CORRELATION BETWEEN HORMONAL AND LIPID STATUS IN WOMEN IN MENOPAUSE

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Abstract

It is widely accepted that menopause leads to changes in hormonal status, metabolism and lipid profile. The aim of this study was to analyze the influence of menopause on the concentrations of lipids, lipoproteins and, the influence of estradiol, progesterone, FSH, LH on lipid profile in menopausal women as well. The menopausal women had higher but non-significant ($p>0,05$) concentrations of total cholesterol, VLDL, LDL, and triglycerides than women with regular menstruation. The concentration of HDL was significantly lower in menopausal women than in women with regular menstruation ($p<0,05$). Also, the concentration of apolipoprotein B was significantly higher in menopausal women ($p<0,05$), but the concentrations of apolipoprotein and lipoprotein (a) were lower but without significance ($p>0,05$). Estrogen concentration has significant negative correlation with VLDL and triglycerides ($p<0,05$) and significant positive correlation with HDL ($p<0,05$) in menopausal women. Progesterone concentration has shown no correlation with concentrations of lipids and lipoproteins in menopause. We can conclude that menopause leads to changes in lipid profile by reducing HDL, and elevating apolipoprotein B levels, thus increasing the risk for cardiovascular disease. These changes were caused by reduction of estrogen concentrations in menopause.

KEY WORDS: menopause, lipid status, triglycerides, FSH, LH, HDL, LDL.

Introduction

Menopause is defined by cessation of menstruation for a period longer than one year, and begins with changes in ovarian function. Increased levels of cholesterol, triglycerides, LDL, apolipoprotein B and decreased levels of HDL and apolipoprotein A are characteristics of lipid profile in menopause. With increase in LDL concentration, the composition of LDL molecule also changes so that participation of low density lipoprotein is increased by 30-40% (1). During menopause, concentration of triglycerides also increases, which is related to the increase of the abdominal fat amount and insulin resistance. Menopause causes decrease of HDL concentration and changes in HDL structure as well. The concentration of HDL2 decreases while concentration of HDL3 increases. HDL concentration is in inverse proportion with abdominal fat level (2). Current understanding is that brain and ovaries are in the center of hormonal changes after menopause. Functional changes in suprarenal glands also have important role, as well as adipose tissue. In brain, neurotransmitters (dopamine, neuropeptide Y) and neuromodulators concentrations (prostaglandins) decrease, while norepinephrine and somatostatine levels increase. The results are development of appetite and thermoregulation disorders, pulsation in GnRH secretion and adenohypophysis hormones secretion, and decreased secretion of growth hormones. With cessation of follicular genesis and menopause, FSH level rises by 10-20 fold, and LH by 3-5 fold. High levels of gonadotropines are maintained during two or three years after menopause. In later age, levels of gonadotropines decrease again, or remain only mildly elevated. LH stimulates ovaries to produce androgens, which persists until advanced years, so that ovary preserves its function of an endocrine organ. Of course, production of estradiols and progesterone by ovary ceases. Estradiol level in circulation is 12-20 pg/ml. Estradiol is formed by conversion of estrone. Growth hormone secretion decreases after the age of 40. In postmenopause, level of growth hormone is by 30-40% lower than in reproductive age. It is caused by the increase of somatostatin level and decreased secretion of growth hormone releasing hormon (GHRH). In menopause, level of ACTH, melatonin and prolactin decreases. Decreased secretion of ACTH leads to decreased secretion of dehydroepiandrosterone (DHEA) and dehydroepiandrosterone sulfate (DHEAS). In women of senior age, level of adrenal androgens is lower by 80-90%. Lower number of women in menopause (15-20%) have symptoms of hyperandrogenism. This group of women is also at higher risk of cardiovascular diseases (3), but it is yet unclear whether increase in risk is caused by increased androgen level or decreased estrogen level (4). There is proportionally small number of studies that investigate correlation between hormonal and lipid status in women in menopause, and this study represents an attempt to clarify this problem.

