свидетельствуют об определяющем значении токов, активируемых при гиперполяризации (If) в адренергической регуляции ритма сердца.

Ключевые слова: регуляция работы сердца, If-токи, показатели работы сердечной деятельности, симпатическая иннервация сердца.

Aims. Studying of the effect of phenylephrine (FE) against the background of blockade of If-currents on the cardiac activity of rats of different ages.

Materials and methods. White non-fertile rats of 1-, 3-, 6-, 20 weeks of age in the amount of 35 individuals participated in the experiment. At the age of week 1, rats do not have sympathetic heart innervation. In 3-week-old rats, sympathetic innervation of the heart develops. The 6th week of postnatal development is the age of puberty, and the regulation system of the heart becomes unbalanced. 20-week-old animals have a fully established cardiovascular system. Use in experiments of both females and males was based on data showing no sex differences in the heart rate of male and female white rats between the ages of 1 and 24 months. For animal anesthesia, a 25% urethane solution was used, which was administered intraperitoneally at a dose of 800 mg/kg animal body weight. If ZD 7288 blocker (Sigma) 0.07 mg/kg, non-selective agonist α -AP FE (Sigma) 0.1 mg/kg was injected into the right femoral vein. Throughout the experiment, computer processing of the ECG and the indicators of the variation pulsogram was carried out.

Results. Administration of FE against the background of the action of the If ZD-7288 blocker causes a reliable reduction in cardiac activity of 6 and 20-week-old rats. In adult rats, α -AP agonist was administered against the background of ZD-7288 action, a two-phase cardiac rhythm gain was observed. In 3 and 1-week-old rats, no change in heart rate after FE administration was observed against the background of If blocker action.

Conclusions. The results allow expanding ideas about the mechanisms of regulation of heart function. Blockade of If in adult animals had no effect on the stimulation effect of α -AP. In 3 and 1-week-old rats, the If blockade removed the bradycardic effect of FE. The data confirm the presence of synthesis of HCN4 channels as the equivalent of If currents long before the formation of a full-fledged sympathetic innervation of the heart.

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Shakirova A.T., Zamirbekova K.Z., Khalikova A.U.

The using of ursodezoxicholic acid in treatment of acne rosacea

*I.K. Akhunbaev Kyrgyz State Medical Academy
(Kyrgyz Republic, Bishkek)*

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Abstract

Under clinical observation were 30 patients with different clinical forms of acne rosacea. A lot of patients have functional and organic disturbances of hepatobiliary system, which were confirm by laboratorical tests. The using of ursodezoxicholic acid leads to regress of clinical signs and normalization of labolatoric analyses.

Keywords: rosacea, ursodezoxicholic acid, ultrasonic research, liver enzymes, lipid fractions.

Аннотация

Проведено клиническое наблюдение 30 больных различными формами розацеа. У большинства больных выявлены функциональные и органические нарушения со стороны гепатобилиарной системы, подтвержденные лабораторными методами исследований. Применение препаратов урсодезоксихолевой кислоты способствовало регрессу клинических проявлений и нормализации лабораторных анализов.

Ключевые слова: розацеа, урсодезоксихолевая кислота, УЗИ, печеночные тесты, липиды.

Introduction. Rosacea is a chronic recurrent dermatosis of the skin of the face, characterized by erythema, papules, pustules, nodules, as well as foci of hyperplasia of the sebaceous glands and connective tissue. The defeat of the central part of the face is associated with the maximum susceptibility of this zone to various external influences, intense vascularization, high receptor sensitivity, inactive muscles and functional disorders of venous outflow.

Rosacea refers to middle-aged dermatoses, the first signs of the disease can be observed at 25-35 years old, reaching maximum severity by 40-50 years. Traditionally, it is believed that the disease often occurs in women, which is due to the more frequent use of medical care compared to men [1,3]. Later forms (rhinophyma, Morbigan's disease) are more marked in men.

Despite the fact that the etiology of rosacea remains completely undefined, various triggers contribute to the development of this condition [Morgulis Yu.V., Potekaev N.N., Korsunskaya I.M., 2009, Adaskevich V.P., 2005], namely : burdened heredity, immunity disorders, psychosomatic disorders, diseases of the gastrointestinal tract and hepatobiliary system, pathology of the endocrine system, vascular pathology. Also influenced by alimentary (alcohol, coffee, hot drinks, spices, seafood), physical (insolation, heat, cold, ionizing radiation), demodex folliculorum - glandular, which is an optional saprophyte [3,8]. A significant role is played by disturbances in the regulation of cerebral effects on the blood vessels of the facial skin (slowing down the redistribution of blood flow, the development of venous stasis in the outflow area of Venae facialis sive angularis; this area also includes the conjunctiva) [5].

The development of rosacea leads to severe psychological trauma, which reduces the social adaptation of patients [Darvey E., Chu T., 2005]. Acne rosacea is not a disabling and fatal disease, but they often cause anxiety, depression, which can sometimes lead to suicidal attempts [Thiboutot D.M., Diane M., 2003].

