I.M. KALMENEVA, S.U. KAMENOVA, N.K. KLIPITSKAYA, D.A. KLEPIKOV, E.B. ATANTAEVA, M.M. IBRAGIMOV

Department of internship and residency in neurology of KazNMU named after S.D. Asfendiyarov, City Clinical Hospital №7, Almaty.

## STUDY OF EFFECTIVENESS OF CITICOLINE IN TREATMENT OF ISCHEMIC STROKE IN ACUTE STAGE

Stroke - one of the most important health and social problems, it one of the leading causes of death, and often of disability of patients. Here presented study of the effectiveness of Citicoline (Difosfocin) in 20 patients with ischemic stroke. The drug was administered at a dose of 1000.0 mg intravenously 2 times a day for 14 days. Among them were 12 men and 8 women. The average age of patients was 38-50 years Difosfocin contributed to the restoration of consciousness, the normalization of functions of vital organs, improvement of the movement in the paretic limbs, a significant decrease of coordination and sensory disorders.

Keywords: cerebral infarction, ischemic stroke, citicoline (Diphosphocin).

**Introduction.** The problem of stroke is very actual because of medical and social significance in connection with a increasing incidence, a consistent trend of lowering age of patients, a high percentage of disability and mortality. Unsolved problem of it's treatment results in the inability of a stroke patient live a full life, to work effectively, to perceive and retain information; patient suffering because of narrowing social circle, lowered social status. Often this disease makes people unable to basic self-care, relatives and friends of the neurological patient must care for helpless relative for many years.

Currently in the world are recognized that a stroke is largely preventable, and with proper treatment has far less tragic consequences - but mortality is still high. Achievements of clinical medicine currently allows to provide effective care for patients with the most severe forms of vascular disease, based on the use of a whole arsenal of modern pharmacological agents.

A significant increase in the frequency of ischemic stroke, including people of working age, leading to disability and frequent patient deaths determines the relevance of the creation and application of new drugs to treat it, including neuroprotectors. Therapeutic tactic: fastest possible recovery of cerebral blood flow by pharmacological or mechanical means.

In patients with ischemic stroke a change of oxidation-reduction processes, oppression of oxidant system, disruption of phospholipid metabolism at the level of cell membranes and some depression of neurotransmitter systems, such as GABA are found. Care for stroke patients there are a number of therapeutic tasks: 1) restoration of the structure and functions of the brain after a stroke; 2) restoration of the vascular system in the area of the brain with impaired circulation. Pathogenetic treatment of ischemic stroke in the acute period include neuroprotective therapy. Neuroprotection used for the treatment of ischemic stroke as a pre-hospital (on the onset of first symptoms of the disease), and during hospital stay. The purpose of neuroprotection to prevent neuronal death in the penumbra due to excitotoxicity, inflammation and apoptosis. Real evidence of effectiveness are very few on drugs with neuroprotective effect. From this point of view, of great interest are the data on the use of Difosfocin (citicoline).

Diphosphocin (cyticoline, sodium cytidine diphosphocholine) is a compound which is normally present in all human cells. It consists of cytidine and choline linked by diphosphate bridge and is essential intermediate compound in the synthesis of phosphatidylcholine, a major brain phospholipid in phospholipid synthesis pathway (Kennedy pathway). Choline, which is part of citicoline, is the basis for the formation of acetylcholine, the lack of which in the brain is of great importance in the development of disorders of neurotransmitter homeostasis and focal neurological pathology. Ingested difosfocin well absorbed, its concentration in the plasma after oral administration has two peaks - one hour after the administration, and the second 24 hours later.

The aim of the study was to evaluate the clinical efficacy and tolerability of Diphosphocin in the treatment of acute stage ischemic stroke.

**Methods**. The study included 20 patients with ischemic stroke who were hospitalized in the neurovascular unit of city clinical hospital #7 in Almaty. The diagnosis of cerebral infarction was established on the basis of complaints, anamnesis, objective research, medical history, including age, duration, risk factors for stroke, coronary heart disease. To determine the etiology of stroke were taken coagulation tests and MRI or CAT study.

