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Efficacy of Multifactorial Treatment of Dyslipidemia, Type 2 Diabetes Mellitus and Arterial Hypertension in Prevention of Expected Complications of Type 2 Diabetes and Endothelial Dysfunction in Elderly Patients

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ABSTRACT. The aim of the investigation was to study simultaneous treatment effectiveness of dyslipidemia, diabetes mellitus type II and arterial hypertension in elderly patients with CHD.

We studied 82 patients (mean age from 65-91, male/female 54/28) with dyslipoproteinemia, diabetes mellitus type 2 and arterial hypertension II (JNC VII), mean indices of T-C, HDL-C, LDL-C and TG were: 275.28±29.1 mg/dl, 30.09±3.1mg/dl, 190.25±21.8mg/dl and 298.1±19.05mg/dl respectively, glycated hemoglobin varied from 6.5% to 7.0% and the levels of creatinine varied from 120 to 150 μmol/l. Patients were randomly assigned and divided into two groups: The first group patients received hypolipidemic drugs (atorvastatin 20mg), hypotensive drugs (ACE inhibitors, Ca-antagonists, diuretics) and metmorphine, diabeton during 8 weeks. And the second group patients received only hypotensive drugs and antidiabetic drugs.

In the first group target levels of lipid profile, glucose concentration and arterial pressure were reached in 64%, 68% and 71% respectively. As for the second group, lipid profile did not change in 86%, and target levels of arterial pressure and glucose concentrations were reached in 51% and 54%, respectively.

Therefore, every patient with type 2 diabetes, must be treated with the above mentioned scheme in the early period of the disease, in order to reach target levels of lipid profile and our treatment will be furthered not only against dyslipidemia, but against the risk factors of type 2 diabetes and arterial hypertension, because these diseases create a vicious circle and aggravate each other and simultaneous treatment of the above-mentioned pathologies facilitates their management and provides better prognosis. Thus, our effort must be directed toward achievement of appropriate target levels, which may be reached after composite treatment. Complex treatment should be regarded as a guaranty, for the target levels may be reached via very low doses of medicines which predicts the safety of long-term treatment, improvement of life quality and stabilization of already reached results. © *2010 Bull. Georg. Natl. Acad. Sci.*

Key words: *dyslipidemia, diabetes mellitus, vascular dysfunction.*

Morbidity and mortality in diabetes mellitus are caused mainly by its vascular complications: micro- and macroangiopathy. Diabetic retinopathy and nephropathy are the hallmarks of microangiopathy, with blindness and renal failure as their ultimate consequences. Microangiopathy of the vasa nervorum is important in the pathogenesis of diabetic neuropathy. Macroangiopathy in diabetes consists mainly of an accelerated form of atherosclerosis. This affects all clinically important sites (i.e., the coronary, the carotid and the peripheral arteries), thus increasing the risk of myocardial infarction, stroke, intermittent claudication and ischaemic gangrene. Both

in insulin-dependent (IDDM) and in non-insulin-dependent diabetes (NIDDM), the presence of nephropathy, even in its early stages (so-called 'microalbuminuria'), identifies a group of patients at very high risk of developing severe complications (i.e., proliferative retinopathy, renal insufficiency, and cardiovascular disease) [1,2]. On the other hand, about 50% of IDDM patients never develop diabetic nephropathy—i.e., they appear 'protected' [2]. In other words, the risk of vascular disease is not distributed equally among diabetic patients; subgroups exist with a relatively normal versus a very high risk of cardiovascular disease.

Adequate management of arterial hypertension in elderly patients, carried out according to the recommendations of the European Society of Cardiology (2007) significantly reduces the risk of cardio-vascular diseases (CVD) and their complications, mainly CVD mortality in these patients. This population belongs to a high risk group for development of CVD and their complications. Heart failure is registered in 15% of these patients while it is observed only in 3% general population. In patients over the age of 80, arterial hypertension is found in about 80% of cases [3]; though the management of arterial hypertension in these patients is not a main problem. Elevated blood pressure is associated with heart failure, blood vessel rigidity and endothelial dysfunctions that are aggravated by dyslipidemia and diabetes mellitus. They are the main risk factors that affect life expectancy. It should be mentioned here that recommendations suggested by international and national societies do not describe precisely which drugs and their combinations should be used in the elderly to prevent and manage the above mentioned pathologies and their complications.

