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THE EFFECT OF ANTIDEPRESSANT THERAPY ON ANXIETY AND DEPRESSIVE DISORDERS IN PATIENTS WITH CORONARY HEART DISEASE

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ABSTRACT: The purpose of the study. An open, randomized, comparative study of the efficacy, safety and evaluation of the effect of paroxetine and hydroxyzine hydrochloride therapy on platelet serotonin levels in patients with coronary heart disease (CHD) with comorbid anxiety and depressive disorders with a predominance of the anxiety component was conducted.

Materials and methods. The study included 40 patients with chronic coronary heart disease with comorbid mixed anxiety and depressive disorders. Diagnosis of anxiety-depressive disorders were established according to ICD-10. The study included patients who scored 18 or more points on the Hamilton anxiety and depression scales. Results. During treatment with both hydroxyzine hydrochloride and paroxetine, a significant decrease in scores on the Hamilton anxiety and depression scales was observed after 4 weeks, and after 8 weeks the decrease reached 50%. Side effects were observed during treatment with both drugs and quickly passed after their withdrawal. Platelet serotonin decreased significantly during paroxetine therapy.

Conclusions. It is established that treatment with both paroxetine and hydroxyzine hydrochloride is characterized by high anti-anxiety and antidepressant activity. Treatment with paroxetine is characterized by a significant decrease in platelet serotonin.

Keywords: depression, anxiety, coronary heart disease, paroxetine, hydroxyzine hydrochloride.

INTRODUCTION

The problem of comorbidity of coronary heart disease (CHD) and affective disorders of the anxiety-depressive spectrum is widely discussed in modern scientific literature. Various studies have proven that depression is an independent risk factor for the development and progression of coronary heart disease. Anxiety is also associated with dangerous cardiovascular events, being their predictor in patients with coronary heart disease. Often there are mixed anxiety-depressive

disorders. Both selective serotonin reuptake inhibitors (SSRIs) and various tranquilizers, including non-benzodiazepine ones, are used to treat these disorders.

At the same time, only 10% of CHD patients with comorbid affective disorders receive adequate therapeutic care. Currently , the number of studies that have studied the

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effectiveness and safety of treating anxiety-depressive disorders with drugs from these groups in patients with coronary heart disease is small. In this regard, an open, randomized, comparative study was conducted efficacy, safety and evaluation of the effect of paroxetine and hydroxyzine hydrochloride therapy

on platelet serotonin levels in patients coronary heart disease with comorbid anxiety-depressive disorders with a predominance of the anxiety component.

MATERIALS AND METHODS OF RESEARCH

The study included 40 outpatient patients aged 38 to 75 years with chronic Coronary heart disease: angina pectoris of functional class II — 22 people, angina pectoris Functional class III — 18 people, all patients had suffered a myocardial infarction in the past. The study included patients who had received standard CHD therapy for at least two previous months: beta-blockers, statins, disaggregants, angiotensin converting enzyme (ACE) inhibitors.Comorbid pathology in the study participants was mixed anxiety and depressive disorder, established according to ICD-10. The intensity of affective disorder was determined using the anxiety scales and Hamilton depression. The study included patients who scored 18 points or more on two Hamilton scales. All patients signed an informed consent to participate in the clinical trial. The study did not include patients with unstable angina pectoris, functional class II–IV heart failure, impaired cerebral circulation in the past, and heart attack myocardial infarction, suffered less than 6 months before the start of the study, and patients with other severe somatic diseases.

Patients were randomized to therapy with paroxetine (20 people) or hydroxyzine hydrochloride (20 people), using random number tables, using the "asymmetric coin" method. The initial dose of paroxetine was 10 mg, hydroxyzine hydrochloride — 25 mg. If necessary, at subsequent visits conducted at 2-week intervals, the dose of paroxetine was titrated to 20 or 40 mg, the dose of hydroxyzine hydrochloride to 37.5 or 50 mg. The duration of therapy was 8 weeks. Clinical and psychological examination using Hamilton scales was carried out during the visits. At the first and final visits, the patients, having come to the visit

on an empty stomach, donated blood in the morning to study the concentration of platelet serotonin. Venous blood was collected in test tubes containing ethylenediaminetetraacetic acid (EDTA). After further sample preparation and removal of the filler liquid, the resulting substrate was stored in a freezer at a temperature of -20 0 With during 4 weeks. Statistical data processing was performed using the statistical package SPSS 15.0. The data is presented in the form of M ± SD, where M is the average value of the value, SD is the standard deviation. Statistically significant differences between groups with continuous parameters were studied using the Mann-Whitney test, and for dependent random variables — the Wilcoxon test.

