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Clinical and Pathogenetic Approaches to Early Rehabilitation of Ischaemic Stroke Patients

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Abstract---*Stroke is the most important medical and social problem, both worldwide and in Uzbekistan, owing to its high morbidity, mortality and disability rates. Uzbekistan's official statistical authorities consider cerebrovascular disease (CVD) to be a single nosological form, without distinguishing it from stroke. Given that the structure of CVDs includes both acute cerebrovascular disorders (ACS) (various types and subtypes of ischemic and hemorrhagic stroke) and chronic CVDs (various forms of so-called dyscirculatory encephalopathy), reliable epidemiological data on stroke prevalence in Uzbekistan are not available. According to the Ministry of Health of the Republic of Uzbekistan, there were 62876 cases of stroke in Uzbekistan in 2019. 15% were fatal, 10-15% relapsed and 55-70% became disabled.*
Keywords---*cognitive impairment, motor impairment, rehabilitation, speech function, stroke*

Introduction

Stroke is one of the causes of permanent disability worldwide (Young & Tolentino, 2011). At the same time, disability from stroke ranks first among the causes of primary disability, reaching, according to different authors, up to 40% (Ilkhomovna et al., 2020). The stroke treatment system consists of emergency hospitalisation of patients with suspected stroke in hospitals with departments for the treatment of AMI patients, providing baseline and specific stroke therapy, identifying and implementing measures for early secondary stroke prevention, as well as early activation and rehabilitation of patients (Kadyrovich, et al., 2021).

The basic therapy is understood to be patient care as well as the control and timely correction of vital functions (correction of oxygenation disorders, maintenance of adequate haemodynamic, volaemic, acid-base and electrolyte status, etc.), body temperature, glycaemia, prevention and treatment of neurological (cerebral oedema, occlusive hydrocephalus, etc.) and visceral complications (infectious complications, etc.). The two strategic directions for the specific treatment of neurological (cerebral oedema, occlusive hydrocephalus) and visceral complications (infectious complications, lower extremity venous thrombosis, thromboembolic complications, aspiration complications in patients with swallowing disorders, etc.). The two strategic directions of stroke specific therapy are reperfusion, i.e. improvement of blood supply to the area of ischaemic brain injury by restoring vascular patency and preventing thrombosis, and neuroprotection, i.e. maintenance of brain tissue metabolism and its protection from structural damage. In recent decades, there has been an increase in the incidence of acute cerebrovascular events affecting the most able-bodied part of the population - middle-aged (40 to 60 years), usually professionally mature professionals. The importance of chronic CVDs as a medical and social problem is increasing every year, which is associated, on the one hand, with improved care for patients in the acute period of stroke, but also with an ageing population and an increasing number of people in the population with risk factors for the development and progression of cardiovascular disease Chauhan et al. (2016); Young & Tolentino (2011), the main among which is arterial hypertension (AH) (Gauthier et al., 2006; Marazziti et al., 2010).

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Material and Method

Rehabilitation is a set of measures (medical, pedagogical, psychological, socio-legal and others) aimed at the restoration of functions impaired by illness and injury and the social re-adaptation of the patient. Three main types of disorders can be distinguished in patients with the consequences of stroke or other diseases and injuries Kuznetsov et al. (2010):

1) Damage (impairment). Stroke damage includes motor (paresis, ataxia), cognitive, speech, emotional-volitional, visual and sensory impairments. Sensory, bulbar and pseudobulbar (dysphonia, dysphagia, dysarthria), pelvic, sexual and other disorders, as well as complications such as epilepsy, falls, thalamic pain, urinary tract infections, thromboembolic episodes, post-stroke arthropathies. The aim of rehabilitation is the full or partial restoration of impaired functions, and the prevention, treatment and minimisation of any complications that may occur.
2) Disability (disability). The impairment is expressed in the impairment of walking, self-care, defined as activities of daily living or impairment of more complex life skills. Self-care includes the ability to dress oneself, eat, maintain personal hygiene, use the bathroom and toilet, control the sphincters, move independently (with or without a stick or wheelchair) indoors and outdoors and sit and stand independently. The ability to perform complex daily living skills may include helping with cooking and cleaning, shopping, working in the garden, driving, etc. The aim of rehabilitation is to teach walking and self-care skills.
3) Social functioning disorder (handicap). Impairment of social functioning is expressed in the restriction of the social role that was the norm for the patient before the illness (according to age, gender, education, social position, profession, cultural level) and includes restriction of social role in the family and society, restriction of social contacts, restriction or inability to work (Gusev et al., 2003; Kobayashi et al., 2006).

