საქართველოს მეცნიერებათა ეროვნული აკადემიის მოამბე, ტ. 7, №1, 2013
BULLETIN OF THE GEORGIAN NATIONAL ACADEMY OF SCIENCES, vol. 7, no. 1, 2013

Medical Sciences

Metabolism Peculiarities in Postmenopause Period after Hypolipidemic Therapy

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(Presented by Academy Member Fridon Todua)

ABSTRACT. The aim of our work was to show some metabolism peculiarities in menopause under 6 month hypolipidemic treatment. 156 women(average age 58.4±5.3) in postmenopause were included in our tests. Their total cholesterol exceeded 6.2 mmol/l . The patients were divided into 2 groups. Group I consisted of 80 women with subclinical hypothyrosis where TSH was more than 4.0 mkIU/ml), group II consisted of 76 women with clinical hypothyrosis, TSH was less than 4.0 mkIU/ml. Both groups were divided into subgroups. Hypolipidemic treatment with 20 mg Atorvastatin was carried out in the I and III subgroup women, while in the II and IV subgroups no specific hypolipidemic treatment was done. The patients were given the general diet recommendations. Besides, all the patients were treated with L-Thyroxine(the average dose 12.5-100.0 mg) for hypothyrosis.

Research has shown that the dynamics of blood lipid spectrum changes at different stages of hypothyrosis in postmenopause women points at the influence of thyroid hormone deficiency. In thyroid dysfunction, atherogenic processes in carotid arteries, namely, intima media- thickness(IMT) are proved to be interparallel processes. 6-month hypolipidemic therapy with Atorvastatin in hypothyrosis appeared to be much more effective than diet. Taking into consideration the findings, we may conclude that hypothyrosis in postmenopause accelerates atherogenic processes in carotid arteries, hypercholesterolemia, increases atherogenic lipoproteins and apolipoproteins along with the decrease of antiatherogenic lipoprotein and corresponding apolipoproteins. Therefore, this may be considered as the factor that helps to develop cardiovascular pathologies. Carotid arteries IMT may be a particular risk factor for developing cardiovascular complications in women with postmenopause. *© 2013 Bull. Georg. Natl. Acad. Sci.*

Key words: *lipids, hypothyrosis, postmenopause, hypolipidemic therapy.*

An increased interest should be mentioned lately in the studies of hormonal problems in women of postmenopause period. The menopause syndrome is considered to be a polysymptomic state which is mostly characterized by the glucose tolerance disorders, 2 type diabetes mellitus, hypothyrosis, cardiovascular diseases, abdominal obesity, dyslipidemia, etc.

In this respect, particular attention is given to thyroid gland function disorders specifically hypothyrosis which is frequently followed by dislipidemia[1-6]. It is well known that thyroid hor-

Table 1. Lipid spectrum parameters of the patients studied.

Groups	Subgroups	Tch Mmmol/l	HDL Mmmol/l	LDL Mmmol/l	TG Mmmol/l	ApoA1 Mmg/dl	ApoB Mmg/dl
Group I (n=80) TSH > 4.0 mkmE/ml Subclinical hypothyrosis	Subgroup I Before treatment with Atorvastatin (n=50)	6.9 ± 0.7	0.99 ± 0.11	5.0±1.0	1.8±0.29	133.5±6.2	200.0± 5.2
	Subgroup I After treatment with Atorvastatin	4.9 ± 0.2	1.2 ± 0.2	3.0 ± 0.2	1.64 ± 0.3	169.8±7.2	175.1±4.1
	Subgroup II Before treatment (n=30)	6.8 ±0.6	0.97 ±0.10	4.9 ±0.9	1.85 ±0.4	135.8±6.2	195.7 ±4.1
	Subgroup II After treatment	5.9 ±0.4	1.0 ±0.2	4.1 ±0.5	1.77 ±0.36	140.5±5.4	188.3±3.7
Group II (n=76) TSH < 4.0 mkmE/ml Clinical hypothyrosis	Subgroup III Before treatment with Atorvastatin (n=36)	6.6 ±0.5	1.0 ±0.3	4.2 ±0.4	1.77 ±0.3	143.1±5.4	183.2±5.1
	Subgroup III After treatment with Atorvastatin	4.3 ± 0.4	1.3 ±0.2	2.8 ±0.4	1.68 ±0.4	165.4±5.9	167.2±5.2
	Subgroup IV Before general dietary recommendations (n=40)	6.5 ±0.6	1.0 ± 0.2	4.0 ± 0.3	1.70 ± 0.3	142.2±5.3	181.9±6.0
	Subgroup IV After general dietary recommendations	6.0 ± 0.5	1.0 ±0.1	3.6 ±0.5	1.60 ±0.4	150.2±6.0	142.2±5.3

