Prospects Of Pharmacological Treatment Of Vascular Dementia In Patients With Arterial Hypertension

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Abstract - The article presents research data from 60 patients with vascular dementia. All subjects were divided into 2 groups: 1st group - 30 patients who received choline alfoscerate on the background of basic therapy; and group 2 - 30 patients who received only basic therapy. The effectiveness of therapy was evaluated twice: before treatment and on day 40 of treatment. The status was assessed using the VAS scale (visual-analogue scale for pain), according to the questionnaire for identifying vegetative disorders and determining the vegetative dystonia syndrome (VDS), according to the severity of vegetative reactivity according to the Danyini-Ashner test, and the Hamilton anxiety and depression test. A reliable nootropic effect of the drug was revealed, as well as its effect on cerebrosthenic and somatovegetative manifestations. There were no serious adverse events requiring additional measures.
Key words - vascular dementia, arterial hypertension, vegetative dystonia syndrome, headache, choline alfoscerate.

1. INTRODUCTION

Vascular dementia (VD) is a fairly common condition among the elderly and is characterized by severe cognitive dysfunction [3]. Patients with VD often require constant outside care and supervision, and their quality of life and social functioning are reduced. Despite significant investments in experimental and clinical neurobiology, the search for effective pharmacological agents for treating this condition continues.

VD is a clinical syndrome that includes a wide range of cognitive impairment. VD occurs as a result of necrosis of brain tissue after ischemia, which is caused by a vascular disease. This distinguishes this type of dementia from its other types, most of which are caused by the deposition of toxic substances in nerve cells. It is believed that the symptoms observed in diabetes differ from those characteristic of dementia in Alzheimer's disease (AD), dementia with Levi bodies and frontotemporal dementia, although elements of VD can also be noted in these diseases [2].

It should be noted that drug treatment of VD has been widely reported in the literature (Broich, 2003; Malouf, Birks 2004; Pantoni, 2004; Schindler, 2005). The main conclusion of the authors is that most of the research results in VD were contradictory. It is also important to emphasize that so far, regulatory agencies have not approved a single drug for the treatment of this disease (Pantoni, 2004). From the point of view of epidemiology, VD is regarded as the second most common type of dementia after AD, although this conclusion has been questioned by the growing study of dementia with Levi bodies (Zesiewicz et al., 2001; Henriksen et al., 2006). From a clinical point of view, VD presents significant difficulties, since its prevalence is increasing, and there are no possible options for effective treatment.

The most important section of the treatment of VD is the impact on existing risk factors for cerebrovascular diseases [1, 9]. Among the corrected factors, arterial hypertension (AH) is of the greatest importance. In those cases when the leading component of the pathogenesis of VD is hypertension, the most characteristic is the predominance of a step-like development of symptoms against the background of periodically developing hypertensive cerebral crises [12]. In this case, intracerebral arteries with a diameter of 70-500 microns and a microvasculature of the brain are mainly affected; the segmental nature of vascular lesions is typical. Developing vascular lesions are divided into primary - acute, repeated destructive changes caused by vascular crises (plasmorrhagia, fibrinoid necrosis with swelling of the wall and the development of acute hypertensive stenosis, isolated necrosis of the myocytes of the middle membrane of the arteries, miliary aneurysms, rupture of the wall, thrombosis); and secondary - chronic reparative processes (arteriosclerosis, hyalinosis with thickening of the walls and narrowing of the lumen of the arteries up to obliteration), compensatory-adaptive changes (myelastofibrosis, hyperelastosis, muscular-elastic "pillows" at the points of branching, hypertrophy of the middle membrane, vascular proliferation of the microvasculature). Thus, multiple diffuse and small-focal changes in brain tissue with different pathogenesis, localization, nature and prevalence lead to the formation of hypertensive angioencephalopathy [7, 8].

It is necessary to achieve normotonia in a patient with AH to prevent the progression of cerebrovascular disease [1, 5].

This can be achieved using only non-drug methods or combining them with drug therapy [4].

