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IMPACT OF IODINE-CONTAINING PUMPKIN OIL ON THE COURSE OF CARDIAC ISCHEMIA IN THE RESIDENTS OF ZAKARPATTYA REGION

IMPACTUL CONŢNUTULUI ÎN IOD AL ULEIULUI DE DOVLEAC ASUPRA ISCHEMIEI CARDIACE LA LOCUITORII REGIUNII ZAKARPATTYA

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The purpose of the research was exploration of the impact of the conventional treatment in combination with simvastatin and iodine-containing pumpkin oil "Fortuna vita" on the values of lipid metabolism in cardiac ischemia patients residing in the setting of iodine deficit. The patients were divided into 2 groups: group 1– patients underwent conventional treatment with application of simvastatin of 20mg/day during the whole course of observation; group 2 – same treatment in combination with iodine-containing pumpkin oil "Fortuna vita" of 10ml/day, which contains 200μg of organically combined iodine form. The level of total cholesterol, triglycerides, high-density lipoprotein cholesterol (HDL cholesterol) and low-density lipoprotein cholesterol (LDL cholesterol) in serum, and aspartate aminotransferase and alanine aminotrasferase in patients before treatment, after 10 days, and after 1 month of treatment was measured. It was determined, that simvastatin is an effective and safe cholesterol-reducing preparation for cardiac ischemia patients which results in reduction of cholesterol level by 18% and LDL by 23% in one month. A combination of simvastatin and iodine-containing pumpkin oil appears more effective, probably because of potentiation of their effects, which also facilitate growth of antiatherogenic HDL and consequently decrease the atherogenicity coefficient. The general clinical state of both groups improved as a result of the treatment, though more so for the patients treated in combination with iodine-containing pumpkin oil. We are inclined to explain this fact by normalization of iodine-thyroid status, and consequently, of the general metabolism of the patients in the setting of ecologic iodine deficit because of iodine-containing fatty acids.

Keywords: cardiac ischemia, simvastatin, cholesterol, lipoproteins, iodine-containing oil

Introduction

Cardiovascular pathology remains the main cause of illnesses and mortality in the world. So, according to WHO nearly 17mln people die from cardiovascular diseases every year. In the structure of mortality caused by cardiovascular pathology cardiac ischemia keeps more than 60% (ex. Kovalenko, 2007). At the same time, the results of multiple experimental, epidemiologic and clinical researches conducted recently leave no room for doubts as to the influence of lipidosis on the development and complications of atherosclerosis. Firstly it relates to illnesses and mortality caused by cardiac ischemia. More than 15% of adult population in Ukraine suffer from cardiac ischemia. Dislipidemy, in particular increased level of total cholesterol is registered among 48.5% of males in the age of 40-60 and 56.3% of women, while prevalence and mortality from cardiac ischemia is one of the highest in Europe (ex. Lutaj et al., 2007). Therefore the system of cardiovascular preexposure and postexposure prophylaxis measures directed at correction of hypercholesterolemia as the main aterosclerosis and cardiac ischemia risk factor becomes especially important (ex. Lutaj et al., 2007).

Hypercholesterolemia is regarded as the main risk factor of atherosclerosis development and complications. In particular, hyperlipoidemia lowers nitric oxide bioavailability upsetting the flow-dependent artery dilation. According to modern views endothelium dysfunction is the main factor facilitating increased penetration of low-density lipoproteins (LDL) to the intima of coronary arteries, which triggers a series of normal homeostasis dysfunctions. Hence, endothelium dysfunction is the initial stage of changes leading to formation of atherosclerotic plaque. Prevention of atherosclerosis risk factors is essential for decreasing the risks of cardiovascular diseases. Impact on the high level cholesterol and low-density lipoproteins must be regarded as the most substantiated and effective method of preexposure and postexposure prophylaxis among various approaches to atherosclerotic plaque stabilization (ex. Kovalenko, 2007). This means the necessity of prescribing cholesterol-reducing therapy and reaching target level of cholesterol content in blood.

Decreasing the high level of total cholesterol and its fraction LDL cholesterol is the primary task of hypolipidemic therapy, since there are cogent proofs as to close correlation between these indexes and development and progressing of atherosclerosis and its complications (ex. Metelitsa, 2002; Gotto, 2003). Currently the indexes of total cholesterol <5.0mmole/l and LDL cholesterol < 3mmole/l are considered as normal at the population level. For patients with present cardiovascular diseases, primarily cardiac ischemia, and other atherosclerosis manifestations the target levels of these indexes are set as <4.5mmole/l for total cholesterol, and <2.5mmole/l for LDL cholesterol – achieving these in the process of treatment is reliably followed by reduction of cardiovascular complications and improvement of prognosis.