In relation to these problems, special attention should be paid to a double-blind, randomized, placebo-controlled trial "CORONA" that showed that the use of statins in patients with heart failure, independent of their age, does not significantly affect the early or late prognoses of the condition [3]. Though results of the trial provide evidence-based data that administration of statins is effective and safe in elderly patients with CAD. Besides atherosclerotic changes in blood vessels of the heart, neck and head, around 25% of elderly patients have identical changes of various degrees in arteries of lower extremities and abdominal aorta. In patients with type 2 diabetes mellitus microalbuminuria is observed in 1/3 of cases 5-7 years post diagnosis [1], and 75% of patients have retinopathy when diabetes duration is 10 years [2-5]. The above mentioned local changes in blood vessel could be assumed as microangiopathy. Besides, it is stated that adipose tissue located in the lower part of a man's body indicates directly to decreased insulin reactivity [6, 7]. It is known that three main risk factors for the development of metabolic syndrome are impaired glucose tolerance, reduced HDL-cholesterol levels and arterial hypertension. It is also known that the use of thyazolidinedions, ACE-inhibitors and ARB reduce the rise of development of type 2 diabetes mellitus and specific angiopathies almost by 50% [3, 8, 9).

Microangiopathy of blood vessels feeding nervous cells and tissue plays an important role in the pathogenesis of diabetic neuropathies. Diabetic macroangiopathy is a clinical representation of aggressive atherosclerosis that damages coronary vessels, carotids and peripheral arteries and elevates the risk of heart attack, stroke, intermittent claudication and ischemic gangrene [8, 9]. The authors present information that 4.4% of patients who died of CVD had type 2 diabetes mellitus. Literary data show that diabetes mellitus is a causative factor for development of CVD, mainly ischemic cardiomyopathy, in 27% of cases and of chronic heart failure – in 50% of cases. Data published in literature indicate that diabetes mellitus is revealed in 10% of adult population (determination of glutamatedecarboxilase antibodies level in blood).

The authors came to a conclusion that diabetes mellitus (its both types) aggravates the clinical course of CVD, significantly reduces life expectancy and quality of life and comprises one of the triggering mechanisms of the aethiopathogenesis of the vicious circle of the pathogenesis [10,11].

The aim of our study was to assess the efficiency of the multifactorial treatment of dyslipidemia, arterial hypertension and diabetes mellitus in patients with coronary heart disease (CHD).

The inserted criteria were: no heart attack in anamnesis during the past 3 years; blood creatinine levels ≤ 150 μmole/l; HDAC< 7; arterial hypertension II (5NC VII) and dyslipidemia.

In total, 82 patients were enrolled in the study (m/f; 54/28), age range 65-91 years. Lipid profile indices HBA1c and creatinine levels are given in Table 1.

The patients were randomly allocated to 2 groups (Gr). The Gr.1 patients were treated with hypolipidemic, antihypertensive and glucose lowering drugs; while Gr.2 patients were receiving only antihypertensive and glucose lowering preparations. Daily calorie intake in both groups was almost identical. Observation period comprised 8 weeks; no cases of discharge due to intolerance to any drug or side effects were registered.

Table 1

Lipid profile indices HBA

T-Chol	275.28±29.1
LDL-Chol	30.09±3.1
HDL-Chol	190.25±21.8
TG	298.1±19.05
I.A.	9.1±0.79
HBA1c	From 6.5% to7%
Creatinine	120-150 μmol/l