Choline alfoscerate, which excites cholinergic receptors, predominantly central (has a cholinomimetic effect), refers to drugs that largely meet the above requirements. In the body, it is split into choline and glycerophosphate. Substrate provides the synthesis of acetylcholine and phosphatidylcholine neuronal membranes. It stimulates cholinergic neurotransmission, improves the plasticity of neuronal membranes and receptor function, activates cerebral blood flow, and stimulates the central nervous system metabolism and reticular formation [10, 11]. It improves mood, improves mental activity, concentration of attention, memorization and ability to reproduce the information received, optimizes cognitive and behavioral reactions, and eliminates emotional instability, apathy [13, 6]. In the acute period of traumatic brain injuries, it contributes to the normalization of blood flow and bioelectric activity of the brain on the affected side, and contributes to the regression of neurological symptoms.

All of the listed positive multifunctional properties of choline alfoscerate were the basis for the inclusion of the drug in the complex treatment of patients with VD, which developed against the background of AH.

2. THE AIM OF THE RESEARCH

was: to study the effect of choline alfoscerate on the indicators of headache severity, quantitative and qualitative indicators of vegetative dystonia syndrome, as well as the level of anxiety in patients with vascular dementia on the background of AH.

3. MATERIAL AND RESEARCH METHODS

The research involved 60 patients with VD, the average age of which was (68.5 ± 0.7 years). The diagnosis of arterial hypertension was established according to the classification of AH by degrees, adopted by cardiologists around the world at a symposium on hypertension at a congress in 2003 [7]. According to this classification, a mild degree of AH was detected in 32 patients, the blood pressure levels of which were in the range 140-159 / 90-99 mmHg; in 28 patients - the second degree, or moderate, their blood pressure ranged in the range of 160-179 / 100-109 mmHg. There were no patients with severe, third degree AH in our studies.

Exclusion criteria for the study were: age less than 40 and more than 80 years, Alzheimer's disease, encephalopathy of another etiology, stroke, diabetes, epilepsy, organic diseases of the brain and spinal cord (hereditary, demyelinating, degenerative, tumors), blood diseases and autoimmune diseases.

All patients were divided into 2 groups.

The 1st group (main) included 30 patients who, on the background of basic therapy, received the drug choline alfoscerate 1000 mg - 4.0 ml intravenous drip for 10 days, then 1 capsule 400 mg 2 times a day for 28 days.

The basic therapy established by the standards for the treatment of AH (in combination) included: 1) acetylsalicylic acid (aspirin); 2) beta-blockers or ACE inhibitors; 3) statins (atorvastatin); 4) diuretics.

Group 2 (comparison group) comprised 30 patients who received only basic therapy.

All patients underwent a thorough clinical and neurological examination. Headache severity indices were evaluated using a visual-analogue scale (VAS), to identify vegetative disorders and to determine vegetative dystonia syndrome (VDS), a questionnaire and a scheme, severity indicators of vegetative reactivity according to Danyni-Ashner were used, and anxiety was used to assess anxiety Hamilton test.

Analysis of the results of the research was carried out twice: before treatment and on day 40 of treatment.

4. RESULTS AND DISCUSSIONS

Cephalgic syndrome occurred in 12 (40.0%) patients of the 1st and in 13 (43.3%) patients of the 2nd group. Vestibular-atactic - in 4 (13.4%) and 3 (10%) patients, respectively. Pyramidal syndrome was detected in 2 (6.6%) patients of the 1st and in 1 (3.4%) patients of the 2nd group. Astheno-neurotic - in 7 (23.4%) and 6 (20.0%) patients, respectively, pseudobulbar syndrome with pathological laughter and crying, namely, it occurred in 5 (16.6%) patients of the 1st group, in group 2 patients, this syndrome was detected in 7 (23.3%) patients.

Patients complained of headaches, often localized in the occipital region, the appearance of a sensation of constriction, a breaking or dull pain, lightheadedness or nausea, irregular dizziness, darkening in the eyes, "black flies" in front of the eyes, blanching of the skin. All this occurs with spasm of the arteries, that is, such an increase in the tone of the walls of the arteries, in which local ischemia and tissue hypoxia occur. In the development of such a headache, not only the arterial wall spasm plays a role, but also the concomitant edema of the vascular tissue and ischemic tissue hypoxia (secondary vascular headache).

Considering that the headache prevailed in the clinical picture of VD, we analyzed it on the VAS scale in the dynamics of treatment.

As can be seen from table 1, the severity of pain according to VDS in patients of the main group before treatment was 6.9 ± 0.2 points, after treatment - 5.0 ± 0.1 points (P <0.001), in the comparison group, respectively – 6.9 ± 0.1 and 5.8 ± 0.3 points (P <0.01).