Statins (HMG-CoA reductase inhibitors) are the main pharmacologic means of dislipidemy prevention these days. They both decrease the level of total

cholesterol and LDL cholesterol, and have a positive effect on LDL subfractions reducing the share of the most atherogenic ones – small dense particles and triglycerides (ex. Gotto et al., 2003). It must be noted, that hypertriglyceridemia and low HDL cholesterol level are also the risk factors of atherosclerosis and cardiac ischemia, which must be taken in consideration when selecting the therapy. Cardiovascular risk is known to increase in case of triglyceride growing > 1.7mmole/l and HDL cholesterol level dropping < 1.0mmole/l for men and <1.2mmole/l for women.

Now appropriateness of statins application for preexposure prophylaxis of arterial hypertension patients is beyond any doubt. Meta-analysis of multicenter researches conducted during the recent year demonstrates possibility to decrease the general death rate by 9 to 30% and stroke development risk by 19 to 31% in case of applying statins therapy (ex. Sirenko et al., 2008; Duovne et al., 2000; .Moron et al., 2000; Cholesterol treatment, 2005).

Lipid-reducing effect of statins is connected with reverse blocking of HMG-CoA reductase enzyme which enables intracellular cholesterol synthesis. The total cholesterol level in plasma is decreased same as cholesterol fractions, in particular LDL by 25-40% on average, and lipoproteins with high triglyceride content. Therapy with statins is characterized by moderate growth of HDL cholesterol (by 5-15%) and decrease of triglyceride level (by 15-30%). Statins lower the risk of atherosclerotic cardiovascular complications by 30% on average (ex. Gotto, 2003).

Wide-range researches of taking simvastatin during 5.5 years demonstrated its effectiveness as to prevention of the main vascular complications (myocardial infarction, stroke, need of revasculization). As a result of this the integrated index of cardiovascular complications rate dropped by 24%. At the same time positive results were observed in various subgroups: men and women; patients of various age; and which is extremely important, regardless of the initial rates of total cholesterol and LDL cholesterol. During taking simvastatin the ischemic risk decreased by 27% (ex. Aronov, 2001), other authors state even higher percentage – 30-40% (ex. Pyorala et al., 2004).

Considering the results of the wide-scale researches, prescription of statins is now recommended for postexposure prophylaxis to all patients with diagnosis of cardiac ischemia and high risk of cardiovascular complications regardless of the age, sex, and initial cholesterol level (ex. Lutaj et al.,2007).

Besides, the effect of omega-3 polyunsaturated fatty acids on lipid metabolism is known to exhibit decreased triglyceride and apolipoprotein B synthesis in liver, LDL excretion from bloodstream. Indirect decreasing of LDL and increasing of HDL is also achieved due to more intense excretion of bile acids. Positive effects of omega-3 polyunsaturated fatty acids were confirmed by randomized placebo controlled researches of cardiologic patients. So, it was demonstrated that cardiac mortality decreased by 50% and nonfatal myocardial infarction lowered by 48% among the patients after myocardial infarction who additionally took polyunsaturated fatty acids. It was additionally determined, that taking omega-3 polyunsaturated fatty acids with food leads to growth of

antiatherogenic HDL in serum and is accompanied by significant reduction of all atherogenic fractions. Multi-aspect effects of omega-3 polyunsaturated fatty acids on cellular membranes were discovered: due to their integration into the structure the biophysical and physiologic properties of cellular membranes change, they become less viscous and more permeable, the structure and functions of ion channels change. Omega-3 polyansaturated fatty acids also slow down free radicals creation and lipid pereoxidation (ex. Rudenko, 2008). Therefore, considering the above data application of omega-3 polyunsaturated fatty acids is reasonable for treatment of dislipoproteinemia patients, particularly during treatment with statins which may exhibit hepatotoxic effect.

Our previous researches demonstrated the effect of iodine-containing fatty acids as effective means for iodine deficit prevention, correction of thyroid gland function, which has antiatherogenic properties, increases resistibility of the organism to the impact of xenobiotics and other unfavorable environmental factors, increases immunologic reactivity of the organism, has an anti-oxidant effect (ex. Turianica et al., 2002, 2002 a).