Degree of impairment of consciousness, degree of disability using the Rankin scale, ability to answer the questions, ability to understand and execute instructions, the function of cranial nerves, the degree of motor, sensory and coordinatory impairments.

All patients received a Diphosphocin in dose 1000 mg intravenously twice a day in 200.0 0,9% saline for 14 days. The effectiveness of the therapy was assessed using dynamics of the neurological status of patients. Results of the study were recorded in an individual patient record.

Of the 20 patients there were 12 men (60%) and 8 women (40%). Average age - 62.7 years. Arterial hypertension was observed in all patients, ischemic heart disease - in 9. 16 patients on MRI and clinical examination had stroke in the middle cerebral artery (80%), 4 (40%) - in vertebrobasilar system.

Neurological examination revealed sensory impairments - 17 (85%), pareses - in 16 patients (80%), ataxia - in 20 patients (100%), speech disorders - in 16 patients (80%) (13 - dysarthria, 3 - motor aphasia), impaired consciousness - in 6 patients (30%), the impaired function of vital organs - in 17 patients (85%). In 19 patients (95%) were observed signs of cranial nerves impairment (in 3 - oculomotor nerve and 16 - the facial nerve).

**Results and discussion.** As a result of the introduction of Diphosophocin 6 patients recovered full consciousness entirely to 2 -3 day and 1 patient in 12 day, although the recovery of consciousness was on day 3 to the extent of stunning. 13 (65%) patients responded incorrectly to a question or two questions - 5 (25%). 5 patients who did not correctly answer two questions, but in 2-4 day began to correctly answer one question, two of them responded to two questions in 3rd day, three - 7-10<sup>th</sup> days. 8 patients to correctly answer one question after 2-5 days correctly answered all the questions. 7 patients (35%) had difficulty in carrying out instructions, respectively, two instructions -2 patients, 5 patients - one instruction. By 2-4 day two of the patients began to carry out an one instruction, execution of two instructions happened in them to 4 -10 day. 5 patients follow all of the instructions to the 2 and 7 day. In 2 patients gaze palsy completely regressed on 2-4 day, one patient day 14 remained with partial gaze paresis. In severe and moderate paresis of the facial musculature (16 patients - 80%) improvement occurred in the 9-11 day, and in one patient with mild facial asymmetry complete regression registered after 3 day of treatment by Difosfocin.

The decrease in motor disorders occurred in 3-5 days. In 9 (45%) patients from 15 to 11 or 12 day strength in hand was restored completely, at the foot all of the strength was restored in 8 (40%) patients in 4-7 days.

Sensory disorders gradually decreased and in 9 (40%) patients to 7- 9 Day sensory disorders regressed completely, in 7 (44%) patients remained hemihypoesthesia, but the degree of it significantly reduced. Ataxia was observed in 19 patients: in 15 (79%) patients in the two limbs, in 4 patients - in either hand or foot. 7 (35%) patients were discharged with disorders of coordination and in 13 (65%) patients, impairments of coordination regressed completely.

6 patients does not have speech disorder. In 12 patients (60%) it was restored completely in 5-10 days, in 2 patients (10%) the severity of dysarthria was decreased. Of the 3 patients with motor aphasia speech was restored only in 1 patient and in 2 observed aphasia remained.

Severe impairments of quality of life were observed in 3 (15%) patients, strong - in 8 (40%), moderate - in 4 (20%), light - in 2 (10%). 2 patients with severe impairments recovered function of the pelvic organs on day 3, on 7-12 day they walked without assistance. 6 patients

with severe disorders of life to 2-4 day did not require the constant help of medical personnel and was able to walk without assistance. By day 6, all patients can do everyday routine tasks without assistance. By 9 -10 day 3 of 8 patients were able to perform all daily duties. In the group of patients (4) with moderate disturbances of life on the 3d day and 1 patient on the 9th day can independently manage their own activities, without considerable help. By 5 -11th day three patients in this group did not require assistance of medical staff

Two patients with mild impairment of life on admission after the first injection of difosfocin can independently perform all procedures.