The aim of rehabilitation is the restoration (full or partial) of a social role (which goes beyond direct medical rehabilitation) in the family and society, social contacts, the opportunity to attend concerts, theatres, exhibitions, various social and religious events, the restoration of old hobbies and the development of new hobbies, and the restoration of the ability to work. There are three levels of recovery:

1) True recovery - when the impaired functions return to their original state. This is only possible if there is no complete death of the nerve cells, but the pathological focus consists of inactivated elements (due to oedema, hypoxia, and changes in the conduction of nerve impulses).
2) Compensation - functional reorganisation, the involvement of new structures in the functional system; re-adaptation - the use of various devices in the form of canes, walkers and prostheses. Rehabilitation is based on neuroplasticity - the ability of the brain to change its functional and structural reorganisation, and the ability of its different structures to engage in different forms of activity.

The reorganisation is based on factors such as:

1) The multifunctionality of the neuron and neuronal pool (Gusev et al., 2003).
2) Hierarchy of brain structures and splicing (sprouting and further anastomosis of nerve fibres) (Kadyrovich, et al., 2021).

The concept of "ischemic penumbra" (penumbra), which has been developed over the past 25 years, is of great importance for understanding the possibility of functional recovery after stroke. The ischemic penumbra is a border zone surrounding the lesion in which neurons and other nerve elements are functionally inhibited but anatomically intact, and which is a potential source of recovery of impaired function. Neuronal function in the ischaemic penumbra can be restored by incorporating collateral blood flow or by reperfusion (Shomurodov, 2018). The basic principles of rehabilitation are Savitz & Caplan (2005); Kobayashi et al. (2006):

1) Early initiation of rehabilitation measures.
2) Early rehabilitation prevents the development of complications of acute stroke caused by hypokinesia and hypodynamia (thrombophlebitis of lower limbs, congestive pneumonia, etc.), development and progression of secondary pathological conditions (spastic contractures, pathological motor stereotypes), development of social and mental disadaptation, astheno-depressive states.

3) Systematicity and duration, which is possible with a well-organised step-by-step structure of rehabilitation. The first stage of rehabilitation begins in the angio-neurological department, where the patient is transported by ambulance. The second stage of rehabilitation is rehabilitation in a specialist rehabilitation hospital, where the patient is transferred after the acute stroke. The second stage can be varied depending on the severity of the patient and the existing neurological deficit.

The first option is to discharge the patient with good recovery to the outpatient clinic of the place of residence or to a rehabilitation centre. The second option is that a patient with severe neurological deficit is transferred to the rehabilitation unit of the same hospital where the patient was admitted. The third option - a patient with moderate neurological deficit is transferred to a rehabilitation centre. The third stage of rehabilitation is outpatient rehabilitation (either in the rehabilitation department of a polyclinic or at home for patients with severe, poor mobility).

1) Complexity and multidisciplinarity. Inclusion of specialists from different specialities in the rehabilitation process (multidisciplinary team): neurologists, therapists (cardiologists), urologists if necessary, specialists in kinesiotherapy (physical therapy), aphasiologists (speech therapists or neuropsychologists), massage therapists, physiotherapists, acupuncturists, occupational therapists, psychologists, social workers, biofeedback specialists and others.
2) Adequacy of rehabilitation measures - requires compilation of individual rehabilitation programmes, taking into account the severity of neurological deficits, stage of rehabilitation, state of the somatic sphere, state of the emotional-volitional sphere and cognitive functions, and age of the patient.
3) Active participation in rehabilitation by the patient and his relatives and friends. It is necessary that specialists in kinesiotherapy, domestic rehabilitation, speech therapists and aphasiologists explain to caring relatives and carers the aims and methods of rehabilitation, and explain the necessity of additional exercises in the afternoon. Families also play an important role in teaching self-care skills and creating conditions for various activities.

The main neurological symptoms of stroke that require rehabilitation are:

1) Movement and walking disorders.
2) Speech disorders.
3) Cognitive impairment.

Rehabilitation of patients with motor impairment

In the acute stage of a stroke, the main aims of rehabilitation are:

1) Early activation of patients.
2) Prevention of the development of pathological conditions and complications associated with hypokinesia.
3) Restoration of active movements.