The purpose of the research was exploration of the impact of the conventional treatment in combination with simvastatin and iodine-containing pumpkin oil "Fortuna vita" on the values of lipid metabolism in cardiac ischemia patients residing in the setting of iodine deficit.

Materials and Methods

The research was conducted according to the clinical research requirements of Ukraine. It included 25 patients with the following diagnosis: cardiac ischemia, exertional angina of functional classes II-III, atherosclerotic cardiosclerosis, essential hypertension II-III, cardiac failure II A, who were subject to inpatient treatment at the general cardiologic department of the regional cardiologic dispensary (Uzhgorod, Zakarpattya region, Ukraine) and who reside in biogeochemical region with ecologically conditioned iodine deficit (ex. Turianica, et al., 2007). The average age of the patients was 56.3±5.8 years.

The patients were divided into 2 groups: group 1 – patients were conventionally treated according to the recommendations of the Ministry of Healthcare of Ukraine with application of simvastatin of 20mg/day during the course of observation; group 2 – same treatment in combination with iodine-containing pumpkin oil "Fortuna vita" of 10ml/day, which contains 20mcg of organically combined iodine form.

According to the research minutes biochemical analysis was performed before treatment, after 10 days of treatment and 1 month after the beginning of treatment.

The level of total cholesterol, triglycerides, high-density lipoprotein cholesterol (HDL cholesterol) and low-density lipoprotein cholesterol (LDL cholesterol) in serum, and aspartate aminotransferase and alanine aminotransferase

was measured with test-kits (PLIVA-Lachema a.s., Czech Republic). Atherogenicity coefficient was estimated by the formula: (cholesterol – HDL)/HDL.

Statistical processing was carried out after a computer database was formed in Microsoft Exel by means of personal computer with calculation of Student's t-test and means comparison.

Result and Discussion

It should be noted that all patients tolerated simvastatin treatment satisfactorily.

Our research determined that after 10 days of conventional treatment with application of simvastatin the patients showed no significant change in lipid blood spectrum, however the levels of alanine aminotransferase and aspartate aminotransferase increased significantly (table 1). After one month of treatment of these patients the cholesterol level decreased significantly by 18% as compared to the values at the beginning of the observation, and the content of the most atherogenic fraction of LDL decreased by 23%, there was also a tendency of triglyceride level decrease ($P>0.05$). It should be noted however, that while HDL level did not change significantly, there was a descending tendency ($P>0.3$). Because of the low level of HDL cholesterol the atherogenicity coefficient did not change either and remained higher than normal (normal is <3). We may not stress that monitoring of enzymes (alanine aminotransferase, aspartate aminotransferase) activity indicated their undesirable significant increase both compared to control and in the observation dynamics, though it did not exceed the safety level (ex. Armitage, 2007). Hence, treatment with simvastatin may be considered as safe and quite effective. Further observation of the patients will allow to obtain more distant results of treatment.

Table 1

Lipid metabolism indices of cardiac ischemia patients in the course of conventional treatment

Indices	Before treatment n=10	After 10 days of treatment n=10	After 1 month of treatment n=10
Cholesterol (mmole/l)	4.8±0.19	4.5±0.28	3.99±0.31 *
HDL (mmole/l)	0.95±0.08	0.89±0.09	0.83±0.07
LDL (mmole/l)	3.52±0.26	3.19±0.31	2.56±0.29 *
Triglyceride (mmole/l)	1.28±0.13	1.15±0.12	0.98±0.11
Atherogenicity coefficient	4.81±0.75	4.87±0.79	4.26±0.71
Alanine aminotransferase (mmole/l)	0.60±0.06	0.77±0.04 *	1.17±0.09 * **
Aspartate aminotransferase (mmole/l)	0.58±0.04	0.74±0.03 *	1.14±0.09 * **

* and ** – reliability indicators compared to control and previous group respectively