mones influence all component aspects of the lipid metabolism – synthesis, mobilization and catabolism. It should be noted that the patients with hypothyrosis in postmenopause are considered as patients with high risk cardiovascular diseases. Nowadays it is stated that, as compared with the persons with the thyroid gland normal function [6-8], in hypothyrosis the parameters of Total cholesterol (Tchol), the low density lipoprotein cholesterol (LDL) and triglycerides (Tg) are higher but the high density lipoprotein cholesterol (HDL) is lower.

Hence, the aim of the work presented was to reveal some peculiarities of metabolism in postmenopause with background of long-term(6 months) hypolipidemic treatment.

Materials and methods. 156 women in menopause were investigated (average age 58.4±5.3) with Tchol exceeding 6.2 mmol/l.

The patients were divided into 2 groups. Group I comprised (n=80) patients with subclinical hypothyrosis, thyroidstimulating hormone (TSH) being more than 4.0 mkmE/l. Group II consisted of (n=76) patients with a clinical form of hypothyrosis, TSH < 4 mkmE/l. Both groups were divided into subgroups. In subgroups I and III hypolipidemic treatment was carried out with 20 mg Atorvastatin per day during 6 months. In subgroups II and IV no specific hypolipidemic treatment was done – the patients were given general dietary recommendations. All the patients under investigation were prescribed L-Thyroxin (average dose 12.5- 100 mg) for hypothyrosis treatment. Our investigation excluded patients with diabetes mellitus, symptomatic arterial hypertension, acute and subacute ischemic heart disease, cardiac insufficiency of III and IV degrees(NYHA), hepatic and renal failures, oncologic diseases.

All the patients mentioned underwent the following biochemical investigations: Tchol, HDL, LDL, TG, apolipoprotein A1(apoA1), apolipoprotein B (apo B), TSH, FT_3 and FT_4. The blood lipid spectrum parameters were defined by biochemical analyser COBAS INTEGRA 400 PLUS(ROCHE DIAGNOSTICS). TSH, FT_3 and FT_4 by electrochemiluminescentic analyzer COBAS E 411(ROCHE DIAGNOSTICS).

Carotid arteries duplex scanning of the patients under investigation was carried out using TOSHBa

Table 2. Carotid arteries intima-media thickness changes in the patients studied.

Groups	Subgroups	IMT
Group I (n=80) TSH > 4.0 mkmE/ml Subclinical hypothyrosis	Subgroup I Before treatment with Atorvastatin (n=50)	1.2 ± 007
	Subgroup I After treatment with Atorvastatin	1.0± 0.06
	Subgroup II Before treatment (n=30)	1.18 ±0.06
	Subgroup II After treatment	1.15 ±0.04
Group II (n=76) TSH < 4.0 mkmE/ml Clinical hypothyrosis	Subgroup III Before treatment with Atorvastatin (n=36)	1.16 ±0.05
	Subgroup III After treatment with Atorvastatin	0.9 ± 0.05
	Subgroup IV Before general dietary recommendations (n=40)	1.15 ±0.04
	Subgroup IV After general dietary recommendations	1.09 ± 0.03

APLIO XG 5-10 mgh transducer. The parameters of the artery lumen, the wall thickness, atherosclerotic damage and the doppler spectrum were defined by the colour and energetic doppler. Carotid arteries intima-media thickness (IMT) was defined from bifurcation 1.0-15cm proximally.

