

# Treatment of the post-stroke speech disorders in the patients with cardiac and cerebrovascular pathology

**Keywords:** blood-stroke, speech disorder, aphasia, arterial hypertension, cerebrovascular pathology, cognitive functions, cognitive defects, memantine

## Introduction

The frequency of blood-stroke incidences in Russia is the highest in the world - up to 3 cases per 100 thousand people each year. The acute cerebrovascular accidents rank the third place after the myocardial infarction and cancer in the list of death causes and they are the key factor of the population's disability: only 20% of post-ischemic stroke patients manage to recover.<sup>1-4</sup> Along with motor and sensitivity defects most of the patients also suffer from cognitive defects that cause social maladjustment, complicate recovery processes, significantly reduce quality of life of both the patient and his family.<sup>5-12</sup> One of the most significant post-stroke cognitive defects is speech disorder. According to the blood-stroke register data of the Neurology research institute of the Russian Academy of the Medical Sciences, by the end of the acute period of the blood-stroke aphasia is reported in 36% of the cases, while dysarthria is reported only in 14% of the cases.<sup>13-17</sup> Speech disorder is the cause of the social and mental maladjustment of the patients, it significantly reduces their communicative capabilities, everyday vitality, contributes to their social exclusion. Recovery after the post-stroke speech disorder is a daunting task and depends on many factors. Unfortunately, the speech disorder is very persistent and the full recovery usually takes from 2 to 6 years.<sup>14-16,18,19</sup> The presence of the gross total sensorimotor aphasia of the patients having the acute period of the blood-stroke (especially, if these defects are refractory during 3-4 months) is an adverse factor for the speech disorder recovery.<sup>20,21</sup> With no regard of the severity of the blood-stroke and the starting date of the speech corrective therapy, speech function recovery is usually poor. In most cases, providing the long systematic psychological corrective therapy by the speech therapist-afasiologist can only induce the limited improvement of the speech function.<sup>21</sup> In view of all these factors, the drug treatment plays a major role in the process of the post-stroke patients' rehabilitation. There are no specific recommendations concerning the treatment of such patients in the present literature on the post-stroke cognitive defects. That's why, specialists follow general approaches to treat the patients with blood-stroke (vascular risk factors correction, antihypertensive therapy, statins etc.). There are a lot of medications used for the recovery of the cognitive functions of the patients with the acute cerebrovascular accident but all of them could be divided into 4 groups: 1) medications that effect on the certain neurotransmitter systems; 2) medications with neurotrophic action; 3) medications with neurometabolic action; 4) medications with vasoactive action. Unfortunately, most of the medications used in Russian clinical practice have no evidence-based guidelines - there are no results of placebo-controlled studies, that's why, there is no objective evidence of the effectiveness. Today there is no consensus on the effectiveness of speech disorder's drug therapy. In recent years many researches, studying the effect of the

Volume 8 Issue 3 - 2018

NN Koberskaya

Chair of Neurology of the Faculty of Medicine of Federal State Autonomous Educational Institution of Higher Education I.M. Sechenov First Moscow State Medical University, Russia

**Correspondence:** NN Koberskaya, Chair of Neurology of the Faculty of Medicine of Federal State Autonomous Educational Institution of Higher Education I.M. Sechenov First Moscow State Medical University, Moscow, Russia,  
Email koberskaya\_n\_n@mail.ru

**Received:** February 15, 2018 | **Published:** May 10, 2018

number of medications on neurorehabilitation's effectiveness, are carried out. The series of scientific researches have proved positive effect of the Paricetam. The Paricetam administration at a dose of 2400 mg twice per day had a positive effect on the expressive speech indicators.<sup>22,23</sup> According to Berthier et al.,<sup>24</sup> Donepezil use at a dose of 10 mg once daily combined with weekly two hour speech corrective therapy improved the parameters of the nominal speech function and reduced the severity of post-stroke aphasia.<sup>24</sup> According to the results of the randomized placebo-controlled studies that were performed by Walker-Batson et al.<sup>25</sup> in 2001, 10 courses of speech therapy combined with 10 mg of the amphetamine during 5 weeks improved the recovery of speech disorder in blood-stroke's recovery phase.<sup>25</sup> With respect to the effectiveness of the antiparkinsonian medications in case of post-stroke aphasia the contradicting results were obtained: the bromocriptine administration did not have a positive effect on the speech functions recovery, but within this study the speech therapy for the patients was not conducted, however, the levodopa administration had a positive effect especially in case of the coronal position of the ischemic foci, but in combination with the speech corrective therapy.<sup>22,26</sup> Akatinol memantine is one of the most advanced modern medications for the cognitive defect recovery. NMDA receptor-mediated excitotoxicity is considered to be an important factor for the neuron death in the ischemic penumbra.<sup>4,27-32</sup> In case of the cerebrovascular pathology there has been observed the enhanced release of the glutamate from the ischemic neurons that causes the increasing of the glutamate activity and the synaptic transmission failure, contributes to the additional damage and untimely cell death. Memantine refers to the uncompetitive low affinity use-dependent NMDA receptor antagonists. Memantine blocks the cation channel of the neuron in the resting state, with the development of membrane depolarization processes the memantine is removed from the channel that provides normal synaptic transmission and recovery of the signal-to-noise ratio.<sup>33-38</sup> Blocking the intracellular calcium current, the memantine has a neuroprotective effect.<sup>33,39-41</sup> For a while this