None of the etiological factors is universal for all rosacea patients. Most likely, rosacea is a certain reaction to various factors, and the main importance belongs to the pathological reaction of the vessels, which develops under the influence of vasoactive peptides, antibodies, circulating immune complexes and other irritants [Kudrina M.I., Potekaev N.N., Potekaev S.N. , Lvov AN, 1998].

Despite the large number of studies on the etiology, pathogenesis and treatment of rosacea, many questions still remain unexplored. Until now, the role of dysfunctions of the organs of the hepatobiliary system in the pathogenesis and clinical course of acne rosacea has not been finally determined [Kolesnichenko SA, 1999; Temnikov V.E., 2000]. Studies devoted to the study of the functional state of the hepatobiliary system in patients with rosacea are fragmentary and insufficiently informative [4]. The pathogenetic significance of metabolic disorders in the liver has not been proven, and therefore a more detailed study of the hepatobiliary system (enzymes of the hepatic profile) and the effect of hepatotropic drugs on the effect of the skin process in rosacea looked relevant.

Modern medicinal products of pathogenetic therapy have aggressive properties, causing undesirable side effects, require the use of high doses in order to achieve a cumulative dose and ensure prolonged remission or cure for a long time [5,6]. Rational treatment of patients with rosacea involves a simultaneous effect on all links of pathogenesis, which increases the relevance of studies to expand possible methods of therapy against the background of disorders of the hepatobiliary system.

The aim of the study was to evaluate the effectiveness of ursodeoxycholic acid preparations in the complex therapy of various forms of rosacea.

In this regard, the possibility of clinical application of ursodeoxycholic acid, which is a tertiary bile acid formed under the action of bacterial enzymes from 7-keto-lithocholic acid, which enters the liver from the small intestine, has been evaluated. Human bile contains trace amounts of UDCA - 0.5-3%. Evaluation of the effectiveness of ursodeoxycholic acid preparations ("Ursofalk", "Ursosan", "Choludexan"), possessing, in addition to the main anticholestatic action, also hepatotropic, antioxidant, immunomodulatory, cytoprotective, hypocholesterolemic, litholytic effects [Nadinskaya M.Yu., 2003; Tkachev A.V., Shavkuta G.V., Bogatyrev V.G., 1999]. Used to treat gallstone disease caused by cholesterol stones, as well as chronic hepatitis, hepatosis and alcoholic liver disease, primary sclerosing cholangitis, biliary gastritis and esophagitis. The use of these drugs is based on numerous observations of patients with a pathology from the gastrointestinal tract, namely the hepatobiliary system.

Material, methods and research results. The study included 30 patients suffering from various forms of rosacea at the age from 33 to 64 years (average age - 48.5 years). Men - 17 (57%), women - 13 (43%). Disease duration ranged from 2-3 to 10 years or more (average duration - 4-5 years). The following forms of the disease were observed: erythematous - 13 patients (43%), papulopustular - 12 (40%), Morbigan's disease - 2 (6.6%), rhinophyma - 1 (3.3%), ophthalmic rosacea - 2 (7 %). Among the trigger factors for the development of rosacea are noted: dysfunctions of the digestive tract - 18 patients with gastritis, cholecystitis, biliary dyskinesia (60%), polyendocrinopathy - 7 patients (23%), insolation - 3 patients (10%), irrational use of corticosteroid ointments - 2 patients (7%). It should be noted that taking hot drinks and alcohol caused erythema on the face in 20 patients (66%). Redness was initially temporary, accompanied by a feeling of heat, but after exposure to provoking factors it reappeared (rosacea diathesis) [Jansen T., Plewig G., 1996].

To identify possible reasons for the development of rosacea and their timely correction in patients, general blood and urine tests, blood glucose, sex hormones (progesterone, estradiol, testosterone), hormones (T3, T4, TSH) and ultrasound of the thyroid gland, ultrasound of the pelvic organs were studied, kidneys. To assess the state of the hepatobiliary system, biochemical and ultrasound examinations were carried out. Biochemical analyzes were carried out in accordance with generally accepted recommendations (V.V. Menshikov, L.N.Delektorskaya, R.P. Zolotnitskaya et al., 1987). Were investigated: the level of concentration in the peripheral blood of ALT, AST, lipid fractions - total cholesterol, triglycerides, high and low density lipoproteins, total bilirubin, direct, indirect, thymol test. Ultrasound of the liver and biliary tract was carried out according to generally accepted methods with the determination of the main echographic parameters: the thickness of the right and left lobes, the structure and echogenicity of the liver parenchyma, its vascular pattern, the diameter of the portal vein. The shape, size, condition of the cavity, walls of the gallbladder and its contractile function were also determined; the size of the spleen and the echogenicity of the pancreas [11,12].

Results and its discussion. Among the concomitant diseases were noted: chronic gastritis - 4 patients (13%), chronic cholecystitis - 18 patients (37%), chronic hepatitis in 4 patients (13%), the phenomena of fatty liver hepatosis were detected in 6 patients (20%), in 4 patients - the presence of chronic pyelonephritis (13%). The course of the disease was aggravated by the presence of an acne tick (*Demodex folliculorum*) - in 9 patients (30%) in the papulopustular stage.

