaluation of the effect of bilateral tubal ligation and bilateral salpingectomy on ovarian reserve

Bilateral tüp ligasyonu ve bilateral salpenjektominin over rezervi üzerine etkisinin değerlendirilmesi

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ABSTRACT

Aim: Aim: We aimed to analyze if the laparoscopic tubal sterilization procedures, bilateral salpingectomy (BS) and bilateral tubal ligation (BTL) had an effect on ovarian reserve, due to affection of anastomoses formed by ovarian and uterine arteries which contribute ovarian perfusion. **Materials and Methods:** This prospective cohort study included 87 women of whom 29 had BTL, 29 BS and 29 control group. Anti-mullerian hormone (AMH) levels and Follicle Stimulating Hormone (FSH) and Estradiol (E2) levels on 3rd day of menses were examined preoperatively (0.month), postoperative 1st month and postoperative 3rd month. **Results:** There were not a statistically significant difference in terms of preoperative, postoperative 1st and 3rd month AMH levels compared in BTL, BS and control group. ($p= 0.906$; $p= 0.81$ and $p= 0.182$, respectively). **Conclusions:** Both of the two procedures are effective sterilization methods and we did not find a negative impact on the ovarian reserve when FSH, E2 and AMH levels were analyzed.

ÖZ

Amaç: Bilateral salpenjektomi ve bilateral tüp ligasyonu laparoskopik tüp sterilizasyon prosedürleridir. Bu prosedürler over perfüzyonuna katkıda bulunan over ve uterin arterlerin oluşturduğu anastomozları etkilemektedir. Çalışmada prosedürlerin over rezervine etkisinin olup olmadığının incelenmesi amaçlanmıştır. **Gereç-Yöntem:** Bu prospektif çalışma 29'u bilateral tüp ligasyonu, 29'u bilateral salpenjektomi ve 29'u kontrol grubu olan 87 kadın dahil edildi. Preoperatif (0.ay), postoperatif 1. ay ve postoperatif 3. ayda adet 3. gününde Anti-Müllerian Hormon düzeyleri ile Folikül Stimulan Hormon ve Estradiol düzeyleri analiz edilmiştir. **Bulgular:** Bilateral tüp ligasyonu, bilateral salpenjektomi ve kontrol grubu ile karşılaştırıldığında preoperatif, postoperatif 1. ve 3. ay AMH düzeyleri açısından istatistiksel olarak anlamlı bir fark bulunamamıştır. (sırasıyla $p= 0.906$; $p= 0.81$ ve $p= 0.182$). **Sonuç:** Her iki işlem de etkili sterilizasyon yöntemidir ve FSH, E2 ve AMH seviyelerine bakıldığında yumurtalık rezervi üzerinde olumsuz bir etki tespit edilmemiştir.

ARTICLE INFO/MAKALE BİLGİSİ

Key Words: Bilateral Tubal Ligation, Bilateral Salpingectomy, Anti-Mullerian Hormone, Follicle Stimulating Hormone, Ovarian Reserve

Anahtar Kelimeler: Bilateral Tüp Ligasyonu, Bilateral Salpenjektomi, Anti-Müllerian Hormon, Folikül Uyancı Hormon, Yumurtalık Rezervi

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INTRODUCTION

Laparoscopic tubal sterilization is a safe and effective contraception method which is one of the most commonly performed methods worldwide. In laparoscopic tubal sterilization, complications such as ectopic pregnancy, tubal re-anastomosis and regret may occur in the early and late periods (1). Vessel anastomoses between ovarian and uterine arteries contributing ovarian perfusion may be affected during this procedure which raises a concern on future menopausal age. Therefore, the potential risk of decreased ovarian reserve due to

surgical interventions on fallopian tubes have been warring of surgeons while counseling patients on tubal sterilization (2, 3).

Ovarian reserve represents the quality and number of oocytes remaining in ovaries at any time in woman's life-span and can be evaluated with several parameters (4). Most commonly used parameters to determine ovarian reserve are basal (3rd day of menses) Follicle Stimulating Hormone (FSH) and estradiol (E2), Anti-mullerian Hormone (AMH), Inhibin measures which are described as static tests (4, 5).

Recently the distal mucosal part of the fallopian tube that extend to ovaries and other pelvic organs has attracted considerable attention as the anatomical location where the majority of serous carcinoma of the ovary develops (6). Salpingectomy, performed for tubal sterilization has been shown to be protective against epithelial ovarian cancers (7). Therefore, in women with indications gynecological operations proposing prophylactic salpingectomy can be reasonable. However, concerns of potential effects on ovarian reserve led us to design this study.

