

THE EFFECTS OF HORMONAL THERAPY IN MENOPAUSE

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Abstract. Through all the immediate and long-term consequences of estrogenic deprivation, menopause is an important public health issue with social, personal and economic impact. If immediate menopausal symptoms are sometimes noisy, the long-term, insidious consequences, especially cardiovascular and bone, are of major importance. In order to eliminate troublesome symptoms and prevent long-term consequences in order to provide a good quality of life for menopausal women, it is nowadays unanimously recognized that hormonal therapy is necessary in the context of adhering to recognized indications and contraindications, also rigorously following the effects of therapy.

INTRODUCTION

Menopause, by modifying the hormonal profile (mainly by lowering estrogen hormones), is a risk factor in the development of atherosclerosis. Endothelial dysfunction plays a key role both in the pre-lesional and lesional stages of atherosclerosis (Atsma, F., et al, 2006; Al-Azzawi, F. & Palacios, S., 2009).

Endothelial dysfunction induced by *dyslipidemia*, especially oxidized LDL, is the first step in the initiation and evolution of the atherogenic process (Kalantaridou, S.N., et al, 2006).

When reaching menopause, women are prone to fluctuations of estrogen that can lead to dyslipidemia (with increased triglycerides, total serum cholesterol, LDL cholesterol, and lower HDL cholesterol) (Crauciuc, E., et al, 2006; Acken, H.S. Jr, 2000). The decrease in estrogen in the menopause leads to a change in the lipid profile, with increases in triglycerides, total serum cholesterol, LDL cholesterol and lower HDL cholesterol (with an antiatherogenic protective role) (Bădoi, D., 2012).

Studies have already shown that in the natural and surgical menopause the atherosclerotic process is based on endothelial damage caused by altered lipid metabolism. Hormonal treatment, mainly by ingesting estrogen, positively influences lipid metabolism and thereby decreases the risk of cardiovascular disease (Atsma, F., 2006; Knowlton, A.A., 2012).

With all the immediate and long-term consequences of estrogenic deprivation, menopause is an important public health issue with social, personal and economic impact. If immediate menopausal symptoms are sometimes noisy, the long-term, insidious consequences, especially cardiovascular and bone, are of major importance.

In order to eliminate troublesome symptoms and prevent long-term consequences, in order to provide a good quality of life for women in menopause, it is nowadays unanimously recognized that hormonal therapy is necessary in the context of respecting some recognized indications and contraindications and in the rigorous following of the therapy effects.

One of the main objectives of the clinical trial was to evaluate the lipid and carbohydrate profile in natural menopause and the effects of hormonal therapy. The evolution of climacteric symptomatology under treatment was also observed.

MATERIAL AND METHOD

In order to conduct the clinical study, we used the extended database of menopausal patients belonging to the Third Clinic of Obstetrics-Gynecology from "Elena Doamna" Hospital Iași and "Medical Life" Obstetrics-Gynecology Practice Iași, a database that records the menopausal patients from all over Moldova for over 15 years. Every patient recorded in the database has a medical chart containing almost 30 indicators; from this database we can extract what we are interested in, namely phytoestrogens and their effects for a certain period; this is how the three lots, the study period, the inclusion and exclusion criteria, the statistical study and the results were established.

Study groups. We studied the patients in natural menopause in 2016, ie 83 patients with anamnestic amenorrhea for at least 1 year, divided into the following study groups:

Lot I - 37 patients with natural menopause treated with Actiwell (1 mg estradiol + 0.5 mg norethisterone acetate);

Lot II - 22 patients with natural menopause fed with natural phytoestrogens;

Lot III - 24 patients in untreated natural menopause.

The inclusion criteria were as follows:

- anamnestic amenorrhoea for at least 1 year;
- absence of hormonal treatment at least for 1 year.

The clinical and paraclinical evolution of the patients was followed. Each patient had a form filled with information about: age, residence, smoking, alcohol consumption, anthropometric data, heredo-collateral history, personal physiological and pathological priors, onset of menopause, previous hormonal treatments, clinical symptomatology, paraclinical assessment, type of treatment in menopause.

At the onset of the study the presence of climacteric symptoms was assessed and we performed the following:

- measuring waist, weight, blood pressure;
- complete clinical and genital examination;
- Babeş - Papanicolau cytological smear;
- ultrasound for measuring the thickness of the endometrium;
- evaluation of lipid metabolism parameters: total serum cholesterol, triglycerides, LDL cholesterol, HDL cholesterol;
- blood glucose, TGP, hemoglobin;
- EKG;
- mammography and osteodensitometry.

