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INFLUENCE OF OMEGA-3-POLYUNSATURATED FATTY ACIDS OF THE BLOOD AND ADIPOKINES CONTENT IN PATIENTS WITH ARTERIAL HYPERTENSION AND OSTEOARTHRITIS

Abstract. *Coincidence of arterial hypertension and osteoarthritis, especially at the background of increased body mass index, leads to worse course of pathology. Aim was to investigate whether therapeutic benefit exists for patients with Arterial hypertension (AH), Osteoarthritis (OA) and their coincidence from omega-3 fatty acid supplementation. 100 patients were investigated, 35 – with AH, 35 – with OA, and 30 – AH + AO. Female: male ratio was 2.5:1, average age 49.6 ± 8.9 years. Average duration of AH – 7.4 ± 3.8 years, clinically II stage and 8.4 ± 4.6 years for OA (2-3 stage by X-ray, no synovitis). Control measurements were carried out in 22 healthy volunteers without exacerbation of any chronic illnesses or acute ones within 3-months period before study. All groups of patients corresponded average ratio by age and gender. All patients depending on nosology were prescribed standard basic therapy, which included: ACE inhibitors (Lisinopril), in AH, non-steroidal anti-inflammatory remedies (Meloxicam, Ibuprofen, Diclofenac Sodium) + chondroprotectors in OA. Patients demonstrating dyslipidemia were distributed randomly to 2 subgroups: those obtaining statins (Rosuvastatin) only (comparison group) and principal group who got omega-3-polyunsaturated acids (Epadol-Neo) as addition to standard therapy. Epadol-Neo includes Eicosapentaenoic Acid (300 mg), Docosahexaenoic Acid (200 mg), other fatty acids – 498 mg, d- α -tocopherol (2 mg) it was taken by patients in QD regimen, 2 caps per intake during 2 months. Application of omega-3-polyunsaturated acids into treatment schedule is effective in patients with arterial hypertension, osteoarthritis and their co-incidence in relation to hyperlipidaemia correction and favours restoration of natural balance of adipokines at the account of potentiation of effects of basic therapy.*

Key words: *arterial hypertension, osteoarthritis, increased body weight, Leptin, Adiponectin, hyperlipidaemia, omega-3-polyunsaturated fatty acids.*

Introduction. Arterial hypertension (AH), osteoarthritis (OA) and their combination are economically unprofitable for the state and patients [1]. AH affects at least one third of the able-bodied population of developed countries of the world, but it is one of the key causes of early dislocation and death. The accusation and mutual burden of these

diseases have been proved: the longer the hypertension, the more often the patient is diagnosed with the associated OA [1,3]. The full correction of manifestations of these nosologies, prevention of complications and rehabilitation without unwanted phenomena is a priority direction of the report. The use of omega-3-polyunsaturated

fatty acids (PUFAs) is not included in the list of recommendations for evidence-based medicine, but today there is much evidence of their clinical efficacy [2].

Materials and methods. 100 patients were investigated, 35 – with AH, 35 – with OA, and 30 – AH in combination with AO. The research design was based on the type of case-control. The ratio of "female: male" was 2.5: 1, mean age – 49.6 ± 8.9 years. The average duration of hypertension was 7.4 ± 3.8 years, the clinical picture of the disease corresponded to the second stage. The long-standing condition for osteoarthrosis was 8.4 ± 4.6 years, the clinical picture corresponded to OA of 2-3 stage, without symptoms of synovitis. The examination procedures met the standards of the Helsinki Declaration in the 1983 review.

The control tests were performed in a group of practically healthy persons ($n=22$), comparable with patients of other groups by age and gender.

Anthropometric measurements – body weight and height – were measured on the day of blood collection. BMI was determined according to the generally accepted formula; the BMI was considered optimal to 25, and the higher – the index is more than 25 kg/m^2 .

Blood for biochemical studies was taken on the first day of the patient's stay in the hospital at about the same time, about 9-10 am in the morning, after 8-12-hour break in the meal. The day before the sampling excluded heavy physical activity, alcohol, greasy food. Biochemical blood tests are performed on the biochemical analyzer "Accent 200" ("Cormay S.A.", Poland).

All patients, depending on nosology, received baseline therapy, which included: for AH – ACE inhibitors (Lisinopril, Enalapril), for OA – non-steroidal anti-inflammatory drugs (Meloxicam, Ibuprofen, Sodium Diclofenac), chondroprotectors (Mucosate, Alflutop). Patients with signs of dislipidemia received hypolipidemic drugs (Rosuvastatin).