medication has proved itself to be good in the geriatric neurology - for the treatment of the patients with Alzheimer's disease, Parkinson's disease, diffuse Lewy body disease etc.<sup>41,42</sup> The clinical evidence testifies that the memantine has the neuroprotective effect not only in case of the neurodegenerative process, but also in the acute local or global cerebral ischemia.<sup>1,4,20,21,28,30,31,33,34,36,38,39,43-45</sup> The large, long-term, placebo-controlled trials of the memantine effectiveness of the patients with vascular dementia (the MMM 300 study that was conducted in France enrolled more than 300 patients with mild and moderate vascular dementia, the MMM 500 study was conducted in the United Kingdom and enrolled more than 500 patients) were performed in Europe. The results of these studies have proved the positive effect of the memantine on the cognitive functions.<sup>43,46</sup> In the series of the memantine effectiveness studies it was reported that the maximum improvement affected by the memantine administration was detected within the tests evaluating the orientation and addressed speech understanding, and also the constructive praxis and the visuospatial functions. Therefore, the memantine administration improved the patients' communication skills and interacting.<sup>41,42</sup> It was also reported the memantine effectiveness in regard to the speech functions of the children with the juvenile myoclonic epilepsy. According to the study of DE Zaitsev et al.,<sup>34</sup> the most significant results of the Akatinol memantine administration for the treatment of the psycho-speech delay in the children with the juvenile myoclonic epilepsy were the speech function improvement, more specifically, improvement of the pronunciation and reduction of the speech tempo disorders.<sup>34</sup> In view of this, the memantine administration in the complex therapy of the post-stroke speech disorders is fully justified. We provide a description of our own study of the Akatinol memantine effectiveness in case of the patient with the post-stroke speech disorders.

## Clinical case

Patient P, was born in 1950 (65 years old), applied for the consultation at the memory laboratory in March 2016. At doctor's appointment she was accompanied by her daughter. She presented the problems with the speech disorder. For 15 years she suffered from the arterial hypertension with a maximum increase in the arterial blood pressure (BP) up to 190/100mmHg, adapted to 120/80mmHg, arterial blood pressure is controlled, the antihypertensive medications administration is chronic. In childhood it was referred to the rheumatic heart disease and the mitral valve defect (the documentation is absent). In summer 2012 -deterioration in the condition, atrial fibrillation of unknown age, labored breathing, swelling of the lower limbs and retrosternal pain. By the examination at the heart station it was revealed the significant degenerative changes of the mitral valve, the wall motion abnormality, the decreasing of the left ventricle systolic function. In November 2013 it was performed the radiofrequency ablation (RFA) of the right and left atriums, the annuloplasty of the tricuspid valve, the mitral valve replacement. The post-surgical period was without complications. Since then the atrial fibrillation has not recurred. The condition was stable, she administered the warfarin, the international normalized ratio (INR) was controlled.

According to the oral information provided by her daughter last December, after the night's sleeping early in the morning it was developed the speech disorder as well as numbness of the right hand. By the emergency medical service team the patient was hospitalized to the resuscitation department of the city clinical hospital. Within one hour (according to the oral information provided by her daughter)

the speech and sensitive disorder was regressed. Upon the multispiral computed tomography (MSCT) of the brain it was detected the repeated ischemic stroke was observed in the left temporal region, the post-stroke changes in the right occipital region were of the unknown age. After 1 day in the stable condition the patient was transferred to the neurology department. During general baseline therapy (medications, rehabilitation and strengthening exercises, 2 courses of the speech therapy) it was reported the favourable evolution in the form of the patient's total activity, she was discharged for the out-patient treatment with the diagnosis: "Repeated brain infarction dated 16.12.2015, left middle cerebral artery syndrome. Cardioembolic development variation". She was under the care of the neurologist, therapist, cardiologist at the place of her residence.