Patients and Methods

Our research aims were to establish differences in lipid status in women in menopause and women with regular menstruation. Also, we intended to establish the influence of estrogen, progesterone, FSH and LH concentration on lipid profile of women in menopause. This prospective research was conducted from September 2000 to September 2004. The study group consisted of sixty women of average age 52,82±8,22 with average menopause length of 49,56±35,65 months. Subjects were selected according to the following criteria:

- No hormonal therapy administered,
- No medications that affect lipid profile administered,
- Smoking maintained below twenty cigarettes per day,
- Body mass index not greater than 35kg/m^2.

Considering that all women included in the study had somatic and psychological changes related to menopause and/or painful syndromes related to osteopenia and osteoporosis, all of them were regularly subjected to gynecological and neuropsychiatric examinations. The control group included 34 women with regular menstruation and average age of 47,92±1,66, who have not been taking any hormone therapy or medicaments that may affect lipid profile. Blood sampling was done at Medical Biochemistry Institute of University Clinics Center Tuzla . Blood was collected from cubital vein. Total cholesterol concentration, triglyceride concentration, LDL (low density lipoproteins), HDL (high density lipoproteins) and VLDL (very low density lipoproteins) concentrations were determined. Total cholesterol, triglyceride, HDL and LDL concentrations were determined using "Dimension RxL" apparatus. Follicle-stimulating hormone (FSH) level, luteinizing hormone (LH) level, estradiol and progesterone levels were determined at Nuclear Medicine Institute of University Clinics Center in Tuzla. FSH, LH and progesterone levels were determined using radioimmunoassay (RIA method), with reagents containing radioactive I^{125}, produced by „NETRIA", London ECIA 7BE. Estradiol was determined using reagents by „CIS

Biointernational". Calculated values were analyzed using standard statistical methods: arithmetic mean, standard deviation, Mann Whitney U test, Student's test, Pearson's test, Spearman-Rank's test of correlation, multiple regression. Statistical significance threshold was set at 5% and 1%. Data was analyzed using statistics program Data Desk version 6.0 (1997, Data Description, Inc,.USA).

Results and Discussion

	MENOPAUSE mmol/dm^3 ± SD	CONTROL mmol/ dm^3 ± SD
Cholesterol	6,08 ± 1,14	5,99 ± 1,44
Triglyceride	1,64 ± 0,68	1,56 ± 0,74
LDL	4,12 ± 1,11	3,99 ± 1,46
HDL	1,44 ± 0,41	1,69 ± 0,50
VLDL	0,69 ± 0,68	0,58 ± 0,39

TABLE 1. Average values of cholesterol, triglyceride, LDL, HDL and VLDL levels in blood of women in menopause and women with regular menstruation from control group

Average values of cholesterol, triglyceride, LDL, HDL and VLDL levels in woman of both groups are shown in Table 1. Total cholesterol concentration in women in menopause is slightly higher than in women with regular menstruation, which is not statistically significant (p>0,05). Triglyceride concentration in women in menopause also is not significantly higher (p>0,05). There are no statistically significant differences in LDL concentration between the two groups (p>0,05). However, HDL concentration in women in menopause is significantly lower than in women with regular menstruation (p<0,05). VLDL concentration difference between the two groups is not statistically significant (p>0,05). Contrary to our observations, many other studies have proved significant deviations in lipid and lipoprotein concentrations in women in menopause (5, 6, 7, 8, 9). Women in our study had lower HDL concentration, which was confirmed by many studies (10), although studies that contradict these findings also exist (11). Apolipoprotein A, apolipoprotein B and Lp(a) concentrations in women in menopause and in women with regular menstruation are shown in Table 2. Apolipoprotein A concentration in women in menopause is lower than in women with regular menstruation, but the difference is not statistically significant (p>0,05). Apolipoprotein B concentration was significantly higher in women in menopause (p=0,003). It is considered that increase in apolipoprotein B concentration is a better indicator of changes in lipid profile and better predictor of cardiovascular risk (12). Apolipoprotein B, together with apolipoprotein A and their correlation, are better predictors of cardiovascular risk than LDL alone (13). However, some authors believe that determination of apolipoproteins does not hold advantage over classical lipid profile determination in cardiovascular diseases prediction. According to their research, women in menopause had lower apolipoprotein A concentrations and significantly higher apolipoprotein B concentrations (14). Lp(a) concentration in women in menopause is higher than in women with regular menstruation, but statistical difference was not significant (p>0,05). Average FSH, LH, estradiol and progesterone levels in blood of women of both groups are shown in Table 3. FSH concentration in group of women in menopause is significantly higher (p<0,001) than in group of women with regular menstruation. LH concentration is higher as well (p<0,001), which, together with significantly lower estrogen concentration, is the expected result and recognized characteristic of hormonal status in this period. Estradiol concentration