It is important to note, that a combination of conventional treatment of patients by simvastatin and iodine-containing pumpkin oil as soon as after 10 days of treatment results in reliable 15% reduction of cholesterol, reduction tendency for atherogenic LDL ($P > 0.05$), and growth tendency for antiatherogenic HDL ($P>0.05$), which probably leads to decrease of atherogenicity coefficient, though not reaching the normal value. The levels of blood enzymes and triglycerides remain without change. After 1 month of the abovementioned complex treatment observed are reliable 19% decrease of cholesterol level, 27% decrease of LDL, 38% drop of atherogenicity coefficient, and 20% increase of HDL. This is a very positive factor since as it is known a 1% decrease of LDL cholesterol decreases the cardiovascular risk by 1%, while a 1% increase of HDL lowers this risk by 3%. Furthermore, it is important that serum transaminase does not change significantly, and even have a tendency to decrease. We tend to explain these revealed additional positive effects by iodine-containing polyunsaturated fatty acids (including omega-3) which are contained in iodine-containing pumpkin oil, since taking of such polyunsaturated fatty acids is know to decrease all atherogenic lipoprotein fractions and increase antiatherogenic ones (ex. Rudenko, 2008). On the other hand presence of iodine-containing fatty acids in pumpkin oil contributes to compensatory inflow of physiologic iodine doses to the organism, and, consequently, to normalization of thyroid regulation of substance and energy metabolism – proteins, amino acids, carbohydrates, lipids, cholesterol, water-salt metabolism, i.e. leveling of iodine deficit consequences (ex. Turianica et al., 2007). Furthermore, omega-3 polyunsaturated fatty acids have anti-oxidant properties which probably contribute to stabilization of hepatocyte membranes, and decreasing the hepatoxic effect of statins.

At the same time triglyceride level did not decrease significantly which may be the consequence of oil intake.

Table 2

Lipid metabolism indices of cardiac ischemia patients in the course of conventional treatment combined with iodine-containing pumpkin oil

Indices	Before treatment n=15	After 10 days of treatment n=15	After 1 month of treatment n=15
Cholesterol (mmole/l)	5.15±0.36	4.39±0.39 *	4.19±0.27 *
HDL (mmole/l)	0.74± 0.05	0.87±0.06	0.93±0.10 *
LDL (mmole/l)	3.84±0.37	3.18±0.40	2.81±0.24 *
Triglyceride (mmole/l)	2.16±0.30	1.8+0.30	1.75±0.41
Atherogenicity coefficient	5.80±0.50	4.08±0.35 *	3.57±0.37 *
Alanine aminotransferase (mmole/l)	0.82±0.08	0.72±0.10	0.63±0.07
Aspartate aminotransferase (mmole/l)	0.70±0.08	0.69±0.08	0.60±0.05

Thus, simvastatin is an effective and safe cholesterol decreasing preparation for cardiac ischemia patients which as soon as after 1 month of application results in 18% decrease of cholesterol level, and 23% decrease of LDL.

Combination of simvastatin and iodine-containing pumpkin oil appears more effective, probably because of potentiation of their effects, which lead to significant 19% decrease of cholesterol, 27% decrease of LDL, 38% drop of atherogenicity coefficient, and, which is particularly important, 20% increase of antiatherogenic HDL which are much more difficult for correction than atherogenic LDL, and, consequently, to decreased atherogenicity coefficient. At the same time it is also important, that during consumption of iodine-containing pumpkin oil the level of serum transaminase did not change significantly, unlike their growth in the first group of patients, which indicates its hepatoprotection effect and lessened side effect of simvastatin.

In both groups of patients the treatment resulted in improved general clinical state, the number and duration of anginous strokes decreased, the need of nitropreparations decreased, physical stress tolerance increased, positive ECG dynamics was observed as decreased number of ST segment depressions, which was more so for patients undergoing treatment combined with iodine-containing pumpkin oil. This fact we tend to explain by normalization of iodine-thyroid status, and, consequently, the general metabolism of patients residing in ecological iodine deficit conditions, because of iodine-containing fatty acids (ex. Turianica et al., 2007).

Conclusions

Simvastatin is an effective and safe cholesterol decreasing preparation for cardiac ischemia patients which as soon as after 1 month of application results in 18% decrease of cholesterol level, and 23% decrease of LDL.

Combination of simvastatin and iodine-containing pumpkin oil appears more effective, probably because of potentiation of their effects, which lead to significant 19% decrease of cholesterol, 27% decrease of LDL, 38% drop of atherogenicity coefficient, and, which is particularly important, 20% increase of antiatherogenic HDL. At the same time it is also important, that during consumption of iodine-containing pumpkin oil the level of serum transaminase did not change significantly, unlike their growth in the first group of patients, which indicates its hepatoprotection effect and lessened side effect of simvastatin.

In both groups of patients the treatment resulted in improved general clinical state, which was more so for patients undergoing treatment combined with iodine-containing pumpkin oil, probably because of normalization of iodine-thyroid status, and, consequently, the general metabolism of patients residing in ecological iodine deficit conditions, owing to iodine-containing fatty acids, in particular omega-3.

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