In the study of a general blood test in 5 patients (16%), a decrease in the level of hemoglobin is observed (anemia of I and II degrees). The study of liver transaminases made it possible to reveal in patients with moderately elevated levels of bilirubin increased AST activity - in 7 patients (23%), ALT - in 3 patients (10%). At the same time, in patients with various forms of rosacea, changes in the concentration of the lipid fraction were noted: there was an increase in cholesterol levels in 13 patients (43%) and low-density lipoproteins in 10 patients (33%); imbalance of triglyceride fractions was observed in 6 patients.

Ultrasound echography of the abdominal organs revealed the following functional disorders: an increase in the size of the liver - 10 patients (33%); heterogeneity of the structure of the liver parenchyma - 12 patients (40%), thickening of the walls (with inhomogeneous contents) - 7 patients (23%), deformities in the neck area - 6 (20%) and the body of the gallbladder - 7 patients (23%); expansion of the intrahepatic bile ducts - 11 patients (37%); an increase in the size of the gallbladder - 8 patients (27%), 20%). this phenomenon is caused either by stenosis of the sphincter of Oddi, or by a violation of the contractile function of the organ, and possibly by the proliferation of fibrous tissue in the neck of the gallbladder, and sometimes by a combination of all these signs [6]; violation of the contractile function of the gallbladder with symptoms of cholestasis was detected in 10 patients (33%); increased echogenicity, heterogeneity of the structure of the pancreas was found in 7 patients (23%); deformation of the image contours of the renal pyelocaliceal system with the presence of salt deposits was found in 4 patients (13%).

When analyzing anamnestic data from 30 observed patients, 22 (73%) had pathology of the gastroduodenal zone, 4 (13%) had previous hepatitis. In 10 (33%) patients, an increase in the activity of AST and ALT was found, which confirms the opinion of a number of researchers about the importance of the pathology of the hepatobiliary system in acne-rosacea [2,7]; 13 (43%) patients showed a change in the shape of the gallbladder. The fact of establishing anomalies in the shape of the gallbladder is considered important, because a clear connection between deformities of the bladder and functional disorders of the hepatobiliary system is determined [3].

All patients received the following treatment:

local

- in the erythematous stage - cold lotions with 1-2% boric acid solutions, dosage forms with metronidazole - 0.75-1% gel;
- funds with ichthyol, clindamycin (in the form of cream "Dalatsin-T", lotion);
- when combined with demodicosis - acaricidal agents - benzyl benzoate ointment 20%, Vidal's milk;
- in the papulopustular stage:
- skinoren - cream with 20% microionized azelaic acid (applied 1 t/d-2 weeks, then -2 t/d, duration - up to several weeks);
- washing the skin of the face with water of a contrasting temperature, wiping it with ice from yogurt, herbal infusions, vegetable and fruit juices.

systemic

- to "cover" the liver - hepatotropic drugs
- ursodeoxycholic acid - 10-15 mg / kg / day in 2 doses or at night - 10-15 days;
- hepabene 1-2 caps x 3 t/d - 14-15 days;
- with papular-pustular rashes - drugs of the imidazole group - metronidazole orally at 1-1,5 g/s during or after meals for 4-6-8 weeks (after 1 month the treatment was repeated) or tinidazole at 4 tablets / day (2,0 g) - 4-7 days under the cover of hepatoprotectors, vitamins C, E;
- antibiotics: roxithromycin 150 mg x 2 t/d - 7-10 days or azithromycin 500 mg x 2 t/d - 10 days.

Ursodeoxycholic acid preparations were prescribed at 10-15 mg / kg / day in 2 doses or at night from the first day of treatment for 10-15 days, were well tolerated, without side effects. Only 2 patients (7%) had loose stools. Significant clinical improvement after the first course of treatment was observed in 22 patients (73%), improvement in 5 (17%) and no changes in 3 (10%) patients. Improvement of the skin process in patients with rosacea was accompanied by a decrease in hyperemia and edema of facial tissues. All patients showed a decrease in seborrhea of problem areas of the skin and regression of papulo-pustular elements. A second course was prescribed 25-30 days after the first one. On average, complete clinical recovery of patients required 3-4 courses of pathogenetic therapy at intervals of 1-1.5 months. After the course of treatment, the dynamics of laboratory parameters was noted in all observed patients, which was accompanied by a decrease in

the level of transaminases, cholesterol and low density lipoproteins to normal values. It should be noted that not only the condition of the skin has improved, but also the psychoemotional state of the patients.

Conclusions. The use of ursodeoxycholic acid preparations in the complex therapy of various forms of rosacea made it possible to obtain a clinical cure in 73% of patients, a significant improvement in 90% of cases. The duration of the first course of treatment was 15-20 days, the subsequent preventive courses for 7-10 days. The observation period is 1.5-2 years. No relapses were observed. The method of treatment did not require high material costs, was simple to administer, highly effective, and did not have a large number of side effects characteristic of retinoids. Treatment with ursodeoxycholic acid preparations can be carried out both in inpatient and outpatient settings.

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