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У збірнику представлені матеріали 100 – ї підсумкової наукової конференції професорсько-викладацького персоналу вищого державного навчального закладу України «Буковинський державний медичний університет», присвяченої 75-річчю БДМУ (м.Чернівці, 11, 13, 18 лютого 2019 р.) із стилістикою та орфографією у авторській редакції. Публікації присвячені актуальним проблемам фундаментальної, теоретичної та клінічної медицини.

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There are several main problems of development of psychopharmacotherapy. The main of them is mass polypragmasy, that is, a widespread use of various combinations of psychotropic drugs. According to our research, up to 80-90% of patients, both in the hospital and outpatient, receive two or more psychotropic drugs. Unfortunately, combined therapy is often prescribed without sufficient grounds and the possibility of drug interactions is not taken into account. Thus, approximately one fifth of outpatients with schizophrenia, in addition to prolonged neuroleptics receive traditional antipsychotics or, more recently, atypical antipsychotics that can completely alleviate positive effects of the clinical effects of the previous ones.

The next problem is an increase in the number of patients in whom a previously effective pharmacotherapy is already ineffective. Despite the variety of psychotropic drugs available at the market and their declared high effectiveness, almost every third patient is not cured. And the reason is not only the development of drug resistance, but also the mainly ineffective combination of drugs. Special studies indicate that about 50% of the ineffectiveness of therapy is due to its inadequate use.

Another problem that causes relapse and contributes to the formation of therapeutic resistance, is the lack of compliance or failure of patients to the recommended treatment regimen. Up to 40% of ambulatory patients violate the treatment regime to such an extent that it significantly affects the effectiveness of treatment, and leads to errors in choosing the following methods.

The probability of development of side effects increases in direct proportion to the number of prescribed drugs. It is now evidenced that most psychotropic drugs are metabolized by the cytochrome P450 system. As a result, the level of drug metabolism decreases during their half-life increases in 4 and more times, which leads to the development of toxic effects. Therefore, the common use of agents metabolized by a single system of cytochrome P450 should be avoided.

Summing up the obtained data, it can be stated that indication of only one etiologically or pathogenetically substantiated medicinal product can deprive the patient of many complications and thus eliminates the need for the administration of a large number of drugs.

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INFLUENCE OF POTASSIUM CHANNELS ACTIVATOR FLOCALIN ON THE FUNCTIONAL STATE OF KIDNEYS IN CONDITIONS OF INCREASED VOLUME OF EXTRACELLULAR FLUID

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The essential characteristic of membrane ATP-sensitive potassium (K_{ATP}) channels is their sensitivity to disturbances in cellular bioenergetics. Subsequently, rapid activation and opening of K_{ATP} channels in response to decrease in ATP level, in particular under the conditions of ischemia and hypoxia, results in plasma membrane hyperpolarization and an increase in voltage dependent inflow of Ca^{2+} ions. The latter event is accompanied by a drastic disturbance of energy metabolism compliance with the functional needs of the cell and opens the metabolic routes for profound cellular pathology. First of all, the regulatory role of K_{ATP} channels in conditions of restriction of the cellular oxygenation was studied on cardiomyocytes and smooth muscular cells of blood vessels. As a result, pharmacological activators of these channels are introduced in the treatment of cardiovascular diseases. In recent years the convincing evidence of cardioprotective and vasolytic effects of the original fluoride-containing K_{ATP} channels activator Flocalin – N-(-4-difluoromethoxyphenyl)-N'-1,2,2-trimethylpropyl-N"-cyanoguanidine were obtained. Due to the presence of fluoride, Flocalin is more selective to K_{ATP} channels and less toxic in comparison to other representatives of potassium channels modulators, which makes it a promising pharmacological substance as physiological regulator and protector of metabolic processes disturbed under hypoxic and ischemic conditions. Overall homeostatic function of kidneys and participation of K_{ATP} channels in the biochemical processes that control kidney cells functions substantiate the research into the effects of K_{ATP} channels activators on the functional state of

kidneys. Our experimental research demonstrates that Flocalin decreases hypercreatininemia, increases creatinine excretion, diminishes sodium loss, and decreases proteinuria on the models of acute nephropathy. Obtained results confirm the ability of Flocalin to modify intrarenal mechanisms of the balance maintenance between glomerular and tubular processes.

The task of research was the investigation of changes in kidney function after repeated administration of ATP-sensitive potassium channels activator Flocalin in conditions of increased extracellular fluid volume.

The experiment was carried out on laboratory white rats on the 7-th day of Flocalin administration at a dose of 5 mg/kg, 10 mg per kg after 5 % water load. Urine and plasma levels of creatinine, sodium and potassium ions, urine levels of protein, pH, titrated acids, ammonium salts were determined. Statistical processing was performed with «Statgrafics». The significance of differences was assessed using parametric Student's t-test with the critical value $p \leq 0.05$.

It has been experimentally shown that multiple administration of the new fluorine-containing ATP-sensitive potassium channels activator Flocalin in conditions of hyperhydration in white rats leads to activation of filtration in nephron with preservation of glomerular permeability without any loss of protein with urine, inhibition of distal sodium reabsorption, maintenance of potassium reserve, intensification of diuresis and acid excretion.

Thus, changes in volume-, ion-, acid-regulatory and excretory kidney functions after administration of Flocalin at a dose of 5 and 10 mg/kg reflect renal effects of the fluoride-containing K_{ATP} channels activator in conditions of hyperhydration, directed on the maintenance of homeostatic activity of nephron due to regulation of glomerular filtration and tubular reabsorption. Our experimental data discover new aspects of pharmacodynamics of a new Ukrainian ATP-sensitive potassium channels activator Flocalin.

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RENAL EFFECTS OF MELATONIN IN CONDITIONS OF TOXIC NEPHROPATHY AND PINEAL HYPOFUNCTION

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It is known, that besides its main regulatory function melatonin possesses immunomodulatory, antioxidant, anti-apoptotic, anti-inflammatory and antitumor activity (Reiter R., 2017). Nephroprotective effect of melatonin has already been established in numerous studies (Kapić D., 2014, Lee I., 2012). On the other hand, there is a few data concerning the influence of pineal hypofunction on the gentamicin nephrotoxicity, as well as efficacy of pineal hormone as a nephroprotector in these conditions.

The task of the research was to study the influence of melatonin on the functional state of rat kidneys under the conditions of gentamicin nephropathy against the background of pineal hypofunction.

Experiments were conducted on 28 non-linear male rats weighting 150-180 g and randomly divided into 4 groups (n=7): the I group – intact control, the II-IV group – simulation of pineal hypofunction (PH) by maintenance of rats in conditions of constant light (24.00 light : 0.00 darkness) for 7 days, the III-IV group – induction of gentamicin nephropathy by daily i/m administration of 4% gentamicin sulphate at a dose of 80 mg/kg for 6 days, animals of the IV group were injected i/p with melatonin at a dose of 5 mg/kg 1 h after every gentamicin injection. Functional state of kidneys was assessed 24 h after the last melatonin injection by the indices of excretory, ion-regulatory, and acid-regulatory kidney functions. Data were compared by Mann-Whitney test using SPSS Statistics 17.0.

Hypofunction of the pineal gland caused desynchronosis of kidney function, manifested by an increase in the excretion of sodium and potassium ions on the background of decreased diuresis and glomerular filtration rate. Administration of gentamicin against the background of pineal hypofunction led to the development of an oliguric form of acute kidney injury, which was