At the end of January 2016, in the afternoon, driving in the country, speech disorder was abruptly developed. The medical attention was observed next day (after returning to Moscow). By the emergency medical service team the patient was hospitalized to the resuscitation department of the city clinical hospital. The multispiral computed tomography (MSCT) of the brain dated 31.01.2016: In the left frontal region it is detected the heterogeneous hypodensity, the boundaries are ill-defined, indistinct, the sulci in this area are mildly flattened. Below, in the left frontal and temporal region it is defined the area of the cystic-cicatricial changes with the dimensions up to 22x24 mm. In the right parietal region it is also defined hypodensity with the dimensions up to 45x36x28 mm of the unknown age. It is reported the periventricular density reduction of the white matter in the form of the leukoaraiosis. In the white matter it is detected the small foci with the vascular density reduction. The brain ventricles are not deformed. The lateral ventricles are symmetrical, moderately dilatated. The sylvian fissures are visible, dilatated, deep. The convexity sulci are visible, dilatated, deep. In all other respects, the differentiation of the gray and white matters of the brain remained constant. There are no signs of the liquor outflow obstruction. CT data can correspond to the ischemic zone in the left frontal lobe. The sequellae of the acute cerebrovascular accident are revealed in the right occipital lobe, left frontal and temporal region. In 3 days after the condition stabilization the patient was transferred to the neurology department. After the performed treatment (medications, rehabilitation and strengthening exercises) she was discharged for the out-patient treatment with the diagnosis: "Cerebrovascular disease: Repeated brain infarction. Left middle cerebral artery syndrome. Cardioembolic development variation». Currently she administers the warfarin 2.5 mg once a day, cardiomagnyl 75 mg once a day, sotahexal 40 mg two times a day, prestartium 2.5 mg once a day, crestor 10 mg before bed.

The patient has secondary education, at the present time she has the 2<sup>nd</sup> disability group. She is married and has an adult daughter.

**Past medical history:** Chronic rheumatic heart disease. Cardiac rhythm disorder: the paroxysmal ciliary arrhythmia. Coronary heart disease. Postinfarction cardiosclerosis of unknown age. Hypertensive disease of the stage 3. Multinodular toxic goiter, coronary-induced. Post thyroidectomy status dated 01.07.2014.

Allergological anamnesis: an allergic hives as the reaction to the lasix and penicillin.

According to the patient, she has no bad health habits. The family history is connected with the cardiovascular diseases.

## Initial examination

General condition is satisfactory. The skin is of the normal colour. Supernutrition. Vesicular breathing, without rales, breathing rate is 16Rpm. Regular heart sounds. Arterial blood pressure is 120\80mmHg; heart rate is 64 beats per minute. The abdomen is soft and painless on palpation. The liver and spleen are not enlarged. The Costovertebral angle tenderness of the lumbar region is negative on both sides.

**Neurologic state:** Consciousness is clear. The cerebral and meningeal symptoms and signs are absent. The patient understands the addressed speech, the instructions are followed. Cranial-cerebral innervation is intact. Muscle strength remained constant. Tendon periosteal reflexes are of the average vivacity, S>D. Muscle tone is not changed. The grasping reflex is revealed in the right. Sensitive disorders are not detected. Coordinator tests in the limbs are performed correctly on 2 sides. The patient is ambulant, leans on the support cane (due to the pains in the left knee joint). Pelvic functions are controlled. She is able to care for herself.

Neuropsychological examination: The patient does not present the active complaints about the memory impairment. She has the complaints of the speech disorder (“it is difficult to speak and think of words”). The patient has the clear consciousness, she is cooperative, behaves adequately in accordance with the examination situation. The work speed is slowed down, rapid fatigability. Attention is not stable. The ability for the condition’s self-examination is reduced. It is revealed the temporal and space disorientation. Memory: it is detected the significant modal nonspecific disorders in the form of the increased extinction of the memory trace by the interference (at all levels of the semantic system), the introduction of the memorizing and prompting strategy during the pronunciation causes only partial memory improvement. 12 words memory and recall test: direct recall of 6+5=11 words, postponed recall of 3+5=8 words (upon the postponed recall of 3 extraneous intrusions). The memory impairments in their nature correspond to the primary (hippocampal) disorder. Speech: The simple situational questions are quite understandable. The complication of the addressed speech causes difficulties. The difficulties in understanding of the comparative and logical-grammatical constructions were revealed. Phrasal speech is defective, it is reported the difficulties in the word choice and agrammatisms, verbal paraphasia, distortion of the syllabic structure of the complex words. Automated speaking is within normal limits. Repetition of the sounds and syllables with the singular literal paraphrases and perseverations. Simplex repetition is unmistakable, the repetition of three words is difficult, it is associated with the volume constriction of the auditory and verbal memory. The word fluency is sharply decreased: literal associations names - one word, categoric associations - 3 words. Significant disorders of the nominal function of the speech - the latent period of the naming is increased, the explanation of the words is through the functional features. The result of the Boston Naming test – is 21 phonemic specific determiners. Bradylexia is with pauses, guessed, with the distortions of the complex words. The ability to write remained constant. Copying is normal. The sound-letter analysis is unaltered. Praxis: Oral-articulatory praxis is unaltered. Symbolic praxis is within normal. The manual kinesthetic praxis - the tests are performed correctly. She has the moderate difficulties in the motor series digestion within the tests for the dynamic praxis, violation of the elements rule and epitomization within the series of motions, replacing by the stereotype. Constructional praxis (drawing

