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Experience in the Use of Actovegin in the Treatment of Patients with Cognitive Disorders in the Acute Period of Stroke

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Forty-three patients with mild-moderate ischemic stroke were studied in the acute period and were divided into two groups. The experimental group consisted of 32 patients who were given Actovegin; the reference group consisted of 11 patients who were given piracetam. Patients were investigated before treatment and at 10 and 30 days; investigations included examination, points assessments of neurological disorders using the original Gusev–Skvortsova scale, neuropsychological tests using the MMSE scale, rheoencephalography, and electroencephalography. Analysis of changes in clinical features in patients treated with Actovegin during the acute period showed that Actovegin had clear positive effects both on general cerebral and on focal neurological symptoms. By the end of treatment, the extent of recovery of impaired functions, assessed in terms of total ischemic points and cognitive functions, was significantly greater in patients treated with Actovegin than in patients given piracetam. These data lead to the conclusion that Actovegin is effective in the treatment of patients with ischemic stroke.

KEY WORDS: ischemic stroke, acute period, cognitive impairments, treatment, Actovegin.

Despite significant successes in basic and applied studies in cerebrovascular pathology, acute impairments of brain blood supply remain an important medical-social problem both in Russia and abroad [1, 3], with high levels of lethality and invalidity. This latter is largely associated with the development of cognitive impairments. The development of cerebral infarcts is accompanied by cognitive impairments in about one third of cases, reaching the level of dementia [5]. Current approaches to the treatment of vascular dementia are based on improving the rheological properties of the blood and improving brain metabolism by ensuring better oxygen and glucose supply and utilization. The corresponding agents, particularly Actovegin, have neuroprotective actions, with direct activatory influences on brain structures, leading to improvements in memory and cognitive functions, also increasing the resistance of the CNS to harmful factors [2, 4].

The aim of the present work was to study the efficacy of Actovegin in correcting cognitive disorders in patients with mild-moderate cerebral infarcts. The tasks were to investigate the effects of Actovegin on changes in the main neurological syndromes in brain infarcts, to assess cognitive functions in patients treated with Actovegin, and to study neurophysiological measures on the background of treatment.

MATERIALS AND METHODS

Studies were performed at the Neurovascular Department, City Clinical Hospital No. 3, Chelyabinsk. A total of 43 patients were studied during the acute period of ischemic stroke.

The inclusion criterion for patients was the presence of mild-moderate ischemic stroke. Exclusion criteria were the presence of speech disorders preventing assessment of neu-

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TABLE 1. Comparative Analysis of the Actions of Actovegin and Piracetam on Cognitive Functions in Patients, MMSE Scale, Points

Parameter	Agent	Time point		
		Before treatment	Day 10	Day 30
Orientation in time	Actovegin	4.7 ± 0.21	4.8 ± 0.35	4.9 ± 0.11
	Piracetam		4.7 ± 0.32	4.8 ± 0.17
Orientation in space	Actovegin	4.9 ± 0.18	4.9 ± 0.23	4.9 ± 0.28
	Piracetam		4.9 ± 0.07	4.9 ± 0.11
Perception	Actovegin	2.2 ± 0.13	2.7 ± 0.24*	2.9 ± 0.29*
	Piracetam		2.6 ± 0.19*	2.8 ± 0.22*
Concentration of attention and counting	Actovegin	2.9 ± 0.24	3.7 ± 0.32*#	4.4 ± 0.28*#
	Piracetam		3.4 ± 0.28	3.8 ± 0.37*
Memory	Actovegin	1.6 ± 0.27	2.1 ± 0.17*	2.6 ± 0.24*#
	Piracetam		1.9 ± 0.25*	2.3 ± 0.19*
Speech functions	Actovegin	5.6 ± 0.27	5.9 ± 0.18	7.2 ± 0.35*#
	Piracetam		5.7 ± 0.21	6.4 ± 0.19
Total points	Actovegin	21.1 ± 0.17	24.1 ± 0.14	29.1 ± 0.16#
	Piracetam		23.2 ± 0.11	25.9 ± 0.24

Notes. *Significant differences before and after treatment, $p < 0.05$; #significant differences between Actovegin and piracetam, $p < 0.05$.

ropsychological status, as well as severe somatic diseases in exacerbation.

Ischemic stroke was diagnosed on the basis of clinical neurological observations, laboratory studies of the CSF and blood, echoencephalographic studies, fundoscopy, and brain CT and MRI scans.

