

# New Technologies in Treatment of Patients in the Acute Period of Stroke

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**Abstract** Among the causes of death, according to the World Health Organization, 56.7% are cardiovascular; 14.4% - cancer, trauma, poisoning and other external causes - 10.7%. In this case, stroke takes second place, second only to coronary heart disease (CHD) with myocardial infarction. The most accessible of modern methods of treating patients with ischemic stroke is systemic thrombolytic therapy (TLT). Werner Hacke, one of the founders of the use of TLT in Europe, notes that systemic TLT has been studied much better than other methods of revascularization. This method is most accessible both economically and technically. Reperfusion therapy for cerebral infarction allows you to increase the chances of a favorable outcome in the form of a decrease in mortality and an increase in the number of individuals independent in daily life. The results of the analysis of thrombolytic therapy carried out in the primary vascular department are presented.

**Keywords** Thrombolytic therapy, Ischemic stroke, Rehabilitation

## 1. Introduction

In the structure of stroke, 80% is cerebral infarction. Moreover, when the cerebral blood flow suddenly stops, loss of consciousness occurs within 10 seconds, bioelectric silence on the electroencephalography after 30–40 seconds, and brain death after 8–10 minutes. In a stroke, the process of irreversible damage to brain matter in the ischemic nucleus is also rapid, but in the area of ischemic penumbra, a part of the brain that is many times larger than the necrosis region, where neurons have not died and can restore vital activity, it lasts for hours.

Currently, hundreds of medical organizations in all over the world have all the necessary conditions for conducting thrombolytic therapy (TLT). One of the reasons that prevent TLT is a relatively short period from the moment the first symptoms of acute cerebrovascular accident (stroke) appear until the onset of thrombolysis. This is only 4.5 hours. It should not be mistaken - although the term "from the first symptoms to the needle" reaches a maximum of 270 minutes, each additional minute of delay increases the volume of dead brain tissue. Therefore, the earlier TLT is performed, the better the result. It is the time interval that is the "stumbling block" in the widespread use of this method throughout the world, including in our country. Minimization of terms gives the best results [2].

The most effective method to reduce the time period for

admission of a patient with a stroke to the hospital and thereby increase the number of patients who undergo TLT is to increase the medical literacy of the population. If the population is constantly informed about the signs of a stroke and teach the algorithm of actions in this condition, then gradually an increasing number of our patients will be hospitalized on time. It is also important in all municipalities, where doctors have mastered the TLT method, to widely inform the population about the possibility of using a new highly effective method of treating stroke. Without the use of radio and television, this is impossible, since the target audience is elderly people, listens to radio more and watches TV shows and uses the Internet less than middle-aged people [1,3].

Another factor that reduces the use of TLTs is the common misconception that circulates both in the medical community and among patients about the effectiveness of various vascular and metabolic drugs for stroke. To date, there has not been sufficient evidence of the effectiveness of neuroprotective agents that have shown good results in the experiment. According to A. Majid (2014), the reason for the mismatch of experimental and clinical data is the duality of the processes that occur during a stroke. So, the activity of microglia and other cells involved in the inflammatory process, the action of metalloproteases, apoptosis and autophagy can be both protective and damaging in nature depending on the duration of their exposure and the stage of development of the pathological process. According to experts, at least a third of studies of potential neuroprotectors give negative or false positive results [3,5]. Unfortunately, we have to admit that after the term for TLT expires with a cerebral infarction, the doctor only has the opportunity for

rehabilitation and secondary prevention of stroke in this patient. Other high-tech treatments for ischemic stroke can only be carried out in selected medical centers.

The pharmacological component of the treatment of ischemic stroke involves the fulfillment of two main tasks - reperfusion and cytoprotection. Reperfusion measures for ischemic stroke are aimed at restoring blood flow during a cerebrovascular accident in the affected pool. The following methods are used as reperfusion methods: the use of thrombolytic drugs (fibrinolytic drugs, anticoagulants, antiplatelet agents, thrombin inhibitors), vascular surgery (endarterectomy, embolectomy), angioplasty and stenting. One of the modern and effective methods of reperfusion in ischemic stroke is TLT [2,3]. In the United States, stroke thrombolysis has been used since June 1996, when the Food and Drug Administration (FDA) approved the clinical use of the drug in neurology [6]. In Europe, the drug was used in 2002. In Russia, thrombolytic therapy has been used since 2005. For thrombolysis in neurology, the only thrombolytic drug is allowed - tissue plasminogen activator rTPA (alteplase). Alteplase activation occurs after binding to fibrin filaments, after which active plasmin acts directly on the fibrin clot and helps to dissolve it. The drug is administered at a rate of 0.9 mg per kg of body weight, with 10% of the selected dose being administered intravenously as a bolus, and the remaining part is drip within 1 hour. The drug proved to be effective with a slight risk of complications [6].