of the geometric figures) is without pathological findings. The clock drawing test: 4 of 10 points (several numbers on the dial are missing, the numbers are disordered, the clock hands are absent). Gnosis: it is reported the moderate disorders of the spatial perception (difficulties in the clock time determination). Cogitation: significant disorders as a result of the inactivity and the block of the intellectual processes, and also as a result of the dysfunction of the performance result’s control. It is reported the cognitive processes slowness, rapid fatigability. The serial counting is flagrantly violated. The result if the Short Test of Mental Status (STMS) is 16 points (upon the orientation study the patient scored 4 of 10 points, the counting is amiss - 0 points, the patient did not remember a single word of 3), the result of the neuropsychological assessment of frontal lobe dysfunction - is 6 points (Verbal Fluency Test is amiss, the dynamic praxis violation, there were the difficulties in the choice reaction test, both simple and complex). The Trail Making Test, part A was performed during 182 seconds, the part B (the connection of the numbers and letters) was amiss.

In view of this, it can be said about the presence of the complex diminution of the cerebral competence. The most significant are the speech disorders in the form of the acoustic and mnestic, semantic, amnesic aphasia with the mild motor component, as well as the disorder of the neurodynamic constituent of the mental activity. The patient has the signs of the hippocampus’s dysfunction and the cognitive impairment of the dysregulatory and neurodynamic nature associated with the subcortical and frontal dysfunction. At the present time the clinical presentation corresponds to the dementia of the moderate intensity. The results of the general blood test and the common urine analysis are without pathological changes.

**Biochemical blood assay:** creatinine 102µmol/l, urea 5.4mmol/l, fasting glucose 5.5mmol/l, total cholesterol 3.6mmol/l, triglycerides 1.3mmol/l. INR is 1.948 (warfarin 1+1\4tablets). Thyroid hormones (thyroid stimulating hormone, Free T4 (Free Thyroxine), Free T3 (Free Triiodothyronine) – are within normal range.

**Electrocardiogram:** normal sinus rhythm. The heart rate is 63 beats per minute. The electrical axis of the heart has the horizontal position. First-degree AV block. Incomplete right bundle branch block. The myocardium changes are moderate.

**Ultrasound investigation of the thyroid gland:** status post strumectomy. Post-surgery area is within normal.

Upon the duplex ultrasonography screening of the carotid arteries it was revealed the presentation of the stenotic arterial sclerotic disease of the brachiocephalic arteries. Stenosis of both internal carotid arteries (ICA) is 30% in diameter on the right and 60% in diameter on the left. Both internal carotid arteries S-shaped curve. Misalignment of the course in the V-segment of both vertebral arteries.

**Findings:** Condition after the recurrent ischemic stroke in the system of the left middle cerebral artery from 30/01/2016. Mixed acoustic-mnestic, semantic, amnesic aphasia with mild (both afferent and efferent) motor component. Mixed dementia of moderate degree of activity (?). Chronic rheumatic heart disease. Condition after the right and left atrial radiofrequency ablation (RFA), tricuspid valve annuloplasty, mitral valve replacement from 06/11/13. Ischemic heart disease. Postinfarction cardiosclerosis of unknown age. Cardiac rhythm and conduction disorder: paroxysmal atrial fibrillation, first degree atrioventricular block (AV block). Stage IIA, NYHA class II chronic cardiac insufficiency (CCI). Stage II, risk 4 hypertensive heart

disease. Atherosclerosis with primary pathologic process in coronary and brachiocephalic arteries. Type 2b hyperlipidemia corrected with statins. Condition after the thyroidectomy from 2014.

**Prescribed:** to continue warfarin intake at a dose of 2,5mg q.d. (under INR control). With due regard to the fact that the patient has arterial hypertension (AH) combined with CCI, it is recommended to continue intake of Sotahexal beta-blocker at a dose of 40mg b.i.d. and angiotensin-converting-enzyme (ACE) inhibitor – Prestarium at a dose of 2,5mg q.d., to continue intake of statins – Crestor at a dose of 10mg q.h.d. Due to the obvious cognitive defect, the patient was prescribed to take Akatinol Memantine according to the following schedule: week 1 – 5mg qAM, week 2 – 10 mg qAM, week 3 – 15 mg qAM and from week 4 – 20mg qAM.