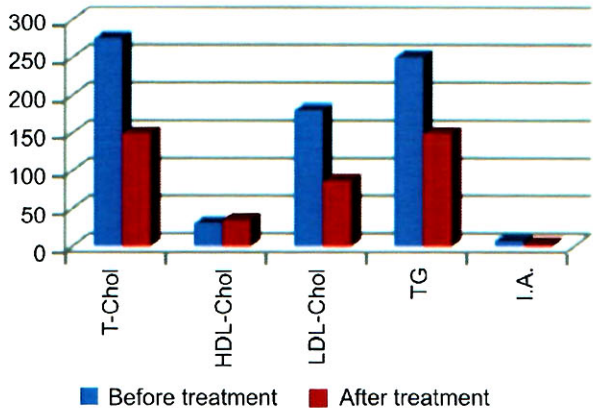

Fig. 1. Dynamic of lipid profile (mg/dl) in Gr.I

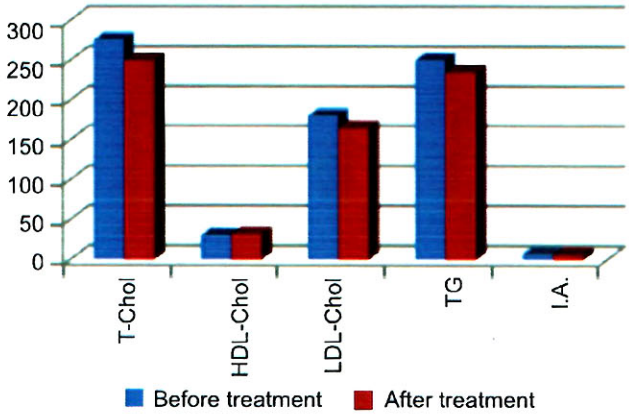

Fig. 2. Dynamic of lipid profile (mg/dl) in Gr.II

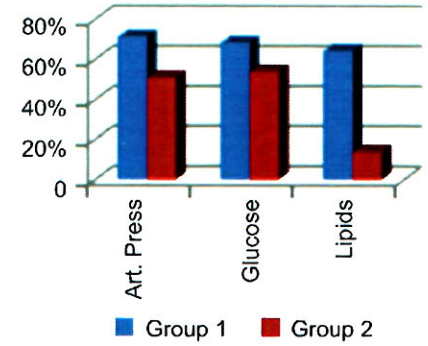

Fig. 3. Gr.1 versus Gr.2 according to the achievement of target levels

Figs. 1 and 2 show dynamic changes in the parameters given above pre and 8 weeks post treatment initiation.

The figures show that in Gr.1 target levels of lipid profile were achieved in 64% of patients; of peripheral blood glucose – in 68% of cases, and arterial blood pressure – in 71% of patients. While in Gr.2 in 86% of cases indices of the lipid profile did not change and target levels of arterial blood pressure and blood glucose were achieved in 51% and 54%, respectively.

Based on the results achieved it may be recommended that all patients with dyslipidemia, diabetes mellitus, arterial hypertension and CHD in anamnesis, should be treated not only based on the "priority" clinical symptoms, that were revealed, as it does not permit to achieve desirable result. All these pathologies comprise parts of a vicious circle that aggravates pathologic processes taking place in the organism. Our intervention should be aimed at achieving target levels of all parameters; this could be done only if multifactorial approach is used. In this case target levels could be achieved with lower doses of drugs administered; this may increase drug safety and permit to use agents for a longer time. This, in turn, will improve the quality of life of patients and provide more stable results.

სამედიცინო მეცნიერებანი

შაქრიანი დიაბეტი ტიპი 2-ის, დისლიპოპროტეინემიისა და ჰიპერტენზიის ერთდროული მკურნალობის ეფექტურობა ხანდაზმულ პაციენტებში შაქრიანი დიაბეტის მოსალოდნელ გართულებათა და ენდოთელური დისფუნქციის პრევენციის თვალსაზრისით

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ჩვენი კვლევის მიზანს შეადგენდა შეგვეფასებინა დისლიპიდემიის, არტერიული წნევისა და შაქრიანი დიაბეტის ერთდროული მკურნალობის ეფექტურობა გულის იშემიური დაავადების მქონე ხანდაზმულ პაციენტებში.