All patients received basic treatment including correction of impairments of systemic and cerebral hemodynamics and the blood clotting system.

Treatment effects were assessed in patients of two groups, one of which received Actovegin (experimental group); patients of the reference did not receive Actovegin.

The experimental group consisted of 32 patients (18 males, 14 females) aged 49–65 years (mean 56.2 ± 2.4 years). These patients received Actovegin (from Nikomed) at a dose of 10.0 ml by i.v. infusion for 10 days with subsequent transfer to p.o. dosage with 200-mg tablets to one month. The reference group consisted of 11 patients (seven males, four females, mean age 55.6 ± 2.4 years). These patients received piracetam at a dose of 10.0 ml by i.v. infusion for 10 days with subsequent oral dosage with tablets at a rate of 1600 mg/day as two doses (at 08:00 and 14:00) for one month.

Patients were investigated before treatment, on day 10, and after treatment was complete, i.e., on day 30. Observations included clinical examination, quantitative assessment of neurological disorders using the Gusev–Skvortsova scale [1], neuropsychological testing using the Mini Mental State Examination (MMSE), rheoencephalography, and electroencephalography. These latter studies were performed using a 16-channel EEG apparatus with standard leads at rest and after functional loading (hyperventilation, photic stimulation).

RESULTS AND DISCUSSION

Use of Actovegin during the acute period had positive influences on both general cerebral and focal neurological symptoms. This was indicated by results obtained on the Gusev and Skvortsova scale: the total points score before treatment was 35.9 ± 0.37, with no difference between groups. On treatment day 10, the experimental group showed a significant reduction ($p < 0.05$) in motor disorders, with an increase in the measure of total ischemic points to 38.9 ± 0.53; the reference group showed a similar change, to 38.3 ± 0.18 points. By the end of treatment (30 days), the efficacy of restoration of impaired functions, measured in terms of total ischemic points, was significantly greater ($p < 0.05$) in patients given Actovegin than in patients given piracetam, i.e., 45.1 ± 0.24 and 42.1 ± 0.15 points, respectively.

Analysis of cognitive functions demonstrated impairments of different severities in 13 (30.2%) of 43 patients. On the MMSE scale, five (85.7%) of these 13 patients had mild dementia and eight (14.3%) had pre-dementia impairments. There were no differences between the experimental group and the reference group. On day 10, both groups showed significant ($p < 0.05$) improvements in measures of the concentration of attention and counting. By the end

of treatment, the experimental group showed a significant ($p < 0.05$) increase in the stability of the concentration of attention and improvements in short-term memory and logical thought. Data on the effects of the two agents on all the cognitive measures studied were summed (Table 1).

Studies of the state of brain hemodynamics and cerebral vessels by rheoencephalography identified significant ($p < 0.05$) increases in the rheographic index in patients given Actovegin as compared with the control group.

Analysis of the EEG in patients with cerebral infarcts before treatment revealed significant abnormalities in bioelectrical activity. Twenty-eight (65.1%) of 43 patients showed an irregular, low-amplitude α rhythm; signs of interhemisphere asymmetry were seen in 11 (25.6%) patients, with slow oscillations in the δ and θ ranges and paroxysmal activity. EEG changes during treatment were particularly marked in the experimental group.

Treatment with Actovegin induced the previously absent regular α rhythm; the slow oscillations in the δ and θ ranges disappeared in some patients. On treatment day 10, paroxysmal brain activity in the form of transient bursts of α and θ waves remained marked, albeit less so than during the pre-treatment period, reflecting changes in the activatory influences of the subthalamus and reticular formation of the brain. On day 30, paroxysmal activity became significantly ($p < 0.05$) lower. A number of patients showed normalization of EEG reactivity to hyperventilation.

Correlation analysis of the relationship between clinical and neuropsychological parameters and the EEG established that there was an inverse relationship ($r = –0.86$) between the severity of stroke and measures of the functions of attention, memory, and the extent of EEG changes during both the initial period of the study and at the final stage.

These studies showed that the tolerance of Actovegin was good. Side effects (as allergic reactions) were seen in only one patient (2.3%).

The results obtained here provide grounds for regarding Actovegin as an agent with great potential for the treatment of patients with mild-moderate ischemic stroke, including for the correction of cognitive disorders.

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