During the repeated consultation in 3 months, the patient and her daughter noted significant amelioration: speech disorder decreased, understanding of addressed speech improved significantly. The patient became more active. Her daughter made specific mention of the patient's memory improvement. Grasp reflex was leveled in the neurological status. Engagement in the random activity and refocusing from one type of activity to another type significantly increased during the neuropsychological study. Impulsive phenomena decreased. In the speech condition: volume of speech comprehension expanded significantly, the patient started to understand comparative and logical-grammatical structures better, her phonemic awareness improved – difficulties remain only in case of producing extensional and complicated speech material. The number of paraphasia and agrammatisms during the phrase construction significantly decreased. Reduction in the word fluency in the literal associations naming test remains unchanged (1 word as well), though the patient named more categorical associations (6 words). Mnestic disorder was almost compensated: in the memory and reproduction test of 12 words: direct reproduction of 2+8=10 words, delayed reproduction of 8+4=12 words (no intrusions). Connect-the-Numbers Test (trail making test, part A) was completed in 98 seconds, part B (connection of numbers and letters) was completed in 215 seconds (during the primary examination, the patient didn't accomplish part B). During testing according to the Mini-mental State Examination (MMSE), the patient scored 20 points (slight disorientation in space and time, calculation disorder, and the patient recalled 1 word out of 3). During the study of the Frontal Lobe Dysfunction Scale (FLDS), total score made up 13 points (reduction in the word fluency and dynamic praxis disorder remains unchanged), which is twice as high as the primary results.

**Decision:** moderately expressed regression of speech disorder, significant regression of mnestic and regulatory defects. Total cognitive defect is assessed as moderate dementia. It is recommended to continue Akatinol Memantine intake at a dose of 20mg qAM.

## Comment

A patient with severe cardiac anamnesis, who suffered two recurrent acute cerebrovascular diseases (ACVD) of cardioembolic origin, is presented. The main post-stroke neurological defect includes marked speech disorders – of both sensory and motor nature. For the first time, we examined this patient two months after the recurrent stroke. And during the examination, primary memory impairments were found apart from speech disorder. As the patient and her daughter said, no serious memory problems had been noticed prior to the strokes. Primary memory impairments include significant difference in the number of memorized words (or symbols during the study of visual

memory) during direct and delayed reproduction.<sup>39,47,48</sup> Introduction of tips that make the process of recollection of the memorized words easier will be ineffective in this case. Such memory impairments are not typical for the vascular brain injury. When the patient who suffered stroke has primary memory impairments, the ischemic source can be supposed to be localized in the hippocampal area. Thus, these impairments are caused as a result of the structural hippocampal damage. Otherwise, onset or progression of the neurodegenerative process induced the stroke. In this case, memory impairments are the first clinical implications of the possible Alzheimer's disease. In the case of our patient, there is a reference to the presence of the ischemic source in the left temporal region specified in the description of the Multislice Computed Tomography (MSCT) of the brain. It cannot be ruled out that ischemic damage also covers hippocampal area. Multiple clinical and experimental studies demonstrated that structure of hippocampal circle were very sensitive to ischemia – their damage occurs not only at cerebral hypoperfusion, but also at chronic obstructive pulmonary disease, cardiac insufficiency and obstructive sleep apnea syndrome.<sup>39,49</sup> Fast positive dynamics of mnestic disorders in the early recovery period in our patient can also indicate that these disorders can be related to the stroke, as the cognitive defects, associated with the development of the neurodegenerative process, often differ in constant progression. However, final decision of this issue requires a longer dynamic follow-up of the patient.

In the given clinical event, the core of post-stroke disorders is surely cognitive disorders, namely mixed speech disorders, both sensory and motor, associated with frontal-subcortical cognitive deficiency. The dominant in speech disorder is an acoustic-mnestic aphasia characterized by dissociation between the relatively remained ability to repeat single words and disorder in repetition of sequence of words not connected in their meaning. Disorder in keeping and retardation of verbal information leads to the difficulty of understanding long composite statements. The above mentioned symptoms are closely related to the disorder of nominative speech function that is evident not only in difficulty of naming single items (results of Boston Naming test in the patient under study), but also in selection of words in own speech, i.e. finding words, replacing them with pronouns, verbal paraphasia considered within the amnestic or nominative aphasia. It consists in that patients cannot name items correctly, but try to describe them by means of words. For instance, when a doctor shows a pencil and asks a patient to name it, the patient in general answers: "This is a thing used for writing". A prompt helps patient to remember correct word. The term "amnestic aphasia" combines acoustic-mnestic aphasia and optic-mnestic aphasia regarded as the varieties of amnestic aphasia.<sup>18,47,50</sup> Since acoustic-amnestic aphasia develops at affection of posterior branches of left medial cerebral artery, it often goes with semantic aphasia (in development of difficulties of understanding grammatical structures, i.e. comparative structures, genitive case structures, prepositions, etc.). The patient under study had difficulties of understanding comparative and logical-grammatical structures. In case of such localization of affection (parietotemporal sections of dominant cerebral hemisphere), acalculia is quite often present, since there is also disorder in analyzing numerical space relations. During primary inspection, the patient has failed even with simple numeric operations. All the above mentioned speech disorders were noted on the background of apparent frontal-subcortical defect resulted from disruption of connection between frontal sections and subjacent structures and development of postprimary frontal dysfunction. The patient had apparent neurodynamic disorders, i.e.