	MENOPAUSE g/dm^3 ± SD	CONTROL g/dm^3 ± SD
Apolipoprotein A	1,52 ± 0,27	1,61 ± 0,28
Apolipoprotein B	1,24 ± 0,33	1,02 ± 0,17
Lp(a)	0,28 ± 0,30	0,24 ± 0,23

TABLE 2. Average values of apolipoprotein A, apolipoprotein B and Lp(a) levels in blood of women in menopause and women with regular menstruation from control group

	MENOPAUSE IU/dm^3 ± SD	CONTROL IU/dm^3 ± SD
FSH	71,37 ± 30,78	14,76 ± 10,38
LH	28,50 ± 13,01	8,31 ± 7,83
	pmol/dm^3 ± SD	pmol/dm^3 ± SD
Estradiol	93,87 ± 120,03	350,42 ± 299,19
	nmol/dm^3 ± SD	nmol/dm^3 ± SD
Progesterone	2,42 ± 6,71	3,13 ± 2,22

In group of women with regular menstruation, estradiol has highly significant negative correlation with lipoprotein (a) concentration (p<0,001) (Figure 1), and significantly positive correlation with HDL and apolipoprotein A concentration (p<0,05).

TABLE 3. Average values of FSH, LH, estradiol and progesterone levels in blood of women in menopause and the control group with regular menstruation

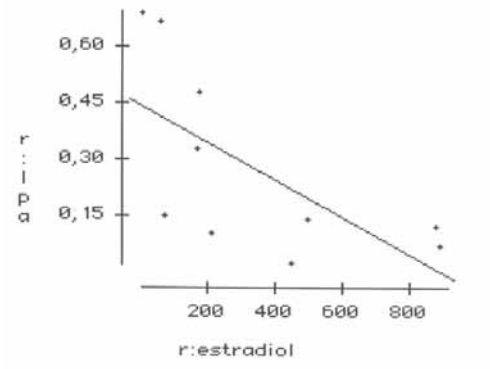

FIGURE 1. Correlation between estrogen and Lp(a) concentration in women with regular menstruation

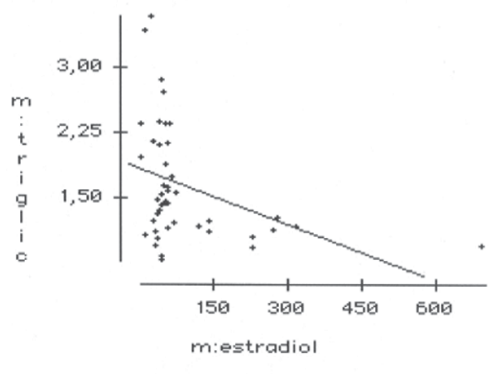

FIGURE 2. Correlation between estradiol and triglyceride concentration in women in menopause

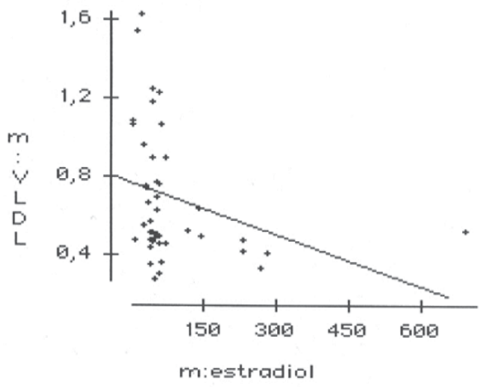

FIGURE 3. Correlation between estradiol and VLDL concentration in women in menopause

