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Kosimov Zafarbek Odiljon ugli
Department of Pharmacology, Clinical Pharmacology and Medical Biotechnology
Andijan State Medical Institute

THE USE OF DRUGS THAT ACTIVATE AND CORRECT METABOLISM

Resume: The article presents modern ideas about the pharmacodynamics of the main groups of antihypoxants. Based on the analysis of literature data and own experimental studies, the mechanisms of antihypoxic activity of direct and indirect energizing drugs are discussed. The issues of clinical efficacy and the use of drugs with antihypoxic activity in medical practice are considered.

Keywords: hypoxia, antihypoxants of direct energizing action; antihypoxants of indirect energizing action; pharmacological correction of hypoxia.

Косимов Зафарбек Одилжон угли
Кафедра фармакологии, клинической фармакологии и медицинской биотехнологии
Андижанский государственный медицинский нститут

ПРИМЕНЕНИЕ ПРЕПАРАТОВ, АКТИВИРУЮЩИХ И КОРРЕКЦИОННЫХ ОБМЕН ВЕЩЕСТВ

Резюме: В статье изложены современные представления о фармакодинамике основных групп антигипоксантов. На основании анализа данных литературы и собственных экспериментальных исследований обсуждаются механизмы антигипоксической активности препаратов прямого и непрямого энергизирующего действия. Рассматриваются вопросы клинической эффективности и применения в медицинской практике лекарственных препаратов с антигипоксической активностью.

Ключевая слова: гипоксия; антигипоксанты прямого энергизирующего действия; антигипоксанты непрямого энергизирующего действия; фармакологическая коррекция гипоксии.

Introduction. In subsequent years, compounds of a different chemical structure (cytochrome C, ubiquinone, hypoxene, mexidol, etc.) significantly expanded the class of antihypoxants, and today it is already quite an impressive independent class of pharmacological substances. Currently, the discussion of the pharmacology of antihypoxants has ceased to be purely experimental and theoretical. The accumulated database of experimental data, successful clinical studies have allowed many compounds to find their clinical application [3,4].

The view of which drugs can be attributed to antihypoxants proper has undergone a number of changes over time. Since the main indicators of hypoxia are violations of energy metabolism, then the protection of the body from hypoxia should consist, first of all, in restoring the energy balance of the cell. Therefore, currently antihypoxants are commonly called substances of a metabolic type of action that can correct energy metabolism disorders and their consequences and thereby increase the resistance of cells, organs and the body as a whole to lack of oxygen and other influences that disrupt energy production. [2,4,5].

Today, antihypoxants are increasingly prescribed as part of combined pharmacotherapy for various diseases accompanied by hypoxia and ischemia. If we outline the range of the main indications for the use of antihypoxants, then we can identify such significant areas of their use as neuroprotection, cardioprotection, hepatoprotection, gastroprotection, angioprotection.

The aim of the study was to evaluate the effectiveness of the use of the calcium antagonist of the dihydropyridine series with extended—acting nifedipine cordaflex RD in relation to blood lipid spectrum parameters.

Materials and methods of research. The study included 40 patients (13 postmenopausal women and 27 men) suffering from grade I-II hypertension [9]. The average age of patients was 52.71+/-9.14 years, the duration of hypertension was 8.11+/-3.14 years. The average baseline systolic blood pressure (SAD) was 168.1+/-17.7 mmHg, DAD - 108,4+/7,21 mmHg. The study did not include patients with symptomatic hypertension, valvular heart defects, autoimmune and endocrine diseases (except for insulin-dependent type II diabetes mellitus in the compensation stage), bronchial asthma, severe rhythm and conduction disorders, circulatory insufficiency of class III-IV (NYHA), unstable angina or stable angina of functional class III-IV, and also, a myocardial infarction suffered less than 3 months before the start of the study.