In current literature, there have been numerous studies on effects of ovarian and tubal surgical procedures on ovarian reserve. Our aim in this study was to analyze and compare the effect of bilateral salpingectomy BS and BTL on ovarian reserve.

MATERIAL - METHODS

This prospective cohort study was conducted between April 2017 and February 2018 in Zekai Tahir Burak Women's Health Education and Research Hospital, Ankara, Turkey. Ethical approval was obtained from institutional ethics committee in 31.03.2017 with the number 57/2017.

Eighty-seven women aged between 30 – 45 years were enrolled in this study after a written and verbal informed consent was obtained. The groups were formed from 29 women who had laparoscopic bilateral tubal ligation (BTL), 29 women who had bilateral salpingectomy (BS) and 29 healthy controls. The patients who had infertility, perimenopausal symptoms, any endocrinological pathology, family history of premature ovarian failure and history of ovarian surgery, endometriosis, myomectomy, history of hydrosalpinx, pyosalpinx, chemotherapy or radiotherapy were excluded.

All laparoscopic tubal sterilization procedures were performed under general anesthesia. The Verres needle was entered in the neutral position. After confirmation of peritoneal access, the abdomen was inflated with carbon dioxide gas to a pressure of 15 mm Hg. After the incision of the umbilical trocar, the patient was placed in the Trendelenburg position and 5 mm trocars were entered. Subsequently in patient group who will be performed tubal sterilization by electrocoagulation method, tubes were cauterized distal (isthmus) 2-3 centimeters (8) from the point where the tubes were combined to the uterus with bipolar cautery (Gyrus ACMI, Southborough, USA). After cauterization, the tubes were cut with the help of scissors and the ends were separated. In the group that underwent salpingectomy, mesosalpinks between the tuba and ovary were coagulated with bipolar cautery and then the coagulated areas were cut and the tubes

were released. After that the tubes were cauterized and removed from the isthmus region

In BTL and BS groups, from venous serum samples of women, Anti-mullerian hormone (AMH) levels were measured preoperatively, postoperative 1st and postoperative 3rd months by using Elisa procedure. Also Follicle Stimulating Hormone (FSH) and Estradiol (E2) levels were measured on the 3rd day of menstrual period of patients preoperatively (0.month), and postoperative 1st and 3rd month. In the control group FSH, E2 and AMH levels were measured on the 3rd day of menstruation and in subsequent 1st and 3rd months after the first blood sample collection. Blood samples were centrifuged at 1000 rpm for 15 min and stored at -80 °C. AMH levels were measured with ELISA method using Elabscience (Elabscience, Houston, Texas, USA). FSH and serum E2 were measured by electrochemiluminescence immunoassay (ECLIA, Roche).

Increasing BMI affects the duration of postpartum tubal ligation surgery. A difference was found between the operation times of women with BMI ≥ 30 and BMI < 30 who underwent postpartum tubal ligation. Therefore, the BMI values of the participants were included in the analysis in our study (9).

There are studies examining the relationship between bilateral salpingectomy and smoking. In our study, smoking was included in the analysis to examine this possible relationship (10).

Statistical Analysis

Statistical Package for Social Sciences (SPSS) 21.0 (SPSS Inc., Chicago, IL, USA) was used for statistical analysis. Normal distribution was analyzed by both visual (histograms and probability graphics) and statistical (Shapiro-Wilk Tests) methods. One-Way ANOVA was used for parametric data and Kruskal-Wallis test was performed for non-parametric data. Post-Hoc Tuckey test was used to compare binary groups in the results of significant parametric data. Chi-square tests were applied to potentiate significant non-parametric data. The results were evaluated in the %95 confidence interval and the significance was evaluated as $p < 0.05$.

Sample Size Calculation

Based on the previous literature, 29 patients in each group would be needed in order to determine the difference between the two groups with 5% significance level and 80% power (11). The appropriate sample size and the strength of the study were calculated by Tools Clinical Tools and Calculators for Medical Professionals.

RESULTS

Patients were evaluated in three groups which were BS group (n=29), BTL group (n=29) and control group (n=29). There were no complications directly attributable to performing salpingectomy or tubal ligation procedures.

The socio-demographic characteristics of the patients are listed in Table 1. The groups were similar in terms of height, weight, BMI, use of medication or presence of chronic disease which are not related with ovarian reserve, history of non-gynecological surgery and use of contraception. Mean age of BS group was higher than the other two groups ($p < 0.001$) and smoking was less common in BTL group ($p = 0.035$).

