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Are serum lipid and androgen levels different in women with natural or surgical menopause?

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ABSTRACT

Menopausal status is associated with the type of menopausal onset. The aim of this study was to investigate whether serum lipid and androgen levels are different in women with natural or surgical menopause. This retrospective case control study was conducted with 376 postmenopausal women with natural onset and 144 postmenopausal women with surgical onset. Each woman was assessed in terms of serum glucose, lipid and androgen levels. The mean serum glucose, cholesterol, triglyceride, HDL, LDL, VLDL and testosterone levels in the surgical menopause group were almost similar to those of the natural menopause group (p=0.510, p=0.873, p=0.807, p=0.950, p=0.807, p=0.972, p=0.086, p=0.778, respectively). The mean serum DHEAS levels in the natural menopause group were statistically higher in comparison with the surgical menopause group (p=0.044). Serum lipid levels in postmenopausal women are not different in terms of the type of menopause onset. Serum androgen levels were decreased more in surgical menopause with lower levels of DHEAS associated with surgical onset.

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1. Introduction

Menopause is the cessation of menstrual periods either following a natural onset of gradual stopping for 12 months or following bilateral oophorectomy so that ovarian hormones are suddenly terminated (Landgren et al., 2004). As life expectancy has increased, women now live at least one third of their lives after menopause (Kulak et al., 2009). Metabolic changes following surgical and natural menopause differ and are associated with risk factors for cardiovascular disease, which is the leading cause of mortality in postmenopausal women (Ozdemir et al., 2009; Farahmand et al., 2015).

Natural menopause occurs at a median age of 51 years due to ovarian follicular depletion with a spontaneous

decline in ovarian hormone secretion. The removal of both ovaries at the time of hysterectomy or other pelvic surgery before the natural age of menopause is known as surgical menopause (Rodriguez and Shoupe, 2015). Although gynecological malignancies are certain indications for oophorectomy, in the setting of benign disease, the decision for removal of the ovaries at the time of hysterectomy is taken according to guidelines for premenopausal patients (ACOG, 2008).

The sudden withdrawal of estrogen, progesterone, and androgens in surgical menopause are associated with more severe, early onset and prolonged menopausal symptoms due to the acute reduction in ovarian sex steroid production (Davison et al., 2005). Hot flushes may even be apparent in the immediate postoperative period (Gallicchio et al., 2006). The intact ovary often maintains hormone production in the natural menopause, which is the transitional period known as the peri-menopause (Taylor et al., 2017). Although estradiol production dramatically decreases, testosterone production continues in the postmenopausal ovaries. The small amount of circulating testosterone seems to have beneficial effects on menopausal symptoms (Fogle et al., 2007). A prior oophorectomy affects lipid, lipoprotein, glucose, and insulin metabolism in women according to the changes in ovarian steroid production and secretion (Carr et al., 2000).

Early and surgical menopause are associated with an increased risk of CVD because of a decline in the natural ovarian hormones (Lobo et al., 2007). The aim of this study was to investigate whether serum lipid and androgen levels are different in women with natural or surgical menopause.

2. Material and methods

This retrospective, cross-sectional study was conducted with postmenopausal women who underwent annual examinations in the Outpatients Clinic of Samsun Women and Children's Health Research and Training Hospital between January 2016 and June 2019. Approval for the study was granted by the Local Institutional Review Board (decision no: GOKA/2019/3/9). The inclusion criteria were accepted as natural or surgical postmenopausal women aged between 40 and 65 years old, and not using hormone replacement therapy (HRT). The exclusion criteria were accepted as use of HRT, exogenous steroid therapy, or anti-lipid drugs, or a history of chemotherapy or pelvic radiotherapy because of a cancer.

Of a total of 550 postmenopausal women, 19 were excluded due to currently use of HRT to eliminate the possible implication of estrogen and progesterone in the relationship between menopause and lipid metabolism, and 11 because of chemotherapy for a malignancy. A total of 376 women with natural menopause and 144 women with surgical menopause were included in the study. Postmenopausal status was accepted as at least 12 consecutive months of amenorrhea with a follicle-stimulating hormone (FSH) level of 40 mIU/mL (Soules et al., 2001). Age, gravidity, parity, time since menopause onset and body mass index (BMI) were recorded as demographic characteristics. The height and weight measurements of women were obtained and BMI was calculated as the ratio of weight (kg) to the square of the height (m^2).

Blood samples were collected by venipuncture after a 12-hours overnight fast, and measurements for serum fasting plasma glucose (FPG), total cholesterol (TC), Triglyceride (TG), High density lipoprotein-cholesterol (HDL-C), very-low density lipoprotein-cholesterol (VLDL-C) testosterone, androstenedione and dehydro-epiandrostenedione-sulphate (DHEAS) were performed. These parameters were quantified using a 7600-110 Automatic Analyzer (Hitachi Inc., Tokyo, Japan). The low-density lipoprotein (LDL) cholesterol was calculated using the Friedewald formula.

Statistical analysis

Data obtained in the study were analyzed statistically using NCSS (Number Cruncher Statistical System) 2007 software (Kaysville, Utah, USA). Descriptive statistical methods (mean, standard deviation, median, frequency, ratio, minimum, maximum) were used to evaluate the study data. The conformity of the quantitative data to normal distribution was tested using the Kolmogorov-Smirnov test, Shapiro-Wilk test and graphic evaluations. The Mann Whitney U test was used in the comparison of two groups of data which did not show normal distribution. The Pearson Chi-square test was used to compare qualitative data. Spearman's Correlation Analysis was applied to evaluate the relationships between variables. A value of $p<0.05$ was accepted as statistically significant.

