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Research Article

Short report of original clinical trial of neurotropic drug: L-dopa efficiency of using in therapy of coronary artery disease

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Abstract

The short clinical study is devoted to the corrective action of the neurotropic drug LEVOPA (L-DOPA) in patients with coronary artery disease (CAD) complicated by atherogenic dyslipidemia (DLP), moderate angina pectoris (AP), arterial hypertension (AH) and other risk factors for the development of atherosclerosis (AS). Purposefully in neurology, drug of L-DOPA - LEVOPA is used in significant doses (3-10 g/day) to treat Parkinson's disease, including atherosclerotic genesis. In this study, the neurotropic drug LEVOPA was used as an active metabolic agent in the complex therapy of CAD in a small dose of 0.5 g 3 times a day, with chronic oral administration for 4 weeks. As a result, an improvement in the lipid profile of blood and the hypolipidemic property of the drug LEVOPA were found. An improvement in hemodynamics and general well-being was noted in treated patients with aggravating risk factors for the development of AS. We had notice the decrease of lipid peroxidation (LPO) too.

Keywords: coronary artery disease; atherosclerosis; dyslipidemia; complex therapy; LEVOPA

Introduction

Lipid-lowering therapy is currently widely used in programs for the primary and secondary prevention of cardiovascular events caused by atherosclerosis (AS), including in ischemic (coronary) heart disease (CAD) due to the high prevalence and mortality [1-4]. AS, arterial hypertension (AH), diabetes mellitus (DM) and obesity (Ob) are “metabolic pandemics” of the 21st century, requiring correction from the standpoint of improving diagnostics and adequate treatment. In patients with CAD aggravated by atherogenic dyslipidemia (DLP) with an improvement in the blood lipid spectrum, the incidence of myocardial infarction (MI) decreases. According to Russian recommendations [5], the goal of complex therapy for CAD associated with AH and atherogenic DLP is to achieve a blood pressure value (<130/80 mm Hg), a normal blood lipid spectrum with targeted achievements, as well as correction of hypoxic and ischemic conditions. For this, in addition to traditional therapy for CAD in the course of treatment, it is rational to use drugs of the metabolic type of action that have antihypoxic and anti-oxidant properties, preventing the increase in energy deficiency and the intensification of lipid peroxidation (LPO) [6].

L-DOPA, a precursor of dopamine synthesis, belongs to physiologically active substances with a nonspecific positive effect on metabolism. Usually, the drug L-DOPA - LEVOPA is used in significant doses (3-10 g per day) for the treatment of Parkinson's disease, including atherosclerotic genesis [7].

Earlier in joint experimental clinical research with employees of the State Medical University named after IP Pavlov (St. Petersburg, Russia) found that L-DOPA stimulates reparative processes, restores the activity of the sympathetic-adrenal system, and reduces the degree of LPO progression. Under the influence of L-DOPA in patients after myocardial infarction (MI), he-modynamic parameters and the clinical course of CAD improve (patentable closed researches). Based on long term studies, a hypothesis was put forward about the possible correction in lipid metabolism disorders with the help of the inclusion of the drug L-DOPA in the complex therapy in patients of AS complicated DLP.

Purpose of the clinical study

The aim of this investigation was to evaluate the effectiveness in complex therapy of the neurotropic drug LEVOPA in CAD patients with DLP and other risk factors of AS.

Material and methods

Object of the study

60 patients with CAD (men, mean age 60.2 ± 5.4 years) with moderate AP I-II degree according to NYHA classification were examined. The reason for hospitalization of patients with CAD was pain syndrome and attacks of AP (3-5 times a day). Upon admission to the clinic, the baseline values of the blood serum lipid spectrum were analyzed for the presence of DLP (phenotyping according to Fredrickson). The assessment of the patient's condition before the start of therapy and after 4 weeks of treatment was carried out according to the results of electrocardiographic, biochemical studies and general well-being. 17 out of 60 CAD patients did not have the significant lipid metabolism disorders. The selected cohort in 43 patients was complex in terms of the number of comorbidities.

In an open, comparative, placebo uncontrolled study of 60 patients, 43 men were selected with chronic CAD, aggravated by DLP II and IV phenotypes, AH and other associated risk factors for the development of

AS. Due to the high risk of developing AS, in this sample of patients, the target values of the blood spectrum were tightened: total cholesterol <4.0 mM/l, triglycerides <1.7 mM/l, HDL cholesterol>0.95 mM/l, LDL cholesterol <1.8 mM/l. All patients underwent a thorough medical examination and were on a lipid-lowering diet for 2 weeks before starting treatment. Electrocardiograms in patients with CAD and individuals in the control group were recorded in 12 standard conventional leads. In patients, the following were instrumentally determined: AH, impaired carbohydrate tolerance or uncompensated type 2 DM and Ob. A contingent of long-term smoking patients was identified (75%). 31 people (72%) were people of mental labor, 15 of them held leadership positions, which determined the dominance of manifestations of psycho-emotional stress and reactive anxiety. 40 men (93%) had waist circumference more than 102 cm and increased body mass index – risk factors of Ob.

The exclusion criteria from this study were acute MI, chronic cardiac insufficiency with an ejection fraction below 40%, severe AH (>170-180 mm Hg), as well as chronic diseases of the liver, biliary tract, kidney, hypo- and hyper function of the thyroid gland.