Biochemical determinations used serum obtained after blood collection in "activator clot" tubes and centrifugation at 4000 rpm for 10 minutes. An automated clinical chemistry analyzer, RX Imola model, with the use of calibrators and control serum, was used to determine the biochemical parameters.

Hormonal estrogen therapy

Estrogen administration is the main way to treat menopause (Bădoi, D., 2012).

Classification of estrogen types:

- *natural*:
 - estrone; estriol;
 - 17-β estradiol;
 - estradiol valerate;
 - piperazin estriol sulfate;
 - phytoestrogens;
 - conjugated equine estrogens.
- *of synthesis*:
 - ethinylestradiol;
 - mestranol;
 - estrogen esters;
 - non-steroidal synthesis estrogens.

Foods with natural phytoestrogens

Whole grains, hops, humus and soybeans, through proven health benefits, are being used increasingly in the human diet and can be given the name of nutritional supplement (Bădoi, D., 2012; Cardenau, H, 2010).

Also, phytoestrogenic products from raspberries and sage leaves were consumed.

Administration requires individualized dosing and is performed in the form of cures of at least one month, usually in combinations with other plants (depending on individual needs), under the strict indication and supervision of a specialist (Crauciuc, E., et al, 2006).

Retrospective study. The data were selected from the observation sheets and processed using the statistical functions of the SPSS 18.0.

In calculating the significant difference between two or more groups, based on the distribution of the value series, to the significance threshold of 95% for the quantitative variables we apply: the t-Student test– parametric test that compares recorded mean values in 2 groups with normal distributions; F test (ANOVA) used when three or more groups with normal distributions are compared; "Pearson" correlation coefficient (r) is the correlation of two variables in the same group (direct / indirect correlation).

RESULTS

Structure of groups by age. Analyzing the age of the patients on the three study groups using the ANOVA test, the following aspects show (tab. I):

- group I: women with natural menopause treated with Activelle, the age varied between 40 and 62 years, with a moderate variation in the value series (9.46%); the mean age of the group was 51.70;

- group II: women with natural menopause fed natural phytoestrogens, the age varied between 48 and 58 years old, with the smallest variance in the range of values (4.94%); the mean age of the group was 51.68;
- group III: women with natural menopause without treatment, the age varied between 45 and 56, with a reduced range of the value series (6%); the mean age of the group was 52.13.

Table I. Statistical indicators of the age (years) of the patients on study groups

Group	Mean	std Dev.	Std Err.	Min	Max	IC95%	variance %	Median
I	51.70	4.89	0.80	40	62	49-54	9.46	52
II	51.68	2.55	0.54	48	58	50-53	4.94	51
III	52.13	3.13	0.64	45	56	50-55	6.0	52

The distribution according to the place of origin has shown the following aspects:

- in the groups of treated menopausal patients, the proportion of patients from rural areas was between 4.5 and 8.1%;
- 29.2% of patients with untreated natural menopause originated from rural areas, significantly higher distribution compared to other groups.

Evaluation of lipid metabolism parameters under hormonal treatment

The clinical study aimed at evaluating the parameters of lipid metabolism and the effect of hormonal treatment.

Total serum cholesterol (mg/dL)

In the untreated natural menopause group, if at onset the mean cholesterol values were significantly lower compared to those recorded in the groups chosen for hormone treatment, at the end of the study the mean values were significantly higher, suggesting the beneficial effect of the treatment (tab. II).

During the monitoring, mean cholesterol values showed significant differences, showing the beneficial effect of treatment:

- in the group of patients with naturally occurring menopause treated with ActiVelle mean total cholesterol levels decreased significantly from mean values of 196.95 mg/dL to 146.49 mg/dL ($r = -0.99$);
- in the group of natural menopausal patients fed with natural phytoestrogens, there was a significant decrease in mean total cholesterol values from about 202 mg/dL to 149 mg/dL ($r = -0.51$);
- to note that in the untreated group of patients with untreated natural menopause the evolution of the mean total cholesterol had an increasing trend during the monitoring, ranging from 165.83 mg/dL to 189.17 mg/dL ($r = +0.78$).