Of the hundred surveyed in AH, OA and their combination was created by the random method of two groups, which included an equal number of persons with all variants of the nosology. The comparison group (50 people) received baseline therapy depending on nosology, which included: for AH – ACE inhibitors (Lisinopril), for OA – non-steroidal anti-inflammatory drugs (Meloxicam,

Ibuprofen, Diclofenac Sodium), chondroprotectors (Mucosate, Alflutop). Patients with signs of dislipidemia received hypolipidemic drugs (Rosuvastatin). Patients in the main group (50 people) additionally prescribed a drug containing omega-3-PUFAs – Epatol Neo 1 capsule 2 times a day for a period of 2 months as a source of ω -3-PUFA.

The actual processing of the obtained results was carried out using a variational citation analysis. All data were approved statistically with PC Pentium III, standard Excel 2010 software.

Research results. Patients in both groups – comparisons and well-being – overcame 2-course courchemic treatment well, without any undesirable events.

Patients in the control group at the end of the standard course of treatment of their normal pathology revealed a significant improvement of the available indicators of the lipidogram, indicating that the efficacy of the cured treatment was effective. Thus, the level of total cholesterol decreased significantly by 18.9% (from 5.8 ± 0.41 to 4.7 ± 0.32 mmol/L) ($p < 0.05$). The removal of PUFAs has led to a further progressive decrease in total cholesterol in the blood of patients in the standard group (up to 4.4 ± 0.22 mmol/L), which was pre-differentiated from the indicator before treatment, but the difference in comparison with the indicator of the comparison group was not confirmed statistically. The same positive dynamics was observed when analyzing the level of HDL cholesterol after completing the treatment. Thus, the level of HDL in the group of comparisons is 13% (the difference is not confirmed), and 20.5% – in the ordinary group ($P < 0.05$) (Table 1).

The treatment in different ways influenced the level of adiponics – leptin and adiponectin – in patients with AH, OA and their combination. Thus, therapeutic complexes with the use of the standard set of medicines did not change the level of leptin in patients with hypertension with optimal BMI. The tendency to decrease by one third of the given indicator in the usual group for the treatment group was detected, however, it was not confirmed by the citation (Table 2). The combination of AG and OA changes in the treatment process was also found only in patients with excessive body mass: the dynamics in the group did not exclude the comparison, in the normal group prescribed leptin for treatment decreased by 21.9%.

Table 1

Changes of lipidogram under the influence of combined treatment with additional inclusion of PUFA

Indicator/ (one dimension)	Before treatment n=100 (0)	Group of comparisons for treatment n=50 (I)	Main group for treatment n=50 (II)	P (I-0)	P (I-II)
Cholecetin, mmol/L	5,8±0,52	4,9±0,56	4,4±0,50	P<0,05	P>0,05
Lipoproteins of high density, mmol/L	1,46±0,14	1,65±0,21	1,76±0,11	P>0,05	P<0,05
Low density lipoprotein, mmol/L	3,5±0,93	3,2±0,58	2,8±0,52	P>0,05	P>0,05
Lipoproteids are very low glucose, mmol/L	0,58±0,171	0,44±0,152	0,41±0,163	P>0,05	P>0,05
Triglycerides, mmol/L	2,26±0,121	1,82±0,083	1,61±0,111	P<0,05	P<0,05

Notes: n – number of measurements; p_1 – the level of pre-test variables according to the data before treatment; p_2 – is the level of interconnection of the indicators according to the data of the comparison group.

Table 2

Concentration of leptin in the blood in patients with osteoarthritis, arterial hypertension and their combination with optimal and excessive index of body mass and before treatment

Indicator/ (one dimension)	Results before treatment	Compariso n group	Main group
AH, optimal BMI n = 17	17,9±4,36	16,6±5,86	12,7±4,36
AH, advanced BMI n = 18	49,2±5,48	42,4±1,73	16,5±3,48 $P_1<0,05$ $P_2<0,05$
OA, optimal BMI n = 17	16,4±4,87	18,2±1,53	17,3±2,87
OA, advanced BMI n = 18	40,5±4,3	40,6±4,73	34,3±4,3
OA + AH, optimal BMI n = 15	33,0±4,94	32,0±2,63	34,1±4,94
OA + AH, advanced BMI n = 15	55,4±6,62	51,2±3,51	38,6±3,62 $P_1<0,05$ $P_2<0,05$

Notes: n – number of measurements; p_1 – the level of pre-test variables according to the data before treatment; p_2 – is the level of interconnection of the indicators according to the data of the comparison group.

Even adiponectin was more susceptible to treatment. Positive, statistically significant changes – attribution of the indicator – were recorded in the normal group in comparison with the results of the treatment and with the results obtained in the comparison group, among the patients in each of the subgroups included (isolated over the AH, OA or their combination, independently from the IMT). The most pronounced changes in adiponectin were

isolated pathology – AG and OA, in patients with optimal body mass: the rate increased by 44.4% and 54.5%, respectively. A convenient way of assessing the precision of adiponectin in the blood was found in patients with a combined pathology – OA and AG: in them the concentration of it was increased by 84.4% in patients with optimal BMI, and in 2 times in patients with excessive body mass.