If a patient has no general contraindications for rehabilitation measures (CHD with frequent angina attacks, high poorly correctable arterial hypertension, acute inflammatory disease, psychosis and marked cognitive impairment), then rehabilitation measures such as positional treatment (antispastic limb stacking), passive exercises and selective massage are started from the first hours and days. The multicentre evidence-based AVERT trial Shomurodov (2010); Khamdamov (2020), has shown that the use of very early rehabilitation (within the first 14 days of stroke) reduces disability, reduces mortality, reduces dependence on others, reduces the frequency and severity of complications and adverse events, and improves patients' quality of life by the end of the first year after stroke. The indication for activation of patients and their transfer to an upright position is stabilisation of haemodynamic parameters, to determine which it is desirable to use ECG and BP monitoring. With medium and small infarcts and small limited hematomas (without blood breakthrough into the ventricles) activation of patients can begin on the 5th day of the disease. In this case, vertical lízers are widely used, e.g. ERIGO-type vertical lízers (with pulse and arterial control). (With pulse and blood pressure monitoring) are widely used. In parallel with the activation of the patient and his transfer to an upright position, active therapeutic exercises are used to restore movement in the paralyzed limbs, electrical stimulation of the neuromuscular apparatus. In addition to the restoration of movement, therapeutic gymnastics aims to teach walking and self-care. In recent years, computerised robotic orthoses (LOCOMAT) have

become available, which initially provide passive movements in the lower limbs, simulating a step. As movements are restored, the patient's active participation in locomotion increases. At the end of the acute period of stroke (after 21 days) comes the early recovery period (the first 6 months after the stroke), the main tasks of which are: further development of active movements, overcoming synkinesia, reducing spasticity, improving walking, training stability of upright posture. During this period, kinesotherapy is continued, aimed at activation of movements in the paretic limbs. The electromyogram method of bio control is widely used. In addition to their conscious suppression, orthopaedic fixation and special antiseptic passive and passive-active movements are widely used to suppress synkinesias (Chauhan et al., 2016).

To improve walking function, the patient is taught to walk first along the wall bars, then with a four-legged support, a regular stick, then without support (if possible). Various types of balance therapy are used to improve the stability of the upright posture. The main remedy for spasticity is the administration of muscle relaxants (Silakarma et al., 2021; Iurii et al., 2021). The most common are tizanidine, baclofen and tolperizone. Physiotherapeutic methods (ozokerite and paraffin applications, cryotherapy, and hand whirlpools) are also used. In cases of severe localised spasticity, botulinum toxin type a injections are used. Self-care is taught in parallel, starting in the acute phase of the stroke, when active movement becomes possible. This begins with learning how to get out of bed, wash, eat, dress, put on shoes and use the toilet. Gradually, these activities are extended: the patient learns to fold things, tidy up the bed, use the refrigerator, the lift, dress and go out, etc. Rehabilitation is carried out against a background of adequate drug therapy, including:

1) Etiological therapy - hypotensive drugs, disaggregants/anticoagulants to prevent recurrent strokes.
2) Pathogenetic therapy, including metabolic and neuroprotective agents (cerebrolysin, nootropics, choline alphoscerate, actovegin, citicoline); antioxidants (mexidol, citoflavin); vasoactive drugs (pentoxifylline, cavinton).

Rehabilitation of patients with speech disorders

According to recent data from the Republican Scientific Centre for Emergency Medical Care, Bukhara Branch, by the end of the acute period of stroke, aphasia is observed in 35.9% of patients, dysarthria in 13.4% of patients [5]. The main method of correction of speech disorders is speech, reading and writing rehabilitation sessions conducted by speech therapists-apphasiologists or neuropsychologists. Speech rehabilitation is longer and lasts for up to 2-3 years. The methods of rehabilitation training depend on the stage of rehabilitation. Early on, special "disinhibiting" and stimulation rehabilitation techniques are used (Ilkhomovna et al., 2020). Speech understanding is restored by understanding individual words and restoring the ability to understand situational speech, and in the next stage, by understanding extra situational phrases. Parallel to this, the patient learns to understand written language. Speech comprehension is stimulated not only in the classroom, but also in normal everyday life situations. The recovery of the patient's own speech is based on naming particular objects and activities using pictures, repeating individual sounds and words, and composing sentences and phrases. The next stage of recovery is dialogue. The final stage is teaching a monologue (making up stories, retelling what you have read). In the acute phase, short sessions (15-20 min each) are indicated due to the high level of exhaustion. Later on, the duration of the sessions is increased to 30-45 minutes. Speech rehabilitation is carried out with medication that has an activating effect on the integrative functions of the brain. These include nootropics (piracetam), cerebrolysin and gliatilin (Allder et al., 1999; Lenzi et al., 2008).

