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CITICOLINE CLINICAL EFFICIENCY IN COMPLEX TREATMENT OF POSTRESUSCITATION SYNDROME

Summary. The problem of global cerebral dysfunction at postresuscitation syndrome (PRS) remains topical today. Until recently for the correction of central nervous system disorders there was used, and is used by most doctors, piracetam. We had carried out the examination of 2 groups of patients (group A and B) with PRS after successful resuscitation. They were administered with Citicoline and piracetam secondary to standard set of intensive care. The use of Citicoline in intensive care of PRS was proved. The Citicoline positive influence on the level and duration of impairment of consciousness was shown as well as promotion to more progressive recovery of mental functions at PRS.

Key words: postresuscitation syndrome, global cerebral dysfunction, Citicoline, piracetam.

Introduction

To this day, one of the most important problems of reanimatology is the problem of minimizing the residual phenomena of postresuscitation syndrome (PRS). Disorders of a complex nature (hypoxic, dysmetabolic, circulatory, etc.) arising in the process of clinical death and immediately before it (critical condition, pre-agony and agony), and subsequently determine the entire completeness of the clinical picture of postresuscitation syndrome ... It is no secret that recently, in a duel between PRS and resuscitators in the arsenal of the latter, a number of drugs have appeared that help in the elimination of the aforementioned disorders on the somatic histoorganic bridgehead, while on the front of the central nervous system these successes are much more modest, due to the structural features , blood supply, metabolism and regulation-autoregulation of this system. The emergence and / or aggravation of encephalopathy of mixed genesis in the early postresuscitation period significantly complicates the work of a doctor, and indeed of all medical personnel, with this category of patients [6, 9]. Until now, the modern pharmaceutical industry has not offered clinicians a drug with a significant, proven neuroprotective effect from the standpoint of evidence-based medicine (Controlled Clinical Trials, CCT; Good Clinical Practice, GCP; The Cochrane Collaboration) [11].

Resuscitators are forced to use outdated, from our point of view, drugs with unproven efficacy, such as piracetam, to solve this problem. Piracetam is a nootropic drug, is a derivative of y-aminobutyric acid and belongs to the racetam class, used to improve metabolic processes in the cerebral cortex. The drug is used in neurological, psychiatric and narcological practice. As a result of

the drug's action, the concentration of ATP in the brain tissue increases, the biosynthesis of ribonucleic acid and phospholipids is enhanced, and glycolytic processes are stimulated. The randomized, multicenter, placebo-controlled PASS (Piracetam in Acute Stroke Study) study showed no efficacy of piracetam in the treatment of acute ischemic stroke. The revealed results of the use of piracetam are similar to the action of placebo. Currently, piracetam is excluded by the FDA from the list of medicines and belongs to biologically active additives (BAA) [7, 8, 11]. Since 2008, a new representative has appeared in our arsenal of medicines - citicoline (Ceraxon), a fundamentally new drug with a polymodal mechanism of action.

Under conditions of ischemia, under the action of phospholipases, activated by a sharp increase in the concentration of calcium in cells, phosphatidylcholine decomposes with the formation of free fatty acids (including arachidonic acid) and free radicals, which leads to lipid peroxidation and oxidative stress. Exogenous citicoline introduced into the body as a result of hydrolysis in the intestinal wall and liver breaks down into its main components cytidine and choline, which enter the systemic circulation and participate in various metabolic processes. They cross the blood-brain barrier, after which citicoline is resynthesized from them in the brain cells. The bioavailability of the drug for oral and parenteral administration reaches 100%. Experimental data indicate that citicoline has a pleiotropic effect in cerebral ischemia, counteracting the progression of ischemic tissue damage. First of all, citicoline enhances the resynthesis of phospholipids of the cell membrane (membranotropic effect), contributing to the repair and stabilization of the membranes of neurons and their organelles, primarily mitochondria. Moreover, it was shown that citicoline promotes the restoration of the level of other phospholipids of cell membranes (apparently, by reducing the release of arachidonic acid and preventing the activation of phospholipase A2). Membranotropic action of the drug may be associated with its ability to restore the activity of N + -K + -pumps. In addition, citicoline can increase the level of glutathione and the activity of glutathione reductase, enhancing the activity of antioxidant systems. By reducing the permeability of the blood-brain barrier, the drug can help to reduce the severity of cerebral edema, which plays an important role in the development of secondary brain damage. The neuroprotective effect may also be associated with a decrease in glutamate release, which weakens the ischemic cascade at its early stage [1, 4].

Experimental models of focal ischemia have demonstrated the ability of citicoline to inhibit the activation of procaspases, which counteracts the processes of apoptosis. The joint administration of citicoline and a thrombolytic carried out in the experiment led to a decrease in animal mortality compared with thrombolytic therapy alone and demonstrated the ability of citicoline to reduce the severity of reperfusion brain damage. The ability of citicoline to enhance the activity of the cholinergic, dopaminergic and noradrenergic systems may also be of great importance, which at the stage of restoration of functions can enhance plasticity processes and reduce the severity of neuropsychological

disorders [1-4, 10, 11].

Purpose of the study. The aim of this work is to identify the clinical efficacy of citicoline (Ceraxon) in a complex of intensive therapy with ORS. The study was conducted on 2 groups of patients: group A - standard intensive therapy ORS + citicoline (Ceraxon); group B - standard intensive therapy ORS + piracetam.