The statistical anylisis (M,S,D) of the given results was done using the program STATISTIKA (version 6). Difference $p<0.05$ was considered as statistically valid.

Results and discussion. The analysis of the findings has shown that the parameters of the thyroid gland function FT_3 and FT_4 in both groups of patients did not go beyond the reference range and remained within the norm (consequently 2.5- 5.8 pmol/l and 12.0 -22.0 pmol/l.

In subgroup I patients with hypothyrosis subclinical form, when compared with the subgroup II patients who showed hypothyrosis clinical form, Tchol, LDL and apoB were higher($p<0.05$), respectively 6.9±0.7 and 6.6±0.5 mmol/l, 5.0±1.0 and 4.2±0.4mmol/l, 200.0±5.2mg/dl and 183.2±5.1 mg/dl. In these subgroups the difference between HDL and Tg parameters (0.99±0.11 and 1.0±0.2 mmol/l, 1.8±0.29 and 1.77±0.3 mmol/l was invalid ($p>0.05$). As to apoA1 and IMT the difference between these parameters in the subgroups was insignificant as well.

In subgroups II and IV the dynamics of the parameter changes is as follows. Tchol, LDL and apoB as well as IMT appeared increased. Particularly, Tchol was 6.8±0.6 and 6.5±0.6 mmol/l, but LDL – 4.9±0.9 and 4.0±0.3 mmol/l, difference was statistically invalid ($p>0.05$). ApoB (195.7±4.1 and 181.9±6.0 mg/dl) and Tg (1.85±0.4 and 1.7±0.3 mmol/l) increased as well. ApoA1 in this subgroup was relatively (135.8±6.2 mg/dl and 142.2±5.3 mg/dl). HDL 0.97±0.10 and 1 .0±0.2 mmol/l become equal. IMT increased and reached 1.18±0.06 and 1.15±0.04 mm (Table 2).

With Atorvastatin 6 month treatment we have got statistically valid decrease of Tchol, LDL and apoB in subgroups I and III decreased, while HDL and apoA1 significantly increased. As to Tg and IMT, with hypolipidemic treatment these parameters were observed to decrease (1.64±0.3 and 1.77±0.3 mmol/l;

1.0±0.06 and 0.9±0.05 mm) (Table 1,2).

In subgroups II and IV where hyperlipidemia was treated with common diet only for 6 months, there was observed an insignificant decrease of Tchol, LDL, apoB, Tg and carotid arteries IMT parameters. But HDL and apoA1 increased in significantly. The mentioned parameter changes appeared statistically invalid ($p>0.05$). Thus, in this case we can speak only about the tendency of dyslipidemia and intima-media thickness correlation.

Our research has shown that the dynamics of the blood lipid spectrum parameter changes at different stages of hypothyrosis in postmenopause women investigated by us points at thyroid hormone deficiency.

In thyroid gland dysfunction, atherogenic processes in carotid arteries, namely, intima media thickening, are proved to be interparallel. This point agrees with some auhtors' opinions that in the patients with hypothyrosis under L-Thyroxin treatment IMT appeared to decrease significantly [9-11].

Thus, taking into account the findings of our research, it may be concluded that hypothyrosis developed in menopause assists in the extension of atherogenic processes in carotid arteries intima media layers, hypercholesterolemia, hypertriglyceridemia. It favours as well the increase of atherogenic lipoproteins and apolipoproteins.

Therefore, this fact can be considered as one promoting vascular pathology development. 6-month hypolipidemic therapy with Atorvastatin in postmenopause women with hypothyrosis appeared much more effective than diet. Besides, carotid arteries intima-media thickness may be considered as a particular risk factor of cardiovascular complication development.