Rehabilitation of patients with dysarthria

In the case of an articulation disorder associated with dysarthria, a range of activities are carried out, including:

1) Exercises of the pharyngeal and pharyngeal muscles.
2) Gymnastics and massage of the articulation muscles.
3) Electrical stimulation of the laryngeal and pharyngeal muscles (with vokastim).
4) Exercises in pronunciation of individual sounds, words, phrases, and rhymes.

Rehabilitation of patients with cognitive impairment after stroke

Cognitive impairment often occurs after stroke and is manifested by impaired memory, attention, gnosis, praxis and reduced intelligence. Little attention is paid to this aspect of cerebral circulatory disorders, even though cognitive impairment largely determines the outcome of rehabilitation measures and the quality of life of the patient after stroke (Matsui et al., 2007; Sun et al., 2007). According to various authors, memory impairment following acute stroke occurs in 23-70% of patients in the first 3 months after stroke. By the end of the first year, the number of patients with memory impairment decreases to 11-31%. For example, according to some scientists Young & Tolentino (2011), the incidence of cognitive deficits in stroke patients was as high as 68%. The incidence of dementia in post-stroke patients is 26%, and tends to increase with age (Kamalova et al., 2020). Patients over 60 years of age have a 9-fold higher risk of dementia in the first 3 months after stroke than those without stroke. The incidence of non-dementia cognitive impairment is even higher. Severe cognitive impairment and even dementia can be due to Kuznetsov et al. (2010):

1) Massive haemorrhages and extensive infarcts.
2) Multiple infarcts.
3) Single, relatively small infarcts located in functionally significant areas: anterior-medial parts of the optic tubercle and its proximal regions, frontal lobes, parieto- temporo-occipital regions of the brain, mediobasal parts of the temporal lobe, pale globes.

Cognitive impairment or dementia due to infarcts in functionally significant areas does not increase over time, and even decreases. For example, according to other authors, improvement in cognitive function is seen in 1/3 of patients by the end of the acute stroke period. The degree of regression varies and depends on the localization of the infarction, its location in the dominant or subdominant hemisphere, the unilateral or bilateral lesion, and the presence of a previous brain lesion that was asymptomatic before the stroke. Cognitive deficits associated with stroke can occur at different times: immediately after the stroke (acute cognitive deficits) and in a more delayed period (delayed post-stroke IP), usually due to a concurrent neurodegenerative (more often Alzheimer's) process activated by increasing ischaemia and hypoxia. Post-stroke cognitive impairment worsens the prognosis, increases mortality Ilkhomovna et al. (2020), and the risk of recurrent stroke threefold, and also increases the severity of functional impairment after stroke, making rehabilitation much more difficult (Ming et al., 2007; Chae et al., 2007). Metabolic and neuroprotective agents, drugs affecting neurotransmitter systems that correct cognitive, emotional-volitional, and other psychiatric disorders are widely used to correct cognitive disorders after stroke.

1) Piracetam - improves metabolic processes in brain cells, changes the rate of spread of excitation, improves cognitive processes, especially memory and attention. It is used at the beginning of the course in the form of intramuscular injections (5.0 ml of 20% solution for 20-30 days) or in severe cognitive disorders by IV drops up to 6 g for 2-4 weeks, and then orally at 2.4-4.8 g / day for 3-4 months.
2) Cerebrolysin has a polymodal effect on brain metabolism, stimulates the growth of different populations of neurons, increases the efficiency of associative processes in the brain, improves mental alertness, memory and attention. It is administered as intravenous injections (5.0 v/m every day for 30 days) or intravenous drip infusions of 10-20-30 ml (depending on the severity of cognitive disorders) every day (20-30 injections for a course).
3) Choline alphoscerate is a central cholinomimetic, improves nerve impulse transmission in cholinergic neurons, positively influences neuronal membrane plasticity, improves cerebral blood flow and activates reticular formation. Administered v/m at 4.0 for 2-3 weeks, then orally at 1.2 g/day for 3-4 months.
4) Actovegin - positively affects the transport and utilisation of glucose and stimulates oxygen consumption. At the same time, actovegin does not increase the oxygen requirement of the cells, it itself contains oxygen molecules and acts as an oxygen donor.