3. Results

Evaluation was made of a total of 520 postmenopausal women, as 376 women in the natural menopause group and 144 women in the surgical menopause group. The age, gravidity, parity, abortus, time since menopause onset, and BMI values of the groups are presented in Table 1 ($p=0.065$, $p=0.011$, $p=0.021$, $p=0.069$, $p=0.696$, $p=0.611$, respectively).

The mean serum glucose, cholesterol, triglyceride, HDL, LDL, and VLDL levels in the surgical menopause group were almost similar to those of the natural menopause group ($p=0.510$, $p=0.873$, $p=0.807$, $p=0.950$, $p=0.807$, $p=0.972$, respectively). The mean serum testosterone and androstenedione were lower in the surgical menopause group, with no statistically significant difference between the groups ($p=0.086$, $p=0.078$, respectively). The mean serum DHEAS

levels in the natural menopause group were statistically significantly higher compared to those of the surgical menopause group (p=0.044) (Table 2).

Table 1. Characteristics of women with natural menopause and surgical menopause.

	Natural menopause (n=376)	Surgical menopause (n=144)	p value
Age (years) mean±sd	52.59±6.75	48.40 ±6.48	0.065
Gravidity min-max (median)	0-15 (4)	0-10 (3)	0.011*
Parity min-max (median)	0-12 (4)	0-7 (3)	0.021*
Aborts min-max (median)	0-6 (1)	0-5 (1)	0.069
Time since menopause onset (years) mean±sd	3.10±1.22	3.91±1.31	0.696
Body mass index (BMI, kg/m2) mean±sd	28.10±5.34	29.31±4.29	0.611

Mann Whitney U Test, *p<0.05.

Table 2. Laboratory test results of women with natural menopause and surgical menopause.

	Type of menopause		P value
	Natural menopause (n=376)	Surgical menopause (n=144)	
Glucose (mg/dl)	116.52±50.64	112.62±34.87	0.510
Cholesterol (mg/dl)	243.22±71.23	240.44±60.88	0.873
Triglyceride	179.93±81.91	183.28±90.21	0.807
HDL (mg/dl)	57.68±16.38	57.70±16.56	0.950
LDL (mg/dl)	168.06±64.22	165.31±66.3	0.807
VLDL (mg/dl)	45.27±25.65	46.67±28.44	0.972
Testosterone (mg/dl)	21.35±10.95	19.91±10.54	0.086
Androstenedione (mg/dl)	0.40±0.22	0.38±0.23	0.078
DHEAS (mg/dl)	100.24±66.72	87.13±60.97	0.044*

Mann Whitney U Test, mean ± sd *p<0.05.

4. Discussion

This retrospective, cross-sectional study investigated whether the serum lipid and androgen levels were different in women with natural or surgical menopause. The results indicated that serum lipid levels were not changed with natural or surgical onset in postmenopausal women. Serum androgen levels were higher in the natural menopause group but not to a statistically significant level. However, postmenopausal women with natural onset had higher serum DHEAS levels in comparison with postmenopausal women with surgical onset.

Menopausal transition is known to be associated with higher dense of LDL and higher LDL-C levels in comparison to premenopausal women (Wang et al., 2018). A history of oophorectomy is associated with increased lipid, lipoprotein, glucose, and insulin levels compared with intact ovaries in postmenopausal women (Yoshida et al., 2011). In the current study, there was no difference between the groups in respect of serum glucose, cholesterol, triglyceride, HDL, LDL, and VLDL levels. Nevertheless, close monitoring of lipids in routine examinations can be recommended for all postmenopausal women.

Surgical menopause results in a sudden reduction in ovarian sex steroid production and a complete absence of any steroid production with surgical removal of the ovary. However, intact postmenopausal ovaries often continue limited production of sex steroids, particularly of testosterone (Matsui et al., 2012). In the present study, serum testosterone and androstenedione levels were lower in women with surgical menopause than in women with natural menopause, but not to a statistically significant level. The removal of the premenopausal ovary and the sudden and significant reductions in testosterone and androstenedione are known to have a negative impact on sexual desire (Celik et al., 2009).

The decline in ovarian production of estrogen and increased adiposity may play a role in heightened estrogen synthesis in the adipose tissue by aromatase conversion of androgens after menopause (Castracane et al., 2006). In the present study, a statistically non-significant decline in testosterone and androstenedione levels was determined in postmenopausal women with surgical onset. It can be suggested that as the surgical menopause group comprised more over-weight women although it did not reach statistical significance, more adipose tissue may provoke more aromatization of testosterone and androstenedione. DHEAS is an important androgen and estrogen precursor in postmenopausal women with decreased ovarian production. Despite the low level of estrogen production, utilization of DHEAS is necessary in the postmenopausal period. Lower DHEAS has been associated with the development of atherosclerosis and insulin resistance depending on a higher BMI (Lasley et al., 2002). In the current study, decreased DHEAS levels were detected in the postmenopausal women with surgical onset.

The limitation of this study is that retrospective and cross-sectional nature containing the last three years, meaning that the results are not fully representative of the general population of postmenopausal women. Further prospective studies are needed.

In conclusion serum glucose, cholesterol, triglyceride, HDL, LDL, and VLDL levels are not different according to types of menopause onset in postmenopausal women. Serum testosterone and androstenedione levels were more decreased with surgical menopause although definitively decreased DHEAS levels were seen to be associated with surgical onset in postmenopausal women.

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Conflict of interest

The authors declare no conflict of interests.

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