Table II. Average total cholesterol (mg/dL) values per study lot/group

Lot	monitoring time (months)			
	V0	V6	V12	V24
I	196.95 ± 40.64	179.68 ± 45.75	160.54 ± 40.96	146.49 ± 38.75
II	201.68 ± 33.44	187.73 ± 44.50	167.73 ± 46.39	148.64 ± 41.67
III	165.83 ± 30.63	176.25 ± 23.37	183.33 ± 22.00	189.17 ± 21.85

Triglycerides (mg/dL)

The evolution of mean triglyceride values during monitoring has shown significant decreases in hormone-treated natural menopausal groups, highlighting the beneficial effect of treatment (tab. III):

- in the group of patients with natural menopause treated with Activelle (group I), mean triglyceride levels decreased significantly during monitoring, from mean values of 132.10 mg/dL to 104.59 mg/dL ($r = -0.56$);
- in the group of natural menopausal patients fed with natural phytoestrogens (group II), there was a significant decrease in mean triglyceride levels from approximately 116 mg/dL to 103.81 mg/dL ($r = -0.63$);
- it should be noted that in the group of untreated natural menopause patients (group III) the evolution of the mean triglyceride values had an increasing trend during the monitoring, ranging from 149.20 mg/dL to 167.50 mg/dL ($r = +0.77$).

Table III. Average triglyceride (mg/dL) values per studied group

Lot	monitoring time (months)			
	V0	V6	V12	V24
I	132.10 ± 55.86	124.58 ± 41.83	115.32 ± 34.93	104.59 ± 28.79
II	115.50 ± 42.75	116.45 ± 43.31	110.18 ± 40.11	103.81 ± 35.41
III	149.20 ± 18.86	156.25 ± 25.52	162.67 ± 29.70	167.50 ± 24.36

The fact that, regardless of the time of the study, the highest mean triglyceride values were observed in the untreated group, significantly higher than in the treated groups, underlines the importance of estrogens in the metabolism of triglycerides.

LDL cholesterol (mg/dL)

The mean LDL cholesterol values during the study showed significant decreases (tab. IV):

- in the group of Activelle-treated natural menopausal patients (group I) mean LDL cholesterol values decreased significantly from 121.86 mg/dL to 102.27 mg/dL ($r = -0.63$);
- in the group of natural menopausal patients fed with natural phytoestrogens (group II) there was a significant decrease in mean LDL cholesterol from 126.95 mg/dL to 95.91 mg/dL ($r = -0.89$);

- it should be noted that in the batch of untreated natural menopause patients (group III) the evolution of mean LDL cholesterol had an increasing trend, ranging from 91.67 mg/dL to 117.08 mg/dL ($r= +0.83$).

Table IV. Mean LDL cholesterol (mg/dL) values per studied group

Lot	monitoring time (months)			
	V0	V6	V12	V24
I	121.86 ± 33.24	122.32 ± 36.32	111.19 ± 34.19	102.27 ± 32.31
II	126.95 ± 30.83	115.73 ± 29.81	107.73 ± 26.37	95.91 ± 24.23
III	91.67 ± 25.14	102.92 ± 21.56	111.25 ± 22.32	117.08 ± 22.16

At the start of the study, in the untreated natural menopausal group, the mean LDL cholesterol levels were significantly lower compared to those of the groups chosen for hormone therapy or phytoestrogens.

At the end of the study, mean LDL cholesterol values were significantly higher in the untreated group.

These results show that, due to lack of estrogen in menopause, hypercholesterolemia is an atherogenic risk factor.

HDL cholesterol (mg/dL)

In hormone treatment groups, during the monitoring, mean HDL cholesterol values showed significant increases (tab. V):

- in the group of Activelle-treated natural menopausal patients (group I) mean values of HDL cholesterol significantly increased from 54.20 mg/dL to 71.41 mg/dL ($r = +0.96$);
- in the group of natural menopausal patients treated with natural phytoestrogens (group II) there was a significant increase in mean HDL cholesterol values from 57.36 mg/dL to 69.91 mg/dL ($r= +0.81$);
- it should be noted that in the group of untreated natural menopausal patients (group III) the evolution of mean HDL cholesterol had a decreasing trend during the monitoring, ranging from 44.17 mg/dL to 41.08 mg/dL ($r = -0.66$), which shows the lack of protective effect of estrogen in this context.