attention deficit, sluggish mentality and rate of mental processes. During primary inspection, general cognitive disorder corresponded to dementia according to the criteria of the International Classification of Diseases, 10 revision (ICD-10) and criteria of DSM-IV (Diagnostic and Statistical Manual of mental disorders).<sup>51</sup> During MMSE (Minimal State Examination) testing, the patient had 16 scores that corresponded to dementia of mean intensity. Within the specific therapy of cognitive disorders, the patient was put on acatinol memantine, a noncompetitive antagonist of NMDA receptors. Efficacy and safety of memantine in medication of dementia of moderate and severe intensity has been repeatedly proven in randomized double blinded placebo-controlled studies.<sup>20,41–43,46,52.</sup> Clinical practice of acatinol memantine administration during reduction period of Acute Cerebrovascular Event was reported in paper of VA Parfenov et al.<sup>31</sup> The study involved 40 patients (middle age was 68.5±3.4 years old) with neurological disorders of mild and moderate intensity and post-stroke cognitive disorders. 20 patients received acatinol memantine at a dose of 20mg per day as an addition to baseline therapy, aimed at prevention of repeated blood stroke. Acatinol memantine was prescribed on the seventh-tenth day after blood stroke progression for a period of three months. The control group included 20 patients adapted according to gender, age, education level and intensity of cognitive disorders. These patients received only baseline therapy. The patients who received acatinol memantine were reported to have faster and more apparent regression of cognitive disorders according to all used neuropsychological tests as compared to the control group. The presented data is consistent with the assumption that administration of acatinol memantine in the recovery period after ischemic stroke contributes not only to decrease of cognitive disorders intensity, but at large to the regression of disablement caused by neurological disorders.<sup>31</sup> However, this study did not include patients with speech disorder. In discussion of our clinical event it is necessary to mention the study conducted by EV Lukianuk et al.<sup>21</sup> who showed the evident effect of acatinol memantine on the recovery of higher mental functions, including speech, in patients with sinistrocerebral blood stroke.<sup>21</sup> The study included 50 patients at the age of 34–68 with blood stroke in the left brain dated 1–12 months ago with aphasia in clinical presentation with possibility of verbal contact in the absence of nootropics, neuroprotectors, acetylcholinesterase inhibitors and parasympathomimetics prescribed. All patients in addition to complex neurorehabilitation (NR) (vasoactive, symptomatic agents, logopedic classes, exercise therapy, massage therapy, reflexotherapy, ergotherapy) received acatinol memantine during 90 days at an initial dose of 5–10mg per day with gradual escalation up to 20mg per day. Control group included 10 patients who underwent a course of NR and did not receive acatinol memantine, nootropics and neuroprotectors. Cognitive state of the patients was examined three times, i.e. before treatment, in 1.5 months and at the end of three-month course of NR. The logopedists who conducted classes reported quality changes of speech disorder in most patients on the 2–3 week of drug administration. At 1.5 month after drug administration, the patients reached the spike of improvement resulting in peak growth in scores according to the neuropsychological test data, indicators of electroencephalography spectrum analysis and level of brain constant potentials. The maximum growth in scores was reported in case of disorder of verbal dominant functions as compared to non-verbal and subdominant functions. However, it was noted that drug administration is preferable when combined with active trainings. Based on the results obtained, the authors concluded that acatinol memantine is the most effective when it is prescribed as soon as

possible after brain injury. It appears that timely complex therapy with acatinol memantine activates spare capacity of injured hemisphere.<sup>21</sup>

In the given clinical event, we have recorded the health-promoting effect of acatinol memantine with regard to not only mnesic disorder (up to complete recovery), dysregulation disorders, but also significant regression of speech disorders. It was manifested in reduction of symptoms of acoustic-mnesic, amnesic and semantic aphasia, improvement of neurodynamic aspect of activity, expansion of oral-aural memory, increase in active vocabulary. Overall score of MMSE has increased from 16 to 20 scores, and the same indicator of FDSE (Frontal Dysfunction State Examination) has increased from 6 to 13 scores. It should be noted that the patient had no classes with logopedist during drug administration. It is likely that administration of acatinol memantine might be more effective when combined with logopedic correctional classes. Thus, inclusion of acatinol memantine in complex therapy of post-stroke speech disorder along with logopedic recovery work can benefit the recovery of speech disorder. To improve the quality of rehabilitation measures in case of post-stroke cognitive disorder, it is reasonable to conduct further placebo-controlled studies of the drug efficacy with regard to speech disorder.

## Acknowledgements

This article is devoted to the clinical case that illustrates the effectiveness and the safety of Akatinol memantine treatment of the patients with the post-stroke speech disorders associated with cardiac and cerebrovascular pathology.