A randomized, double-blind, placebo-controlled study of NINDS confirmed the effectiveness of TLT in the first 3 hours from the onset of ischemic stroke. According to NINDS, the rate of hemorrhagic transformations was 6.4% (compared with placebo -0.6%), and mortality -17% (placebo-21%). It was found that the degree of functional recovery in the group of patients receiving TLT was 30% higher. Currently, all information on the results of TLT is analyzed through the SITS (Safe Implementation of Thrombolysis in Stroke) register. The SITS register unites more than 500 centers in Europe, Asia, Australia. According to the SITS register, hemorrhagic transformation occurs in 16.9% of cases, however, it does not always lead to a deterioration of the patient's condition after thrombolytic therapy. Clinically significant hemorrhagic transformation is considered to be a deterioration in the patient's condition, estimated by a stroke scale (NIHSS) of more than 4 points. Such a complication was registered in 4.9% according to the SITS register, and good functional recovery (on the Rankin scale 0–1 points) was found in 54.8% of patients who received TLT [1,5].

A clinically significant improvement in TLT is considered to be a decrease in the severity of symptoms on the scale of stroke (NIHSS) by 4 points or more. However, in case of violation of the protocol of the procedure, the risk of complications significantly exceeds the possible benefit. The main complications of thrombolytic therapy for stroke are cerebral hemorrhages, symptomatic (clinically expressed) hemorrhagic transformation of ischemic cerebral infarction, and Quincke edema, significantly worsening the course of

stroke [2,7].

To perform thrombolytic therapy, it is important to observe a number of conditions, one of which is a temporary criterion. The use of thrombolytic therapy is limited, the so-called period of the therapeutic window. Currently, the "therapeutic window" for systemic thrombolysis is 4.5 hours from the onset of the disease. The shorter this time, the more efficient and safer the TLT. NNT is the number of people who need to be treated to get a positive outcome in each case. When conducting TLT in the period up to 90 minutes from the onset of a stroke, NNT is 4-5 people; at a time of 180 minutes - 8-9 people; with a 270 minute interval before the start of TLT - 14 people.

In accordance with the concept of "time is the brain," the help with a stroke should be emergency, with minimal delays at all stages of its provision. The time interval from the appearance of the first symptoms of a stroke to a call to an emergency medical service is one of the significant delay factors at the prehospital stage [5]. Timely delivery of the patient during the period of the "therapeutic window" allows reperfusion and cytoprotective therapy at the very initial stages of the onset of stroke [7]. To reduce the time costs from the onset of the disease to the start of treatment, we carried out organizational work on the logistics of patients, as well as active information work with the population [3]. The main ways of informing are: conversations with patients and their relatives, conducting recreational activities as part of World Stroke Day, using the media, posting basic information on the problem of stroke on the website of the medical institution, organizing and participating in the work of the society of relatives of patients with stroke and schools of stroke patients. The use of information posters and newsletters in crowded places has not lost its significance [2,4].

In order to optimize the provision of medical care and reduce the time of diagnosis, a scheme for the delivery of a patient to a hospital has been developed. The ambulance service, delivering the patient with signs of stroke, collects a full medical history and informs the patient in advance of the call to the on-duty neurologist of the department for stroke patients. Patients with signs of stroke when examined on an emergency basis are examined by a neurologist on duty, who: assesses the vital functions (if there are medical indications, they are corrected), the patient's general condition and neurological status; organizes electrocardiography, blood sampling to determine platelet count, glucose in peripheral blood, international normalized ratio, activated partial thromboplastin time. The content of the above indicators is determined within 20 minutes from the moment of blood sampling, after which the result is transmitted to the neurologist on duty at the department. After examination, patients with signs of stroke are sent to the department of radiation diagnostics, where multislice computed tomography or high-field magnetic resonance imaging of the brain is performed to clarify the diagnosis. The expert's opinion is transmitted to the doctor on duty at the department. The time from the moment a patient with signs of stroke is

admitted to the department until the doctor receives the results of neuroimaging and blood tests is no more than 40 minutes.

In the absence of signs of stroke, at the time of examination of the patient after stabilization of the condition and vital functions, for further examination and treatment, the patient is transferred to the general reception and diagnostic department under the supervision of a physician or neurologist. With the stabilization of the patient's condition, it is possible to refer the patient under the supervision of outpatient services. Patients whose signs of hemorrhagic stroke are established according to neuroimaging data are given an emergency consultation by a neurosurgeon, after which a decision is made on treatment tactics. In the presence of medical indications for surgical treatment, the patient with stroke is transferred to the specialized department. When confirming the diagnosis of stroke, patients are hospitalized in the intensive care unit or intensive care department, depending on the severity of the condition.