Table V. Mean values of HDL cholesterol (mg/dL) per studied group

Lot	monitoring time (months)			
	V0	V6	V12	V24
I	54.20 ± 17.60	58.95 ± 14.40	65.84 ± 11.93	71.41 ± 11.80
II	57.36 ± 19.66	63.45 ± 16.57	66.41 ± 12.17	69.91 ± 8.96
III	44.17 ± 6.02	46.04 ± 7.94	43.92 ± 7.95	41.08 ± 8.04

Other biochemical parameters

À jeun glycemia (mg/dL)

The glyceimic values determined on study groups show the following (tab. VI):

- the mean glycemia levels were initially significantly higher in group II (treated with phytoestrogens) (101.68 mg/dL) compared to the other groups;
- after 6 months of treatment, the mean values of glycemia were significantly more reduced for the group treated with Activelle (group I) (90.95 mg/dL);
- after 12 months of treatment, the mean values of glycemia were significantly increased for the group with natural menopause without treatment (group III) (101.33 mg/dL) when compared with the other groups;
- 2 years post-treatment the highest mean blood glucose levels are found in patients with natural menopause without treatment 103.08 mg/dL).

Table VI. Mean values of glycemia (mg/dL) on studied groups

Lot	monitoring time (months)			
	V0	V6	V12	V24
I	90.67 ± 19.54	90.95 ± 7.69	91.03 ± 5.44	90.08 ± 5.30
II	101.68 ± 10.75	94.51 ± 5.73	92.00 ± 6.13	91.18 ± 5.18
III	93.38 ± 4.48	96.71 ± 7.30	101.33 ± 10.98	103.08 ± 8.16

The evolution of the mean values of glycemia showed the following aspects:

- for the group of patients with natural menopause treated with Activelle, the mean values of glycemia decreased slightly during monitoring ($r = -0.17$);
- for the group of patients with natural menopause fed naturally with phytoestrogens there was a significant decrease in mean glycemia levels ($r = -0.64$);
- it is noted that in the group of menopausal patients without a hormone treatment, there was a significant increase in mean blood glucose levels after 2 years ($r = +0.76$).

TGP (UI/L)

The following must be noted about the studied groups, regardless of the moment of studying (tab. VII):

- the highest mean values of TGP can be found in the group without treatment (group III);
- for the groups following treatment, the highest mean values of TGP can be found in the patients treated with Activelle (group I).

Table VII. Mean values of TGP (UI/L) on studied groups

Lot	monitoring time (months)			
	V0	V6	V12	V24
I	23.90 ± 7.78	25.52 ± 9.21	25.70 ± 9.41	25.86 ± 8.55
II	23.77 ± 8.45	21.55 ± 1.84	21.14 ± 1.17	21.09 ± 1.19
III	27.71 ± 3.38	28.67 ± 3.21	28.79 ± 3.40	29.21 ± 3.45

During monitoring, the groups with natural menopause with hormonal treatment, showed the following evolution of the mean values of TGP:

- for group I of patients with natural menopause, treated with Activelle, the mean values of TGP increased significantly, from 23.90 UI/L to 25.86 UI/L ($r= +0.75$);
- for group II of patients with natural menopause treated with, the mean values of TGP decreased from 23.77 UI/L to 21.09 UI/L ($r= -0.16$);
- the evolution of mean TGP values had an increasing trend during the monitoring, ranging from 27.71 UI/L to 29.21 UI/L ($r= +0.73$).

Hemoglobin (g/dL)

The following aspects have been found after studying the groups (tab. VIII):

- at the start of the study, in the batch treated with synthetic or natural phytoestrogens the mean hemoglobin values were significantly lower than the untreated group;
- after 12 months of treatment, mean hemoglobin values became homogeneous on the study groups (11.14-11.31 g/dL), which is maintained at 2 years post-treatment (11.09-11.26 g/dl)

Table VIII. Mean hemoglobin (g/dL) values on study groups

Lot	monitoring time (months)			
	V0	V6	V12	V24
I	11.70 ± 0.75	11.30 ± 0.77	11.26 ± 0.69	11.26 ± 0.65
II	11.80 ± 1.09	11.40 ± 0.58	11.18 ± 0.50	11.09 ± 0.53
III	12.00 ± 0.26	11.70 ± 0.46	11.31 ± 0.46	11.21 ± 0.41

The evolution of the mean values of hemoglobin revealed the following aspects:

- in the group of patients with natural menopause treated with Activelle, mean hemoglobin values decreased significantly during follow-up ($r= -0.69$);
- also the group of natural menopausal patients treated with natural phytoestrogens showed a significant decrease in the mean values of hemoglobin ($r= -0.67$);
- it should be noted, however, that also in the group of hormonal untreated menopausal patients, there is a significant decrease in the mean values of hemoglobin after 2 years ($r= -0.66$).