## Conflict of interest

The author declares no conflict of interest.

## References

1. Vakhnina NV, Nikitina Llu, Parfenov VA. et al. Post-stroke cognitive disorders. *Stroke*. 2008;22:16–21.
2. Zakharov VV, Vakhnina NV. Specific aspects of post-stroke cognitive disorders management. *Atmosphere Nervous diseases*. 2011;3:14–20.
3. Zakharov VV, Vakhnina NV. Stroke and cognitive disorders. *Neurology Neuropsychiatry Psychosomatics*. 2011;2:8–16.
4. ZA Suslina. *Vascular neurology articles*. Moscow: Atmosphere; 2005. 368 P.
5. Klimov LV, Parfenov VA. Cognitive disorders in acuity of ischemic stroke. *Neurology Journal*. 2006;1:53–7.
6. Iakhno NN, Levin OS, Damulin IV. Comparison of clinical and MRI data in case of dyscirculatory encephalopathy. Report 2: Cognitive disorders. *Neurology Journal*. 2001;3:10–9.
7. Henon H, Pasquier F, Leys D. Post-stroke dementia. *Cerebrovasc Dis*. 2006;22:61–70.
8. Kooten F, Koudstaal PJ. Epidemiology of post-stroke dementia. *Haemostasis*. 1998;28:124–133.
9. Madureira S, Guerreiro M, Ferro JM. Dementia and cognitive impairment three months after stroke. *Eur J Neurol*. 2001;8(6):621–627.
10. Pendlebury ST, Rothwell PM. Prevalence, incidence, and factors associated with prestroke and post-stroke dementia: a systematic review and meta-analysis. *Lancet Neurol*. 2009;8(11):1006–1018.
11. Reitz C, Bos MJ, Hofman A. Prestroke cognitive performance, incident stroke, and risk of dementia: the rotterdam study. *Stroke*. 2008;39(1):36–