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regulation of the elevated level of leptin in patients with a metabolic syndrome. Thus, lactate reduced the level of hyperlipidemia by reducing the level of C-reactive protein, LDL- α and LPDH, and total cholesterol by 40-50%. The level of leptin corrected by lovastatin was much higher and the dynamics at the end of the three-month therapeutic course was 20% this year. Simvastatin, due to the inoculation of monotherapy in hyperlipidemic patients, reduced the plasma concentration of the C-reactive protein, proinflammatory cytokines and lipoproteins, and to a lesser extent influenced the administration of leptin [2].

The results we receive are similar: the appointment of standard therapy - baseline therapy of communicable disease and patients – with patients with hypertension, OA or their combination was completely effective against the correction of hyperlipidemias, but did not lead to a complete restoration of the natural relationship of adipocytes, slightly contributing to the desired adiponectin in the sample.

The formal function of omega-3-PUFA is to reduce the synthesis of triglycerides and their transcript of apolipoprotein B in the liver, as well as in the increase of the total glucose and lower lipoprotein excretion in particular.

According to various observations [3-5], ω -3-PUFAs in a number of biological applications or enriched in their activity are able to reduce the levels in the blood of leptin and resicants, and the level of adiponectin is somewhat elevated. Such a law has been found for ICC patients, non-alcoholic cateo-hepatose. At the same time, in tissues of target organs (liver, fatty tissue), they significantly improve the concentration of matrix RNA, which encode the synthesis of these adipocys.

The regulation of the adopic compounds ω -3-PUFAs significantly reduces the expression of hypertriglyceridemia, in comparison with other gipolipidemic drugs and affects the administration of glucosylated hemoglobin in patients with diabetes mellitus and increases the intake of HDL. The same law was found in the course of the investigations: the inclusion of PUFA in a combined treatment of patients with OA and OA from the adjacent AG revealed additional, in comparison with the effect of the subjects, the hypolipidemic action: led to a decrease in the severity of both hypertriglyceridemia and hyperholesterolemia; It

contributed to the renewal of the natural balance of adipocytes: normalized the level of leptin in patients with oesophagitis, hypertension with OA with excessive BMI, and contributed to the addition of adiponectin to all patients in need of treatment [3-5].

Conclusions. Application of PUFA in the combined treatment of patients with OA and OA with the arterial hypertension reveals additional hypolipidaemic conditions, and also helps to restore the natural balance of adipokines: normalizes the level of leptin in patients with osteoarthritis, hypertension with OA with excessive BMI, and helps to increase adipokines in the examined contingent of patients.

Referens

1. Bazylevych AD, Kuleshir Mla, Hdyria OV, Kamins'ka KhA. *Yevropeic'kyi konhres kardiologiv [European Congress of Cardiologists]. Liky Ukrainy. 2016;7-8:34-41.*
2. Mitchenko OI, Romanov Vlu, Yanovs'ka KO, Hel'medova MM, Yakushko LV, Beliaieva TV, ta in. *Indekc leptyn/adyponektyn yak novyi dodatkovyi curohatnyi marker aterocklerotychnoho urazhennia [Insert leptin/adiponectin as a new additional cohort marker of atherosclerotic lesions]. Ukrainc'kyi kardiologichnyi zhurnal. 2012;2:40-7.*
3. Molinar-Toribio E, Pérez-Jiménez J, Ramos-Romero S, Romeu M, Giralt M, Taltavull N, et al. *Effect of n-3 PUFA supplementation at different EPA:DHA ratios on the spontaneously hypertensive obese rat model of the metabolic syndrome. Br J Nutr. 2015;113(6):878-87. doi: 10.1017/S0007114514004437*
4. Krysiak R, Zmuda W, Okopien B. *The effect of simvastatin-ezetimibe combination therapy on adipose tissue hormones and systemic inflammation in patients with isolated hypercholesterolemia. Cardiovasc Ther. 2014;32(2):40-6. doi: 10.1111/1755-5922.12057*
5. Vafeiadou K, Weech M, Altowajiri H, Todd S, Yaqoob P, Jackson KG, et al. *Replacement of saturated with unsaturated fats had no impact on vascular function but beneficial effects on lipid biomarkers, E-selectin, and blood pressure: results from the randomized, controlled Dietary Intervention and Vascular function (DIVAS) study. Am J Clin Nutr. 2015;102(1):40-8. doi: 10.3945/ajcn.114.097089*