DISCUSSIONS

Cholesterol is an organic alcohol, sterol that is identified in the cell membrane and body tissues and transported in the blood. It is concentrated in the marrow, brain and plaque of the atheroma, leading to atherosclerosis.

Triglycerides are an essential component of the lipid profile, included on the list of risk factors for the metabolic syndrome by most current guidelines. Hypertriglyceridemia is associated with endothelial dysfunction and increased risk of cardiovascular disease, particularly associated with lowering HDL cholesterol and elevating LDL cholesterol.

HDL cholesterol plays an important role in the metabolism of cholesterol, participating in its transport from extrahepatic tissues to the liver for catabolism and excretion (Hayward, C.S., et al., 2001). Together with LDL, it helps maintaining cellular cholesterol levels (Farhat, M.Y., et al., 1996; Jairath N., 2001).

High LDL cholesterol contributes to favoring the development of endothelial dysfunction, with a role in the pre-lesional stage of atherosclerosis (Carl, B. & Laven A., 2007).

The most important studies on hormonal therapy in menopause are (ACOG, 2004):

- the observational study Nurses Health Study (NHS) (70.000 de femei women analysed), in which treated women were cardiac asymptomatic and showed a lower incidence of cardiovascular disease and overall mortality in women under hormone therapy compared to those without hormone therapy. It is important to know that most women in this study started TH in perimenopause and had no cardiovascular disease detected at the beginning of the study.

- HERS (The Heart and Estrogen/Progestin Replacement Study) was the first published trial of secondary prevention in a group of 2763 women with known cardiovascular disease, monitored right from the time of appearance. For an average period of time of 4.1 years there was no significant difference between those taking hormone therapy and placebo. There was a possible improvement on the longer term, but the study did not last for more than 7 years.

- the largest randomized study is WHI (Women's Health Initiative), which included 16,608 women with an intact uterus who used only conjugated equine estrogens and medroxyprogesterone acetate as hormonal therapy versus placebo, over a period of time of over 5.6 years. The study was stopped earlier due to an increase in the number of cases of breast cancer and a lack of cardiovascular benefits in women with hormone therapy. An additional group of 10,739 women hysterectomized women with the same therapy, conjugated equine estrogens + medroxyprogesterone acetate versus placebo, was analyzed, showing that there are no cardiovascular benefits for these women.

WISDOM study that was taking place in England in that period and that used the same therapy was interrupted after the WHI results were published.

WHI study is considered a very important one because it changed the perception about TH, but this study had many limitations: the mean age of the women of 63 years old, more than 10 years later than the age when menopause begins, significant differences among the women taking part in the study, only one type of treatment, and one administration manner.

Thus, at the beginning of the 21st century, prescribing and using TH is still controversial, randomized studies (WHI, HERS) showing that estrogen may be beneficial for preventing early atherosclerotic lesions, but are ineffective and even harmful if the disease is installed.

Based on the results of the randomized trials, the observational studies (PEPI, NHS) and their comparison showed that the relative risk of coronary artery disease increases with years of menopause and that in the hormone therapy-coronary / cardiovascular disease equation, the beginning of hormonal therapy means everything: hormone therapy should begin before the fibrous capsule formation of the atheromatous plaque, which was found to be between 45 and 55 years of age; women starting hormonal therapy around menopause have a significant reduction in the risk of coronary artery disease (RR= 0.66 for single estrogens and 0.72 for estrogens+ progestative).

Hormonal therapy is beneficial in postmenopausal women, taking into account the results validated over time in observational studies and is being discussed as primary prevention in cases without coronary artery disease at the age of 50 years under 60 years of age during the 10 years from the onset of menopause. For elderly women, therapy is individualized, the benefit being relative to the recommended age and dose.