Table 1

Headache indicators on a visual analogue scale

Indicator	Treatment	Main group (n=30)	Comparison group (n=30)
Headache by VAS scale	Before	6.9±0.2	6.9±0.1
	After	5.0±0.1*** (27.5%)	5.8±0.3** (15.9%)

Note.   - significantly relative to the data before treatment (** - P <0.01; *** - P <0.001). Hereinafter in the remaining table. in parentheses indicate the percentage of dynamics

Thus, in patients of the main group, the dynamics of improvement was 27.5%. In patients of the comparison group, the dynamics was 15.9%.

In patients with VD, vegetative disorders are dominant in both qualitative and quantitative indicators of VDS. In the dynamics of treatment, a decrease in the severity of VDS was observed in the examined patients. The dynamics of indicators in patients of the main group, according to the questionnaire was 55.2%, according to the scheme - 45.6%, in patients of the comparison group, the dynamics of the indicators was 23.3% and 20.8%, respectively.

Thus, in the patients examined by us, the initial high severity of VDS according to the questionnaire and scheme was initially observed. In the dynamics of treatment with the inclusion of choline alfoscerate, this indicator changes more distinctly than in patients who received only basic therapy. From this it follows that choline alfoscerate has a vegetative stabilizing and antioxidant effect.

Table 2

Indicators of the presence and severity of VDS according to the questionnaire and scheme

Indicator	Treatment	Main group (n=30)	Comparison group (n=30)
VDS on the application form	Before	33.0 ± 0.9	31.7 ± 1.2
	After	14.8 ± 0.4*** (55.2%)	24.3 ± 1.1*** (23.3%)
VDS according to the scheme	Before	40.1 ± 1.0	41.8 ± 1.7
	After	21.8 ± 0.4*** (45.6%)	33.1 ± 1.7*** (20.8%)

Note.   * - significantly relative to the data before treatment (*** - P <0.001); in parentheses indicate the percentage of dynamics.

As for the indicators of vegetative reactivity (VR) according to Dagnini-Ashner, then against the background of treatment in patients of the main group, they approached the norm, equal to 6. In patients of the comparison group, VR before treatment was 2.2, after treatment - 4.2, those no improvement was noted (Table 3).

Table 3

The severity of vegetative reactivity according to Dagnini-Ashner

Group	The severity of autonomic reactivity			
	before treatment		after treatment	
	peace of mind	reactive	peace of mind	reactive
Main group (n=30)	81.1 ± 1.0	-4.7	80.6 ± 0.7	-6.0
Comparison group (n=30)	84.7 ± 1.7	-2.2	83.6 ± 1.1	-4.2

Next, we analyzed the assessment of the psychoemotional state in the dynamics of treatment. The severity of anxiety in patients of the main group before treatment was 20.5 ± 0.5 points, after treatment - 7.3 ± 0.2 points (P <0.001). An improvement in anxiety in patients of this group was 64.4%. In the comparison group, indicators of anxiety before treatment were 21.2 ± 0.8 points, after treatment - 17.2 ± 0.9 points (P <0.01), the dynamics of treatment was 18.9% (Table 4).

Table 4

Indicators of the anxiety rates on a Hamilton test

Indicator	Main group (n=30)		Comparison group (n=30)	
	before treatment	after treatment	before treatment	after treatment
anxiety	20.5±0.5	7.3±0.2*** (64.4%)	21.2±0.8	17.2±0.9** (18.9%)

Note.   * - significantly relative to the data before treatment (** - P<0,01; *** - P<0,001); in parentheses indicate the percentage of dynamics.

Thus, in patients of the main group there was a regression of anxiety syndrome with an improvement in anxiety rates according to the Hamilton test.

5. CONCLUSIONS

1. The mechanisms of action of choline alfoscerate against the background of basic therapy, positively realizing their influence, complementing each other's intensity, have one goal and are aimed at restoring impaired functions, normalizing hemodynamics, improving microcirculation and rheological properties of blood, and of course, optimizing metabolism in brain tissue in VD. This was confirmed by an improvement in the severity of headache according to the VAS, VDS scale, indicators of vegetative reactivity according to the Danyini-Ashner, and also anxiety indicators according to the Hamilton test.

2. The complex therapy of VD in patients with AH with the inclusion of the drug choline alfoscerate is pathogenetically substantiated and can be used in clinical practice as a means of choice for improving brain microcirculation and subsequent facilitation of neuroprotective therapy.

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