In Table 2 AMH levels of all three groups were similar in preoperative period, postoperative 1st month and postoperative 3rd month. Preoperative, postoperative 1st and 3rd month E2 and FSH values of all three groups were also compared in Table 2. There was no significant difference between all three groups in terms of preoperative, postoperative 1st and 3rd month E2 levels. Basal FSH levels were higher in BS group ($p = 0.034$) while the postoperative 1st and 3rd month FSH levels were similar between the groups. FSH values of patients were compared among themselves by Tukey's Post Hoc test. In all three groups, FSH levels were similar when basal (preoperative) levels were compared with postoperative 1st and 3rd month results.

AMH values of all three groups were compared among themselves in terms of basal (preoperative), postoperative 1st month and 3rd month values. There were no statistically significant differences when basal (preoperative) AMH levels were compared with postoperative 1st and 3rd month AMH levels.

There were no intra-operative and post-operative complications reported in BS and BTL groups.

DISCUSSION

In this study, we aimed to evaluate the ovarian reserve of women who had undergone bilateral tubal ligation and bilateral salpingectomy, with the hypothesis of disrupted ovarian blood flow due to damage in the vascular anastomoses of uterine and ovarian arteries. The effects of both techniques on ovarian reserve markers were examined individually and also compared with each other. AMH, FSH and E2 levels were not affected by both two procedures in preoperative, postoperative 1st and 3rd months and we shall comment that BS and BTL were not superior to each other in order to maintain ovarian reserve.

The mean age of women with BS was significantly higher than BTL group. Basal FSH levels were also significantly higher but was still in normal range in this group. The difference between the ages of the study groups were caused because of the attitude of surgeons to recommend salpingectomy to women above 37 years of age because of the concerns due to reports on increased risk of ovarian cancer caused by the adjacent tubas (12). In the light of the published studies, decrease in ovarian cancer risk was reported as 13-41% after BTL and 42-78% after BS; and patient based decision for the appropriate method was recommended after discussing the operative risks, complication rates, future benefits and probability of demand for tubal reversal (12). American College of Obstetricians and Gynecologists (ACOG) and the American Cancer Society also recommends extraction of the fallopian tubes in hysterectomy without oophorectomy and counseling women who want tubal sterilization (13, 14).

Table 1. Patient and socio-demographical characteristics in three groups

	Control	BTL	BS	P
Age (year)	36.7±4.3	35.5±3.9	40.4±2.9	< 0.001*
Height (cm)	160.2±6.5	162.0±5.3	160.4±4.8	0.390
Weight (kg)	68.9±13.5	70.7±12.7	69.9±12.6	0.871
BMI (kg/m ²)	27.1±5.6	27.0±9.0	27.1±4.6	0.332
Smoking	10 (34.5)	4 (13.8)	13 (44.8)	0.035**
Medication history	5 (17.2)	4 (13.8)	5 (17.2)	0.830
Additional disease history	6 (20.7)	7 (24.1)	8 (27.6)	0.919
Gynecological surgery history	1 (3.4)	1 (3.4)	4 (13.8)	0.203
Non-gynecological surgery history	18 (62.1)	14 (48.3)	14 (48.3)	0.482
Contraception use	20 (69.0)	13 (44.8)	18 (62.1)	0.158

* Post-Hoc Tuckey test; Control – BS; $p = 0.001$, BTL – BS; $p = 0.001$, Control -BTL $p = 0.394$

** Chi-Square test: Control - BTL; $p = 0.066$, BTL - BS; $p = 0.009$, Control - BS; $p = 0.421$

BMI: Body mass index, BTL: Bilateral tubal ligation, BS: Bilateral salpingectomy. Variables were given as mean ± standard deviation and number (percentage),

P < 0.05 was considered significant.