Material and methods

The study involved 73 patients: 40 men and 33 women, the average age of which was 59 years, who underwent a state of clinical death, with successful resuscitation measures. At the time of the study, all patients were treated in the intensive care unit (RIT) of the St. Trinity ICD in the period from 2008 to May 2010. The severity of the condition of these patients was due to such reasons as the syndrome of endogenous intoxication, the syndrome of acute cardiovascular and / or cardiopulmonary insufficiency, the syndrome of intestinal insufficiency, the ALP / ARDS syndrome, the SVR syndrome, the global brain dysfunction syndrome, etc. 2 groups by blind (random) randomization:

- group A - 36 patients who underwent standard intensive therapy with ORS + citicoline (Ceraxon);
- group B - 37 patients who received standard intensive therapy with ORS + piracetam.

Method of prescribing citicoline (Ceraxon) and piracetam

Citicoline was prescribed in a dose of 1000 mg per 250 ml of physiological solution or 5% glucose twice a day by intravenous drip.

Piracetam was administered at a dose of 4500 mg per 250 ml of physiological solution or 5% glucose twice a day intravenously. Both drugs in these doses were prescribed on time, strictly individually, depending on the regression of neuropsychiatric symptoms, with the subsequent transition to a different dosage regimen and route of administration or complete withdrawal of the drug. The effectiveness of the use of these drugs was assessed daily according to the following parameters:

- neuropsychiatric objective examination using scales;
- Glasgow Coma Scale (GCS);
- Pittsburgh Brain Stem Assessment Scale (PSCM);
- Brief scale for assessing mental status (Mini Mental State Examination, MMSE) [5];
- CT scan of the brain to exclude the development of secondary ischemic and / or hemorrhagic foci;
- EEG in case of convulsive syndrome development.

Research results and their discussion

During treatment in the RIT department, all patients in the early postresuscitation period showed positive dynamics in terms of neuropsychiatric symptoms while taking the above drugs. In group A, regression of symptoms was noted by the beginning of the second day, with its almost complete disappearance by the end of the third - the beginning of the fourth day, which led to a subsequent decrease in doses and frequency of citicoline administration

or its complete cancellation. In group B, the regression of symptoms was somewhat delayed and was noted on the third - the beginning of the fourth day, which caused the continuation of the administration of piracetam in the above dose for 5-7 days, followed by a decrease in the dose and frequency of administration. When piracetam was prescribed at a dose of 9000 mg / 24 hours in 31.7% of cases, such undesirable effects as increased motor and speech excitement, increased spatial and temporal disorientation were observed, which made it necessary to prescribe additional drugs of a sedative-tranquilizing nature. In the case of using citicoline, these effects were observed in 12.2%. Initially, the impairment of consciousness in both groups was "11-12 p. According to the GCS, but in group A the progress of the point up to 15 p. Averaged 26 ± 3 hours, while in group B it was 36 ± 2 hours. According to the MMSE scale, initially, the data in both groups were 24 ± 2 points with an increase to 28 ± 1 points by the end of the second day in the case of citicoline use and by the end of the third to the beginning of the fourth day when using piracetam [5]. In 5 patients, CT examination of the brain revealed bilateral lacunae without signs of a fresh process, and in 3 patients - punctate hemorrhages in the cerebral hemispheres, which did not play a negative role in the evolution of ORS during therapy. EEG, carried out according to the indications of patients of both groups, did not reveal the organic nature of epileptic activity in any of the cases. In the delayed period, 12 patients died from the incurable complications of the underlying pathology.

In conclusion:

1. The use of citicoline in the complex of measures of intensive therapy of ORS causes a shorter duration of the period of impaired consciousness.

2. The use of citicoline is justified from the point of view of a more progressive restoration of mental functions in case of PRS.

3. The polymodal mechanism of action of citicoline makes it possible to practically not resort to prescribing other drugs that affect the central nervous system during the therapy of ORS.

Literature:

1. Warach S.J., Pettigrew L.C., Dashe J.F. et al. Effect of citico-line on ischemic lesions as measured by diffusion-weighted magnetic resonance imaging // Ann. Neurol. - 2000 .-- 48 .-- 713-722.

2. Adibhatla R.M., Hatcher J.F., Dempsey R.J. Citicoline: neuroprotective mechanisms in cerebral ischemia // J. Neurochem. - 2002. - 80. - 12-23.

3. Adibhatla R.M., Hatcher J.F. Cytidine 5'-diphosphocholine (cdp-choline) in stroke and other cns disorders // Neurochem. Res. - 2005. - 30. - 15-23.

4. Fioravanti M., Yanagi M. Cytidinediphosphocholine (cdpcholine) for cognitive and behavioral disturbances associated with chronic cerebral disorders in the elderly. http: //www.cochrane. org / reviews /

5. Mishchenko T.S., Shestopalova L.F. Clinical scales and psychodiagnostic tests in the diagnosis of vascular diseases of the brain // News of Medicine and Pharmacy. - 2009 .-- 277.

6. Gusev E.I., Skvortsova V.I. Cerebral ischemia. - M .: Medicine, 2001 .-- 327.
7. Avrutskiy G.Ya., Niss A.I. Pharmacology of nootropics. - M., 1989. - 112-118.
8. Voronina T.A. Pharmacology of nootropics. - M., 1989 .-- 8-19.
9. Karavaeva I.P., Zhirov I.V., Sterkhova L.M. et al. Successful therapy of posthypoxic encephalopathy after cardiac arrest in acute myocardial infarction // Bulletin of RUDN. Medicine series. - 2002 .-- 2. - 98.
10.http: //www.ceraxon.ru/
11.http: //www2.cochrane.org/