There is an ongoing study called KEEPS (The Kronos Early Estrogen Prevention Study) which uses 0.45 mg conjugated equine estrogens or 50 µg transdermal estradiol in women at most 36 months after the last menstrual period and will show the effects on cardiovascular disease. Today there is scientific evidence that estrogen has effects on almost all systems and apparatuses of the female body (Waren, M.P., 2004). Because of this, various symptoms have been associated with decreased

estrogen, occurring in menopause. It is important to emphasize that not all symptoms occur to any woman, but there are some who encounter the highest frequency, such as vaso-motor and uro-genital symptoms (Peterson HB, 2004).

Even if there is a category of symptoms that are rarely encountered, they can affect the quality of menopausal woman's life (Davey, D.A., 2012).

In this study, patients treated with synthetic estrogens showed an increased frequency of hot flashes, migraines, asthenia, insomnia, reduced libido and vaginal dryness. Hormone therapy removes all these symptoms and besides the immediate improvement in the quality of life, it exerts a long-term protective role on the risks of osteoporotic fractures, cardiovascular disease and the risk of Alzheimer's disease. It is considered today that, with the exception of absolute contraindications and taking into account the necessary precautions in a number of general illnesses, 80% of women could benefit from hormone therapy. For control of menopausal symptoms, hormonal therapy administered for up to 5 years is appropriate, with prolongation for a further 5 years, if the symptom reoccurs at interruption. Hot flushes, palpitations, insomnia and psychological problems improve after estrogen therapy for 3 months in 90% of cases (Hudiță, D., et al, 2003; Christenson, E.S., et al., 2012).

The major beneficial effects of hormonal therapy in menopause are represented by (Maki, P.M., et al, 2004; Gruber, C.J., 2002):

- *resolving menstrual irregularities and perimenopausal bleeding*

Continuous-combined therapy (only after histological investigation of the cause of bleeding) with sequential estro-progestative preparations solves the problem, effectively controlling the proliferation of the endometrium and restoring the regularity of menstrual cycles. Continuous-combined TH can be recommended after a year of amenorrhea; the continuous-combined treatment is safe for the endometrium when it is proposed for the long term (Bodinet, C. & Freudenstein, J., 2004).

- *the immediate, common symptoms of menopause*

There are publications that signal the results of experimental and clinical studies on the efficacy of phytoestrogens in the postmenopausal woman (Clarkson, T.B. et al, 2001).

The evaluation of the effectiveness of the therapy is done clinically, asking the patient about his / her general condition, the persistent symptomatology or the ones appeared under therapy.

Clinical evaluation shows evidence of underdosage or overdose, which should be noted in the patient's follow-up sheet, estrogen doses then being adjusted according to the type of patient-indicated signs (tab. IX).

Table IX. Criteria for clinical assessment of estrogen tolerance
(according to Pelinescu-Onciul D, 2001)

Signs of underdosing	Signs of overdosing
- persistence or recurrence of heat waves	- mastodynia
- vaginal dryness	- weight gain
- asthenia	- abdominal bloating
- headache	- "heavy" lower limbs
- feeling cold	- nervousness, irritability, insomnia
- lack of tone, depression	
- joint pain	
- urinary disorders	

CONCLUSIONS

Based on the cases studied, the epidemiological characteristics revealed a slightly higher mean age of the patients treated with synthetic or natural phytoestrogens, coming predominantly from cities or towns, married and with an average educational status.

The patients started therapy in less than 5 years after the onset of menopause, thus respecting the "window of opportunity".

The moment they started treatment was around the age of 50.

Patients fed with natural phytoestrogen had a normal weight, while patients treated with synthetic estrogens were overweight.

Treatment with estrogen, synthetic or natural, has resulted in an improvement in the onset symptoms: hot flushes, migraines, asthenia, reduced libido, insomnia and vaginal dryness.

The climacteric symptomatology resolved under treatment.

In patients with natural menopause, hypercholesterolemia is an atherogenic risk factor due to estrogen deficiency.

The highest mean triglyceride values are noted in the untreated group, which shows the importance of estrogens in triglyceride metabolism.

Patients with natural menopause, whether or not treated with estrogen, recorded significant decreases in mean hemoglobin level.

Under hormonal treatment, changes in lipid profile have been achieved with a cardiovascular protective role, by the antiatherogenic effect of lowering total serum cholesterol, triglycerides and LDL cholesterol, and especially by the increase in HDL cholesterol.

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