Table 2. Comparison of AMH, FSH and E2 levels of the three groups in preoperative period, postoperative 1st and 3rd month

	Control*	BTL	BS	p
Preoperative AMH value (ng/dl)	2.2±1.2	2.2±1.0	2.3±1.5	0.906
Postoperative 1 st month AMH value (ng/dl)	2.8±1.2	2.7±1.4	2.5±1.3	0.81
Postoperative 3 rd month AMH value (ng/dl)	2.6±0.6	2.6±1.8	2.2±1.2	0.182
Preoperative (Basal) E2 (pg/ml)	69.7±57.8	79.4±45.5	93.8±57.5	0.243
Postoperative 1 st month E2 (pg/ml)	71.6±53.8	62.4±28.2	55.7±18.1	0.258
Postoperative 3 rd month E2 (pg/ml)	94.4±64.4	75.5±50.0	64.5±22.8	0.069
Preoperative (Basal) FSH (mIU/ml)	4.9±2.5	4.8±1.8	6.5±3.8	0.034**
Postoperative 1 st month FSH (mIU/ml)	5.5±2.5	5.8±3.2	5.9±2.4	0.825
Postoperative 3 rd month FSH	5.2±2.3	5.0±2.4	5.9±2.2	0.302

* The preoperative section in control group refers to the hormonal examination first visit of the patient

** FSH values were compared by Tukey's Post Hoc test among themselves in Table 3.

BTL: Bilateral tubal ligation, BS: Bilateral salpingectomy. E2: Estradiol FSH: Follicle Stimulating Hormone

Variables were given as mean ± standard deviation, P <0.05 was considered significant.

Venturella et al. examined the long-term effects of prophylactic BS combined with laparoscopic hysterectomy on ovarian reserve up to post-operative 5th year in 70 women with the parameters; AMH, FSH, 3D AFC, vascular index, flow index and vascular flow index by using OvAge method (12). They concluded that performing prophylactic BS to patients while laparoscopic hysterectomy would not affect the ovarian reserve up to post-operative 3rd and 5th years (15). Among women who had total abdominal hysterectomy with ovarian and tubal preservation, significant decrease in AMH levels were reported in postoperative 1st month but not the 3rd month, and this was commented as a temporary effect on ovarian reserve (16). Herman et al. compared ovarian reserves of 46 patients who had salpingectomy or tubal ligation during caesarean section; by analyzing AMH levels in preoperative period and post-operative 6-8th weeks. Similar to our study, the mean age of women in the salpingectomy group was higher than in the bilateral tubal ligation group (17). As a result, no difference was reported between groups in terms of post-operative complications and ovarian reserve (17). In literature, an article had evaluated women with hydrosalpinx undergoing in vitro fertilization. In that study laparoscopic proximal tubal occlusion was superior to laparoscopic salpingectomy on ovarian reserve in three years of follow-up (18).

In a prospective cohort study of 53 women who had tubal ligation, ovarian reserve was evaluated by pre- and post-operative 12th month AMH levels and AFC and it was reported that ovarian reserve was not altered by tubal ligation (19). In a rat model which compared the Pomeroy technique and bipolar electro cauterization, AMH levels and AFC were significantly lower in electro cauterization group, proposing that electro cauterization caused higher damage to ovaries (20). Ozyer et al.

compared the AMH and Inhibin-B levels of women who had tubal ligation with Pomeroy technique during caesarian section or by elective mini-laparotomy, and found higher AMH and Inhibin-B levels in favor of tubal ligation performed during cesarean section (21). Ovarian reserve after laparoscopic tubal bipolar electrodissection and transection was also evaluated by Ercan et al. and significant change in AMH levels were not observed (22). Venturella et al. evaluated the ovarian reserve of patients who had bilateral salpingectomy with standard method or with removal of mesosalpinks; and reported the ovarian reserve was not effected by salpingectomy (23). Collectively; the most of the experts reported the ovarian reserve was not affected by any kind of tubal surgery methods despite the few conflicting reports.

Our results were consistent with other published studies that have addressed whether salpingectomy or tubal ligation performed concurrently with hydrosalpinx, myomectomy, hysterectomy or caesarean section operations can lead to impaired ovarian function (2, 15, 17, 24-26). The main limitations of our study were the number of study groups, and the absence of the long-term follow-up after surgery due to unwillingness of patients to collaborate for the study. Although the FSH levels were in normal ranges in all groups, preference of salpingectomy for patients after 37 years of age in our hospital routine may be commented as another limitation. Another limitation of our study was that AFC could not be measured, because most of the patients refused to be examined by transvaginal ultrasound. We think that more significant results can be obtained in the long-term follow-up of patients in large study groups.

In conclusion, tubal sterilization procedures, salpingectomy and tubal ligation procedures were

not superior to each other when the ovarian reserve parameters (AMH, FSH, E2) were evaluated. In addition, there were no difference between groups in terms of intraoperative or postoperative complications. While counseling women who demand tubal sterilization, ovarian reserve should not take concern for decision of appropriate method in the light of our study and the current literature.

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Disclosure

The authors declare no conflicts of interest.

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