**Conclusion.** Citicicoline (Difosfocin) promotes regression of focal neurological symptoms within 7-10 days. Normalization of consciousness occurs at 2-3 days. Regression of motor disorders comes from 3-5 days and reaches a maximum of 11 -12 day. In assessing neurological status was revealed reduction of facial asymmetry, the severity of pareses. Muscle strength tended to increase in patients from 1 to 4 points after 2-4 days. Decrease of coordinatory disorders occurred in the first week, and their full regression was observed in 9 -12 day. At 7-10 day, all patients fully answered all the questions. All instructions was executed by patients on day 2-7. The greatest effect of the administration of the drug obtained in patients with mild to moderate impaired functioning. 8 (42%) to 12 day did not need any help and was able to complete self-care.

Thus, Difosfocin causes regression of neurological symptoms in first days of treatment of ischemic, without observed side effects. High efficiency of Difosfocin combined with a favorable tolerability profile and safety determines the indications of its use for the treatment of patients with cerebral infarction for rapid recovery of neurological function, improving the quality of life of patients and maintaining their social independence.

### REFERENCES

- 1 Виничук С.М. Новые аспекты нейропротекции в острый период ишемического инсульта. Практическая ангиология №4 (33), 2010. С. 31 38.
- 2 Гусев Е.И., Скворцова В.И. Ишемия головного мозга. М., 2001, 586 с.
- 3 Федин А.И. Оксидантный стресс и применение антиоксидантов в неврологии. Атмосфера. Нервные болезни 2002; 1: С. 15-18.

### И.М. КАЛЬМЕНЕВА, С.У. КАМЕНОВА, Н.К. КЛИПИЦКАЯ, Д.А. КЛЕПИКОВ, Е.Б. АТАНТАЕВА, М.М.ИБРАГИМОВ

С.Д. Асфендияров атындағы ҚазҰМУ, жүйке ауруларының интернатура және резидентура кафедрасы, Алматы қаласы, №7 ҚА МКҚК

# ИШЕМИЯЛЫҚ ИНСУЛЬТПЕН ТҮСКЕН НАУҚАСТАРДЫ ЦИТИКОЛИНМЕН ЕМДЕУ

**Түйін:** Инсульт – маңызды медико-әлеуметтік жағдайлардың бірі және өлім себебі, сонымен қатар науқастарды мүгедектікке әкелуші себеп болып табылады. Науқас тірі қалған жағдайда да, олардың жартысында тұрмыстық тәуелсіздік қайтадан қалыптаспайды. Инсульттің маңызды және жиі көріністерінің бірі өмір сапасын айтарлықтай төмендететін қимыл қызметінің бұзылысы. Қимыл қызметінің бұзылысы бар 38 науқасқа нейромидин әсері зерттелді. Дәрі 0,5% 1мл мөлшермен тәулігіне 2 реттен 10 күнге тағайындалды. Олар 24 әйел және 14 ер адамдар. Науқастардың орташа жасы 38-50 жас. **Түйінді сөздер:** ишемиялық инсульт, ми метаболизм, цитиколин (дифосфоцин).

### И.М. КАЛЬМЕНЕВА, С.У. КАМЕНОВА, Н.К. КЛИПИЦКАЯ, Д.А. КЛЕПИКОВ, Е.Б. АТАНТАЕВА, М.М.ИБРАГИМОВ ИЗУЧЕНИЕ ЭФФЕКТИВНОСТИ ЦИТИКОЛИНА В ЛЕЧЕНИИ ИШЕМИЧЕСКОГО ИНСУЛЬТА В ОСТРОЙ СТАДИИ

**Түйін:** Инсульт – одна из наиболее важных медико – социальных проблем и служит причиной смерти, а также часто является причиной инвалидизации больных. Проведено исследование эффективности цитоколина (дифосфоцина) у 19 больных с ишемическим инсультом. Препарат назначался в дозе 1000,0 мг внутривенно капельно 2 раза в день в течение 14 дней. Среди них было 11 мужчин и 8 женщины. Средний возраст больных был 38 - 50 лет. На фоне лечения цитоколином (дифосфоцином) отмечалось улучшение движений в паретичных конечностях, значительное уменьшение чувствительных, координаторных нарушений, нормализация сознания и жизненноважных функций.

Ключевые слова: ишемический инсульт, метаболизм мозга, цитоколин (дифосфоцин).