სამედიცინო მეცნიერებანი

მეტაბოლიზმის თავისებურებანი პოსტმენოპაუზის პერიოდში და ჩატარებული ჰიპოლიპიდემიური თერაპიის ფონზე

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(წარმოდგენილია აკადემიკოს ფ. თოდუას მიერ)

წარმოდგენილი კვლევის მიზანს შეადგენდა პოსტმენოპაუზის პერიოდში მყოფი ჰიპოთირეოზის მქონე ქალებში მეტაბოლიზმის რიგი თავისებურებების გამოვლენა და ჩატარებული ჰიპოლიპიდემიური მკურნალობის ეფექტურობის შეფასება. გამოკვლევაში ჩართული იქნა პოსტმენოპაუზის პერიოდში მყოფი 156 ქალი (საშუალო ასაკი 58.4 ±5.3), რომელთა საერთო ქოლესტეროლი

აღემატებოდა 6.2 მმოლ/ლ. პაციენტები დაყოფილი იქნა 2 ჯგუფად. I ჯგუფი (n=80) შეადგინა სუბკლინიკური ჰიპოთირეოზის მქონე პაციენტებმა, რომელთა თიროიდმასტიმულირებელი ჰორმონი(TSH) აღემატებოდა 4.0 მკმერთ/ლ, ხოლო II ჯგუფი (n=76) კი ჰიპოთირეოზის კლინიკური ფორმის მქონე პაციენტებმა, რომელთა TSH < 4 მკმერთ/ლ. ორივე ჯგუფი დაყოფილი იქნა ქვეჯგუფებად. I და III ქვეჯგუფებში 6 თვის განმავლობაში ჰიპოლიპიდემიური მკურნალობა ტარდებოდა 20 მგ ატორვასტატინით, ხოლო II და IV ქვეჯგუფებში სპეციფიკური ჰიპოლიპიდემიური მკურნალობა არ ჩატარებულა — პაციენტებს ეძლეოდა მხოლოდ ზოგადი დიეტური რეკომენდაციები. ამავე დროს ყველა გამოკვლეულ პაციენტს ჰიპოთირეოზის მკურნალობის მიზნით დანიშნული ჰქონდა თიროქსინი (საშუალო დოზა 12,5 - 100 მგ). ჩატარებულმა გამოკვლევებმა გვიჩვენა, რომ პოსტმენოპაუზის მქონე პაციენტებში, ჰიპოთირეოზის სხვადასხვა სტადიაზე სისხლის ლიპიდური სპექტრის ცვლილების დინამიკა თირეოიდული ჰორმონების დეფიციტის ზეგავლენაზე მიუთითებს. თავის მხრივ ფარისებრი ჯირკვლის დისფუნქციის დროს საძილე არტერიებში მიმდინარე ათეროგენული პროცესები, კერძოდ, იმშ გასქელება, ურთიერთპარალელური პროცესებია. ჰიპოთირეოზის დროს ატორვასტატინის მეშვეობით ჩატარებული 6 თვიანი ჰიპოლიპიდემიური თერაპია, გაცილებით ეფექტური აღმოჩნდა დიეტასთან შედარებით. მიღებული შედეგების გათვალისწინებით, შეიძლება დავასკვნათ, რომ პოსტმენოპაუზის პერიოდში განვითარებული ჰიპოთირეოზი აღრმავებს საძილე არტერიების იმშ მიმდინარე ათეროგენულ პროცესებს, ჰიპერჰომოცისტეინემიას, ჰიპერტრიგლიცერიდემიას, ათეროგენული ლიპოპროტეინებისა და აპოლიპო-პროტეინების რაოდენობის მომატებას, ანტიათეროგენული ლიპოპროტეინებისა და შესაბამისი აპოლიპო-პროტეინების შემცირების პარალელურად. ამიტომ ეს ფაქტი გულსისხლძარღვთა პათოლოგიის განვითარების ხელშემწყობ ფაქტორად შეიძლება მივიჩნიოთ. გარდა ამისა პოსტმენოპაუზის პერიოდში საძილე არტერიების იმშ-ის გასქელება, შეიძლება მოვაკუთვნოდ კარდიოვასკულური გართულების ჩამოყალიბების განსაკუთრებული რისკის ჯგუფს.

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Received December, 2012