## 2. Materials and Methods

During the period from 2015 to 2018, 780 patients with stroke were treated in the intensive care department, of which 579 patients with ischemic stroke (IS), which amounted to 74.2%. The patients with ischemic stroke who arrived from the onset of the disease in the first 3 hours ("therapeutic window") turned out to be 195 (25%).

Systemic TLT for the indicated period was received by 25 patients (3.2%). It is noteworthy that from the beginning of work, this indicator has a tendency to increase (from 0.5% in 2015 to 4.7% in 2018). The target indicator for TLT of the number of people with ischemic stroke is considered to be 5%.

The average age of patients receiving alteplase treatment is 63.8 years. Distribution by gender: men - 17 (68%), women - 8 (32%). Social distribution: disabled people - 14%, workers - 18%, employees - 13%, pensioners and non-workers - 55%. Working age (men under 60 years old, women under 55 years old) accounted for 38.2%. There are 8 people working (32%).

The patient's delivery time about the onset of the disease depended on the distance to the hospital and the speed at which the patient or his relatives made decisions about seeking medical care and ranged from 26 minutes to 188 minutes and averaged 1 hour 23 minutes. The time of TLT from the moment of the onset of the disease ranged from 57 minutes to 203 minutes and averaged 2 hours 02 minutes.

Assessment of the effectiveness of the treatment was carried out on the scale of the stroke of the National Institute of Health USA (No. H<sup>1</sup>) and a six-point scale for assessing Rankin's disability.

In 9 cases (36%), the doctor decided to conduct TLT, relying on anamnestic and clinical data, not having confirmation according to multispiral computed tomography.

It was important to verify the absence of a hemorrhagic component in the brain tissue, thus eliminating subarachnoid or intracerebral hemorrhage, traumatic brain injury or tumor process. A day after TLT, ischemic stroke in such patients was confirmed by repeated computed tomography or magnetic resonance imaging.

## 3. Results

Treatment efficacy was observed in 23 patients (92%). All surviving patients who received alteplase treatment were discharged in satisfactory condition. However, in 2 cases (8%), the effect was regarded as minimal. These patients were discharged with transfer to a rehabilitation department with severe hemiparesis and significant impairment of the self-care function (on a Rankin scale of 3-4 points). Clinically significant complications of TLT in the form of symptomatic hemorrhagic transformation developed in 1 patient. Asymptomatic hemorrhagic transformation occurred in 4 patients (16%), but this complication did not affect the recovery period after a stroke and the rehabilitation prognosis.

The average score on admission to the hospital (before the start of TLT) was 11.4 points (for people of working age -13.7 points), and on the Rankin scale-3.94 points (for people of working age -3.3 points). During treatment, the symptoms of stroke decreased by an average of 7.13 points on the No. II scale, and 2.12 points on the Rankin scale, amounting to an average of 4.27 points on NIHSS when discharged from the hospital (3.2 points for people of working age) and 1.82 points (in patients of working age, 1.3 points) according to the Rankin scale, respectively.

We also took a comparison group of 32 patients with ischemic stroke who did not receive alteplase treatment. The average delivery time for patients from this group was 1 hour 26 minutes, and the average time for the initiation of differential therapy after neuroimaging was 2 hours 11 minutes from the debut of the stroke. The average age of patients with ischemic stroke who did not receive TLT was 65 years. Distribution by gender: 17 men (53.1%) and 15 women (46.9%). Persons of working age amounted to 14 people (43.7%).

The average NIHSS score for admission to the hospital (before the start of TLT) was 11.8 points (for people of working age -14.1 points), and on the Rankin scale-3.88 points (for people of working age -3.5 points). During treatment, the symptoms of stroke decreased, having averaged 6.12 NIHSS points on discharge from the hospital (5.9 points for people of working age) and 2.4 points on the Rankin scale (2.1 points for patients of working age) respectively.

There were situations when the patient acted with a low score on a stroke scale, and was discharged with much worse rates. This was due to the addition of cerebral edema or the progressive course of a stroke, despite its active management. The average duration of treatment with ischemic stroke

during TLT was 14 days. Patients with ischemic stroke from the control group were treated for 16.1 days.

Three patients died after TLT. 6 - a clinically significant hemorrhagic transformation occurred in combination with diabetes mellitus and a history of toxic damage to the nervous system; and 2 patients died due to a combination of ischemic stroke and myocardial infarction. In general, the mortality rate in the department was 12.4%, and among patients with ischemic stroke - 11.8%.

Transferred to the rehabilitation department for further inpatient treatment - 18.7% of patients, and 75.8% of patients for rehabilitation in outpatient clinics (at the clinic) at the place of patient registration. Thus, the rehabilitation of stroke patients was carried out at the subsequent stages of the three-stage rehabilitation system both in the clinic and in the hospital.

## 4. Conclusions

Currently, systemic thrombolysis in ischemic stroke is recognized and remains a highly effective and safe treatment method.

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