Patient`s treatment regimen

All 43 patients with CAD and DLP received basic therapy: antithrombotic agents (aspirin cardio), long-acting nitrates (nitrosorbide, isosorbide dinitrate), antihypertensive drugs (ACE inhibitors), in the presence of myocardial ischemia - alpha-blockers (metoprolol, carvedilol) in individual doses. A cohort of 43 patients was divided into 2 groups: one group of 20 people (group 2) was prescribed basic CAD therapy for 4 weeks, and patients of group 3 of 23 people were given complex treatment: basic therapy + L-DOPA (LEVOPA) 0.5 g 3 times a day for 4 weeks too. For comparison, as a control (group 1), we used the data of laboratory analyzes of 10 apparently healthy men without DLP (55-65 years old).

The Biochemical analysis

The blood levels of total cholesterol (TC), triglycerides (TG), high density lipoprotein cholesterol (HDL-C) and low density lipoprotein cholesterol (LDL-C) were studied by standardized biochemical research methods and in comparison with internal standards of human serum (USA) by analyzer Technicon AA-II (USA). The cholesterol index of atherogenity (IA) was calculated according to the common formula after academician A.N. Klimov (IEM, Russia): [(TC – HDL-C) / HDL-C]. In blood we analyzed with standard generally accepted methods, spectrophotometrically by the analyzer the levels of hormone corticosterone (CS), non-esterified fatty acids (NEFA), glucose (G), the content of diene conjugates (DC), malonic di-aldehyde (MDA) as products of LPO.

Results

The results of biochemical studies have shown the following. In the analysis of venous blood of patients with CAD, hyperglycemia initially on an empty stomach was 8.0 mM/l. By the end of the study, there was a 13-27% decrease in the content of G in serum in 50% of the examined patients in both groups, but the target level of G was not achieved.

Under the influence of antihypertensive therapy, all 43 patients managed to achieve a decrease in blood pressure by 25-30 mm Hg (by the end 138-142 versus 158-162 mm Hg at the beginning).

After 4 weeks of treatment, there was a moderate efficacy of basic nitrate therapy in patients in both groups, characterized by a decrease in the frequency and severity of AP attack.

Initially, the structure of the lipid profile differed from the norm by a pronounced increase in the level of atherogenic LDL-C and a significant decrease in the concentration of antiatherogenic HDL-C. In patients of group 2 (basic therapy) who received only basic standard therapy, there was no improvement in the blood lipid profile, in contrast to patients in group 3 (treatment with LEVOPA), where a significant decrease in elevated lipid parameters was achieved - the level of TC, TG and LDL-C.

By the end of treatment, a corrective effect of the neurotropic drug was noted in group 3 (basic therapy + L-DOPA). In 23 patients treated with L-DOPA, the content of TC by the end of treatment decreased by 23.5%, while the concentration of HDL-C increased by 15%. It is important to note that the content of LDL-C at the end of treatment decreased by 13.9%, and the calculated cholesterol index IA was 2 times lower than that in patients of group 2 who received only basic therapy for CAD.

In the main group 3 of patients under the influence of LEVOPA, in comparison with the initial values, a decrease of 20% in the level of G, by 31.2% in the content of NEFA and by 45% in the concentration of CS in the blood plasma of patients was found, in contrast to patients of group 2 (basic therapy for CAD). Probably, this is due to the stress-protective effect of drug.

It is interesting to notice, in this group of patients who additionally received LEVOPA, there was the significant decrease (19% and 21%) in the level of DC and MDA, reflecting the state of LPO, which indicates the presence of the antioxidant property of L-DOPA.

Conclusion

Should be emphasized, in the short report about the presented clinical study, performed on a small cohort of 43 patients was and remains the only and original one. Until now there are no similar studies with using L-DOPA found.

The drug L-DOPA, which in experimental and preliminary clinical research has a pronounced lipid-lowering effect and anti-ischemic action, was used with positive results in a clinical set-ting as a metabolic drug in patients with CAD in the complex treatment of low doses - 0.5 g 3 times per day for 4 weeks. It is important to point out that in this small cohort of patients with CAD, burdened mainly by DLP and AH, it was possible to achieve a significant correction of biochemical indicators of homeostasis and improve the quality of life of patients.

Patients with comorbid pathology were discharged from the clinic 3-5 days earlier than usual with good well-being.

By the end of the study, patients receiving additional LEVOPA lost an average of 1.7 kilo-grams. This fact is positive, but was not the goal of presented clinical study and in the future would need additional verification.

Thus, as a result of complex therapy with the use of the drug LEVOPA for 4 weeks contributed to improvement in the lipid spectrum of blood.

It was observed accompanying decrease in the levels of G, NEFA and hormone CS were observed with normalization of the values of the studied substrates and increased stress resistance.

The positive effect of the course of treatment with LEVOPA was combined without any side effects from liver and other organs which assessed only visually, but not in details.

The manifestation of the effectiveness of L-DOPA can be explained by the preliminary good preparation of patients for investigation, use of a cholesterol-lowering diet and by the higher sensitivity to drug therapy despite the aggravating factors of residential patients (elderly men). It is possible that the beneficial curative effect was influenced by the ability of L-DOPA to reduce the activity of sympathoadrenal system.

As the main conclusion, L-DOPA can be considered is really active metabolic agent with its own original complex action for the correction of socially significant comorbid diseases.

Inspired by the result, we believe more research is needed and we look forward to further clinical studies and more extensive research will allow us to more deeply assess the multifaceted properties of L-DOPA.

Compliance with ethical standards

The clinic investigation was carried out with humanity and approved by Ethics Committee of the State Medical University named after IP Pavlov. All the patients had informed consent.

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Conflicts of interest

There is no conflict of interest.

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