Results and their discussion. In most patients, certain risk factors for the development of cardiovascular complications were identified: already existing coronary heart disease, type II diabetes mellitus, impaired glucose tolerance, obesity, hypertriglyceridemia. In 80% of patients with hypertension, a combination of 2 or more risk factors was noted. Dyslipoproteinemia of type I and Ib was detected in 32 patients (80%), and hypertriglyceridemia - in 40 (100%). The presence of metabolic syndrome was determined by a combination of insulin resistance, hypertension, abdominal obesity, hyper-triglyceridemia (TG>2.2 mmol/L), a decrease in HDL levels below 0.90 mmol/l.

Patients continued to receive other medications necessary for the treatment of concomitant diseases. All patients included in the study were prescribed nifedi-pin (Cordaflex RD) in individually selected doses of 2040 mg per day with a double intake. The effectiveness criteria were determined: the content of total cholesterol (OHC), triglycerides (TG) and high-density lipoprotein cholesterol (HDL cholesterol) was determined in blood serum using enzyme kits from Randox on the "Centrifichem-600" autoanalyzer. LDL cholesterol was calculated using the formula Friedwald et ai.: LDL cholesterol (mg/dl) = HC-(TG/5+HDL cholesterol). The glucose content in capillary blood

was determined by the glucose oxidase method on the Exan-G glucose meter on an empty stomach and 120 minutes after taking 75 g of glucose. The content of immunoreactive insulin in blood plasma was determined on an empty stomach and 120 minutes after taking 75 g of glucose using standard Rio-Ins-PG-125 kits. The level of glycosylated hemoglobin (NI A1c) was determined by column chromatography using the Bio-Rad kit.

All studies were conducted before the start of treatment, 48 weeks later (when a stable hypotensive effect was achieved), 16 and 24 weeks after the start of taking Kordaflex RD.

When assessing the effect of Cordaflex RD therapy on lipid metabolism, there was no significant positive dynamics in the content of OHC after 8 and 16 weeks from the start of treatment.

One of the most important roles in ensuring the safety and effectiveness of prescribed pharmacotherapy, its rationalization is to determine the activity of metabolic enzymes that directly affect the pharmacokinetic parameters of drugs and the risk of adverse reactions.

Taking into account the urgency of this problem, a large number of methods for determining the activity of SUR isoenzymes by different methods using appropriate equipment have recently been developed.

The results of the research showed that the use of the authors' improved methodology for phenotypic determination of the activity of the isoenzyme SUR2C9 using HPLC with a mass spectrometric detector makes it possible to accurately, quickly and safely obtain all the necessary information about the activity of metabolism in an individual patient, and based on the information received, the doctor will be able to adjust the dosage of the prescribed drug. This will make pharmacotherapy safer, more rational, will help reduce the risk of adverse reactions and save money on their elimination.

It is known that in almost 50% of patients, hypertension is combined with resistance of peripheral tissues to the action of insulin (insulin resistance, IR)

and impaired glucose tolerance (HTG) as part of the metabolic syndrome. In studies conducted by J. Yip et al, it was shown that every fifth patient with insulin resistance develops severe cardiovascular and metabolic diseases (hypertension, coronary heart and brain disease, insulin-independent diabetes mellitus) over the next 5 years. In addition, H.R. Blak, Y.M. Reaven in his works [1] demonstrated facts proving that lowering blood pressure does not lead to a reduction in the risk of coronary heart disease if antihypertensive therapy is not aimed at correcting insulin resistance. In recent years, the question of the positive effect of calcium antagonists on the lipid spectrum and carbohydrate metabolism has been widely discussed [1,4,6]. The available data [3,4] suggest that long-acting dihydropyridine calcium antagonists (AK) may be first-line drugs in the treatment of hypertension in patients with metabolic disorders. Prolonged AK does not have an adverse effect on carbohydrate metabolism, the level of uric acid and lipids in the blood [2,5].

Conclusions. This study showed that 6-month treatment of patients with hypertension with MS with individually selected doses of Cordaflex RD is an effective treatment method, not only in terms of blood pressure figures, but also has a beneficial effect on lipid and carbohydrate metabolism, which may contribute to the wider use of this drug in the treatment of hypertension in patients with MS.

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