- 41.
12. Serrano S, Domingo J, Rodriguez-Garcia E. et al. Frequency of cognitive impairment without dementia in patients with stroke: a two-year follow-up study. *Stroke*. 2007;38(1):105–110.
13. Prokopenko SV, Mozheiko Elu, Vizel TG, et al. Neurodynamic speech disorders in post-stroke period: pathogenesis, clinical picture, diagnostics. *Siberian Medicine Bulletin*. 2011;2:154–161.
14. Stoliarova LG, Varakin Iula, Vavilov SB. Specific aspects of speech disorder and its course in apoplectic patients (Clinical imaging examination). *Neurology and Psychiatry Journal*. 1981;8:1141–1146.
15. Stoliarova LG, Varakin Iula., Nekrasova EM. Speech disorders in case of localization of vascular locus in deep structures of dominant cerebral hemisphere. *Neurology and Psychiatry Journal*. 1985;9:1296–1300.
16. Stoliarova LG, Shokhor-Trotskaia MK. Specific aspects of speech development in patients with various kinds of motor aphasia caused by stroke. *Neurology and Psychiatry Journal*. 1981;1:10–15.
17. Shklovskii VM, Vizel TG. *Recovery of speech function in patients with various kinds of aphasia*. Moscow: Speech Pathologists Association; 2000. 96 p.
18. Tsvetkova LS. *Aphasia and rehabilitation training: Educational Guidance*. Moscow: Moscow Psychological and Social Institute; 2001. 256 p.
19. Savva GM, Stephan BC. Alzheimer's society vascular dementia systematic review group. Epidemiological studies of the effect of stroke on incident dementia: a systematic review. *Stroke*. 2010;41:41–6.
20. Levin OS, Vasenina EE. Administration of acatinol memantine in humans. *STPN*. 2015;1:24–33.
21. Lukianiuk EV, Maliukova NG, Shklovskii VM, et al. Administration of acatinol memantine in residual stroke period. *Neurology and Psychiatry Journal*. 2010;12(2):28–33.
22. Bakheit AM. Drug treatment of post-stroke aphasia. *Expert Rev Neurother*. 2004;4(2):211–218.
23. Berthier ML. Post-stroke aphasia: epidemiology, pathophysiology and treatment. *Drugs Aging*. 2005;22(2):163–245.
24. Berthier ML, Green C, Higuera C, et al. A Randomized, placebo-controlled study of donepezil in post-stroke aphasia. *Neurology*. 2006;67(9):1687–1689.
25. Walker-Batson D, Curtis S, Natarajan RA. et al. Double-blind, placebo-controlled study of the use of amphetamine in the treatment of aphasia. *Stroke*. 2001;32(9):2093–2013.
26. Ashtary F, Janghorbani M, Chitsaz A. et al. A Randomized, double-blind trial of bromocriptine efficacy in nonfluent aphasia after stroke. *Neurology*. 2006;66(6):914–916.
27. Belopasova AV, Shakhparonova NV, Kadykov AS. Speech rehabilitation in patients with post-stroke aphasia and neuroplasticity mechanisms. *Neurology Journal*. 2011;16(1):37–41.
28. Verbitskaia SV, Parfenov VA. Clinical experience of memantine administration in post-stroke dementia. *Neurology Journal*. 2008;4:45–8.
29. Damulin IV, Parfenov VA, Skoromets AA, et al. Impaired circulation in cerebro-spinal axis. In: NN Iakhno, editor, *Nervous system diseases. Guidance for Physicians*. Moscow; 2005. p. 231–302
30. Levin OS, Iunishchenko NA, Dudarova MA. Efficacy of acatinol memantine in case of moderate cognitive disorder. *S.S. Korsakov Neurology and Psychiatry Journal*. 2009;109(7):36–42.
31. Parfenov VA, Vakhnina NV, Nikitina LIu. Cognitive disorders after stroke and treatment with memantine. *Clinical Gerontology Journal*. 2005;11:49–52.
32. Dirnagl U, Iadecola C, Moskowitz MA. Pathobiology of ischaemic stroke: an integrated view. *Trends Neurosci*. 1999;22(9):391–397.
33. Gudkova AA, Sorokina IB, Iakovlev AA, et al. Administration of acatinol memantine in patients with vascular cognitive disorders. *Neurology and Psychiatry Journal*. 2010;12:37–40.
34. Makarov IV, Zaitsev DE. *Psychiatric disorders in children with epilepsy (diagnosis and management)*. Guidance for Physicians. St. Petersburg; 2006. 27 p.
35. Berthier ML, Green C, Lara JP, et al. Memantine and constraint-induced aphasia therapy in chronic post-stroke aphasia. *Ann Neurol*. 2009;65(5):577–585.
36. Culmsee C, Junker V, Kremers W, et al. Combination therapy in ischemic stroke: synergistic neuroprotective effects of memantine and clenbuterol. *Stroke*. 2004;35(5):1197–1202.
37. Lipton SA, Chen HV. Paradigm shift in neuroprotective drug development: clinically tolerated NMDA receptor inhibition by memantine. *Cell Death Differ*. 2004;11(1):18–20.
38. Lopez-Valdés HE, Clarkson AN, Charles AC, et al. Memantine improves recovery after stroke. *Stroke*. 2014;35(3):49–57.
39. Preobrazhenskaia IS. Post-stroke cognitive disorders: causes, clinical signs, treatment. *Pharmateca*. 2013;9(262):49–53.
40. Block F, Schwarz M. Memantine reduces functional and morphological consequences induced by global ischemia in rats. *Neurosci Lett*. 1996;208(1):41–44.
41. Reisberg B, Doody R, Stöfler A. et al. A 24-week open-label extension study of memantine in moderate to severe Alzheimer's disease. *Arch Neurol*. 2006;63(1):49–54.
42. Reisberg B, Doody R, Stöfler A, et al. Memantine in moderate-to-severe Alzheimer's disease. *N Engl J Med*. 2003;348(14):1333–1341.
43. Orgogozo JM, Rigaud AS, Stöfler A, et al. Efficacy and safety of memantine in patients with mild to moderate vascular dementia: a randomized, placebo-controlled trial (MMM 300). *Stroke*. 2002;33(7):1834–1839.
44. Srikanth VK, Quinn SJ, Donnan GA, et al. Long-term cognitive transitions, rates of cognitive change, and predictors of incident dementia in a population-based first-ever stroke cohort. *Stroke*. 2006;37(10):2479–2483.
45. Wilcock GK. Memantine for the treatment of dementia. *Lancet Neurol*. 2003;2(8):503–505.
46. Wilcock G, Möbius HJ, Stöfler A. A double-blind, placebo-controlled multicentre study of memantine in mild to moderate vascular dementia (MMM 500). *Int Clin Psychopharmacol*. 2002;17(6):297–305.
47. Khomskaia MD. *Neuropsychology*. 4th ed. St. Petersburg: Piter; 2005. 496 p.
48. Iakhno NN. Cognitive disorders in neurological clinic. *Neurology Journal*. 2006;1:4–12.
49. Larrieu S, Letenneur L, Orgogozo JM. Incidence and outcome of mild cognitive impairment in a population-based prospective cohort. *Neurology*. 2002;59(10):1594–1599.
50. Tsvetkova LS. *Neuropsychological rehabilitation of patients: Educational Guidance*. Moscow: Moscow psychological and social institute; 2004. 424 p.

51. Roman GC, Tatemichi TK, Erkinjuntti T, et al. Vascular dementia: diagnostic criteria for research studies. Report of the NINDS-AIREN international workshop. *Neurology*. 1993;43(2):250–60.
52. Bhogal SK, Teasell R, Speechley M, et al. Intensity of aphasia therapy, impact on recovery. Aphasia therapy works. *Stroke*. 2003;34(4):987–993.