is significantly lower ($p<0,001$) in group of women in menopause. Progesterone concentrations are not significantly different between the two groups ($p>0,05$). Multiple regression analysis of estrogen and progesterone mutual influence does not show statistical significance in women in menopause ($p>0,05$). Progesterone is not significantly correlated with lipid and lipoprotein concentration in group of women in menopause, and in group of women with regular menstruation as well. Multiple regression analysis also does not show the change in influence of estrogen on some lipids and lipoproteins induced by progesterone, which puts this research into group of those that found no negative progesterone influence on lipid profile and cardiovascular risk in women in menopause (15). Lp(a) synthesis is genetically determined and, in contrast with other lipoproteins, its concentration is not influenced by diet, exercise or drugs that decrease the concentration of lipids (16). Lp(a) concentration reduction in women who used hormone therapies has been proven in several different studies (17). In women with regular menstruation, there is a significant negative correlation between estrogene concentration and Lp(a) concentration, which affirms previously proved dependence of Lp(a) concentration (18). In the same group, there is significant positive correlation between Lp(a) and apolipoprotein B concentration and FSH and LH, and negative correlation between Lp(a) and apolipoprotein B concentration and apolipoprotein A. FSH and LH concentrations are in significant positive correlation with Lp(a) concentration ($p<0,05$) in group of women with regular menstruation, which indicates that, at the first sign of weakened ovarian function, increased FSH level increases cardiovascular diseases risk in women with regular menstruation as well. In the group of women in menopause there is no correlation between FSH and LH and Lp(a). In group of women with regular menstruation, positive correlation between estradiol and HDL and apolipoprotein A affirms mutual performance of HDL, apolipoprotein A and estrogen, which is mentioned in the results of experimental studies (19). In women in menopause there is no correlation between estradiol concentration and HDL, which indicates that estrogens are not the only factor that affect HDL concentration in menopause. There is a significant negative correlation between estradiol concentration and triglyceride, VLDL and apolipoprotein B concentrations ($p<0,01$ and $p<0,05$) in women in menopause (Figures 2, 3 and 4), which affirms already proven influence of estrogen on lipid profile of women in menopause. The fact that VLDL shows significant negative correlation with estradiol concentration in women in menopause indicates that estrogens modify VLDL concentration, as well as triglyceride and apolipoprotein B concentration. VLDL alone is already recognized as cardiovascular diseases risk factor (20). There is a positive correlation between estrogens concentration and Lp(a) in women in menopause, contrary to the results in group of women with regular menstruation. Again, that reiterates that Lp(a) acts as an independent factor of cardiovascular risk.

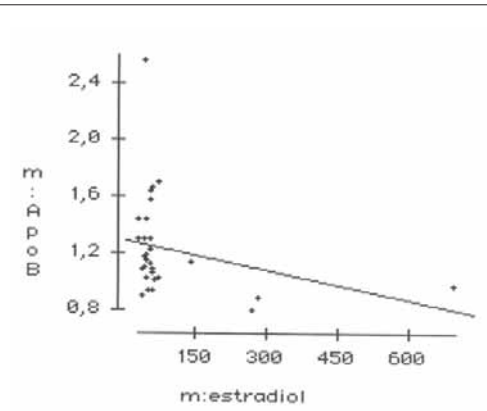

FIGURE 4. Correlation between apolipoprotein B and estradiol in women in menopause

Although it was published that application of estrogens therapy decreases Lp(a) concentration, the question remains whether the ovarian estrogens are the only factor that influence Lp(a) concentration or there are other factors that influence the cardiovascular risk (21). That will be the aim of some future studies.

Conclusion

Women in menopause have lower concentration of HDL ($p<0,05$) in relation to women with regular menstruation. The concentration of apolipoprotein B is higher in women in menopause ($p<0,05$). The concentration of estrogen shows negative correlation with VLDL and triglycerides concentration in women in menopause, while the correlation with HDL concentration is positive. Progesterone concentration shows no known correlation with the lipids and lipoproteines concentrations in either women in menopause or those with regular period.

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