კვლევაში ჩართულ იქნა 82 პაციენტი, მათ შორის 28 ქალი და 54 მამაკაცი, საშუალო ასაკი მერყეობდა 65-დან 91 წლამდე. ლიპიდური სპექტრის, გლიკოზირებული ჰემოგლობინისა და კრეატინინის ლაბორატორიული მონაცემები შეადგენდა: T-Chol–275,28±29,1, LDL-Chol-190.25±21.8, HDL-Chol-30.09±3.1, TG-298.1±19.05, I.A.- 9.1±0.79, გლიკოზირებული ჰემოგლობინ-6,5%-დან 7%-მდე და კრაეტინინი - 120-150მმოლ/ლ. პაციენტები დაყოფილ იქნა ორ ჯგუფად: პირველი ჯგუფის პაციენტები იღებდნენ: ჰიპოლიპიდემიურ, ჰიპოგლიკემიურ და ჰიპოტენზიურ საშუალებებს, ხოლო მეორე ჯგუფის პაციენტები მხოლოდ — ჰიპოგლიკემიურსა და ჰიპოტენზიურს. ორივე ჯგუფის პაციენტების კვების რაციონი თითქმის თანაბარი კალორაჟის იყო. მკურნალობისა და დაკვირვების ხანგრძლივობა შეადგენდა 8 კვირას. შედეგებმა გვიჩვენა, რომ ლიპიდური სპექტრის მონაცემების სამიზნე დონე I ჯგუფში მიღწეულ იქნა პაციენტთა 64% შემთხვევაში. გლუკოზის კონცენტრაცია პერიფერიულ სისხლში — 68%-ში, ხოლო არტერიული წნევის მონაცემები — 71% შემთხვევებში. რაც შეეხება მეორე ჯგუფის პაციენტებს, ლიპიდური სპექტრის მონაცემების სამიზნე დონე მკურნალობის შემდეგ არ იქნა მიღწეული 86% შემთხვევაში, ხოლო გლუკოზისა და არტერიული წნევის მონაცემთა მაჩვენებლებმა სამიზნე დონეს მიაღწიეს 54% და 51% შემთხვევებში, შესაბამისად.

აღნიშნულიდან გამომდინარე, ჩვენი ძალისხმევა მიმართული უნდა იყოს შესაბამისი მაჩვენებლების სამიზნე დონის მისაღწევად, რაც კომპლექსური მკურნალობის შედეგად შეიძლება იქნეს მიღწეული. კომპლექსური მკურნალობა შეიძლება ჩაითვალოს გარანტად, რადგან ცალკეულ სამიზნე მაჩვენებელთა მიღწევა შესაძლებელია პრეპარატთა უფრო მცირე დოზის გამოყენებით, რაც ამ პრეპარატთა უსაფრთხო და ხანგრძლივი გამოყენების საშუალებას იძლევა. ეს კი თავისთავად ცხოვრების ხარისხის გაუმჯობესებისა და მიღწეული შედეგების სტაბილურობას განაპირობებს.

REFERENCES:

1. *M.A. Gall, K.Borch-Johnsen, P. Hougaard, FS. Nielsen, HH. Parving* (1995), Diabetes, **44**: 1301–1309.
2. *C.D.A. .Stehouwer, N.C. Schaper* (1996), Eur. J. Clin. Invest. **26**: 535–543.
3. *T. Deckert, H. Yokoyama, E .Mathiesen, et al.* (1996), Br. Med. J. **312**: 871–874.
4. *T. Omland, RT. Lie, A. Aakvaag, T. Aarsland, K. Dickstein* (1994), Circulation. **89**: 1573–1579.
5. *C.D.A. Stehouwer*. In: CE. Mogensen, ed. (1997), The Kidney and Hypertension in Diabetes Mellitus, 3rd edn. Boston: Kluwer, 155–163.
6. *G.M. Reaven* (1995), Physiol. Rev. 75: 473–486.
7. *D.J. Chisholm, L.V.Campbell, E.W. Kraegen* (1997), Clin. Exp. Pharmacol. Physiol. **24**: 782–784.
8. *G.S. Kozlov* (2009), Kardiologia. **11**: 56–63.
9. *A. Ceriello* (1993), Diabetologia. **36**: 1119–1125.
10. *K. Kario, T. Matsuo, H. Kobayashi, M. Matsuo, T.,Sakata, T. Miyata* (1995), Arterioscl. Thromb. Vasc. Biol. **15**: 1114–1120.
11. *P.B. Leurs, R. van Oerle, K. Hamulyak, BHR. Wolffenbuttel* (1995), Diabetes. **44**: 80–84.

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