THE RESULTS AND THEIR DISCUSSION

The eight-week study was completed by 29 people (15 patients in the hydroxyzine hydrochloride group and 14 in the paroxetine group). Against the background

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of hydroxyzine hydrochloride treatment, 5 patients stopped the study within 2-8 days due to the following side effects, possibly related to taking the drug: one patient had memory impairment; one had irritability, bradycardia; one had sweating, weakness, headache; another patient had weakness, a feeling of intermittent breathing the work of the heart. Two weeks later, one patient's eyesight deteriorated, which it also led to the cancellation of the drug. Early discontinuation of therapy in the paroxetine group during the first days was associated in two patients with increased anxiety; in two more — with the appearance of severe fatigue, weakness; in one patient, hypotension and bradycardia appeared. Contact with one patient was lost during the first two weeks. One patient's eyesight deteriorated, but this did not lead to the cancellation of the investigational drug. All adverse events during treatment with both drugs were considered as possibly related to the studied drug means, and they passed quickly after their cancellation. There were no significant differences in the number of adverse events. During hydroxyzine hydrochloride therapy, after 4 weeks, manifestations of anxiety decreased (from 22.7 ± 1.3 to 12.3 ± 1.2 points) and depression (from 17.4 ± 0.9 to 10.6 ± 1.3 points on the Hamilton scale, $p \leq 0.01$), after 8 weeks this pattern remained, scores decreased by more than 50 % (up to 10.3 ± 2.2 on the anxiety scale and up to 6.3 ± 1.5 on the depression scale, $p \leq 0.01$). Against the background of paroxetine treatment, a similar dynamics was observed: after 4 weeks of anxiety manifestations and depression decreased significantly: on the anxiety scale from 21.5 ± 2 to 15.7 ± 2.1 points ($p < 0.01$) and on the depression scale from 18.9 ± 1.3 to 13 ± 2 points ($p < 0.05$), after 8 weeks this pattern remained and the scale parameters decreased by more than 50%: on the anxiety scale — up to 7 ± 2 points, on the depression scale — up to 4.7 ± 1.7 points ($p < 0.05$). Within the framework of the conducted research, the following has been studied platelet serotonin concentration, which decreased during drug treatment, but only with paroxetine therapy, the platelet serotonin content decreased significantly ($p < 0.05$). The side effects, probably related to taking the drugs, were not serious and passed quickly after their withdrawal. When treated with paroxetine, the side effects were mainly somatic in nature, in particular, weakness, visual impairment, and increased anxiety were noted. According to other studies, the side effects of paroxetine treatment were nausea, headache, agitation, anxiety, asthenia, diarrhea, anorexia, dizziness, dry mouth, tremor, sweating, constipation, visual impairment, decreased libido. Of the side effects associated with cardiovascular system, one patient in our study had bradycardia and hypotension. Perhaps it was a coincidence. In a comparative study of paroxetine and nortriptyline in patients with coronary heart disease with depressive

disorders, no clinically significant side effects were found with respect to the effect on heart rate and blood pressure. During hydroxyzine hydrochloride therapy, our patients noted weakness, headache, sweating, irritability, memory impairment, and visual impairment among the side effects. Placebo-controlled studies evaluating the efficacy and safety of hydroxyzine hydrochloride in patients with generalized anxiety disorder described the following adverse events that prevented participants from continuing the study: colitis, depression, drowsiness, agitation associated with various pains, headache.

CONCLUSIONS

Thus, the use of both hydroxyzine hydrochloride and paroxetine in patients Coronary heart disease with comorbid mixed anxiety-depressive disorders with a predominance of the anxiety component is characterized by high anti-anxiety and antidepressant activity and the

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absence of serious side effects. Paroxetine therapy is also associated with a decrease in platelet serotonin levels.

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