Numerous studies have shown that actovegin has anti-oxidant properties, as it reduces the formation of free radical oxygen fractions. During administration of the drug, a significant improvement in memory, concentration and thinking compared to the placebo group was noted. Clinical improvement of cognitive functions was accompanied by normalization of electroencephalogram and increase in amplitude of evoked cognitive potential P300. In hippocampal lesions, actovegin stimulates the growth of hippocampal cells and improves the energy status of the cells (Ilkhomovna et al., 2020). The drug has an insulin-like effect, as it stimulates the transport of glucose inside the cells without affecting insulin receptors. The product is especially indicated in patients with concomitant diabetes

mellitus and metabolic syndrome, as it still has a pronounced inhibitory effect on the lipolytic effect due to the stimulation of the adrenergic system. Actovegin 2000 mg v/v for 10-14 days, followed by oral administration at 600-1200 mg/day for several months. A course of infusion therapy with Actovegin leads to a more pronounced and rapid improvement in patients with cognitive impairment, so treatment should be started with parenteral administration of the drug (Teasell et al., 2014; Paolucci et al., 1999).

1) Akatinol-memantine is an NMDA-receptor antagonist, it regulates ion transport - it blocks calcium channels, normalises the membrane potential of neurons, has a neuromodulatory effect, stimulates nerve impulse transmission, improves cognitive processes, memory, learning ability, increases daily daily activities. The treatment regimen is as follows: 5 mg daily the first week, 10 mg (in 2 doses) the second week, then 15-20 mg for 3-4 months.
2) Citicoline (ceraxone) is a mononucleotide containing ribose, cytosine, pyrophosphate and choline in its chemical structure. Citicoline administered in the body serves as an exogenous source of choline for the synthesis of acetylcholine. Citicoline positively influences neuronal membrane repair, participates in synthesis of cell membrane phospholipid structures; reduces free fatty acid accumulation, stimulates formation of acetylcholine and dopamine, increases activity of antioxidant systems. In the acute period of stroke citicoline provides neuroprotection, in the subacute and recovery periods enhances processes of neuroplasticity and neuroregeneration. Using neuroimaging studies proved that when using citicoline in the acute period of ischemic stroke there is a reduction in the volume of cerebral infarction. The use of citicoline promotes the recovery of motor function, walking and self-care. A number of placebo-controlled studies have shown the ability of citicoline to reduce the severity of post-stroke cognitive impairment, reduce spontaneity. Patients with post-stroke cognitive impairment are administered citicoline at 1000-2000 mg/day by intravenous drip for 10 days. Then switch to oral administration of 200-300 mg (2-3 ml) 3 times a day for several weeks. Side effects are rare.
3) Galantamine is a selective competitive and reversible acetylcholinesterase inhibitor that increases the effect of acetylcholine on n-cholinoreceptors. Initially taken at a dose of 8 mg/day (in two doses), the dose is gradually increased depending on the severity of cognitive impairment.
4) Rivastigmine is a selective cerebral acetyl- and butyrylcholinesterase inhibitor that slows down acetylcholine degradation, increasing its content in the cerebral cortex and hippocampus. The initial dose is 1.5 mg/day in two doses, the dose is gradually increased to 12 mg/day (depending on the degree of cognitive impairment) over 4-6 months. Recently, the Exelon patch (4.6 mg) has been widely used. In addition to drug therapy, patients with cognitive impairment are given psychological counselling sessions.

Conclusion

Thus, properly organised rehabilitation measures for patients after a stroke help to further correct motor and cognitive impairment, as well as social adaptation. No drug can protect nerve cells or bring back to life those that have died during a stroke. The management of patients with stroke consists of two areas that need to be developed in parallel:

1) Control of risk factors. It is known that even within a single hospital admission - with inadequate control of blood clotting and blood pressure levels - 1-2% of patients develop a second stroke. Up to 15% of stroke patients are susceptible to a repeat vascular event within a year. This is why it is crucial to maintain optimal blood pressure levels, prevent thrombosis and monitor the rhythm of the heart. These actions reduce the risk of swelling and haemorrhage in the stroke area, minimise symptoms, and are also a prevention of recurrent stroke.
2) Early rehabilitation. Restraint, prolonged stay in bed, rest - worsen recovery from stroke. The brain is incredibly plastic and ready to re-learn and restore walking, speech, memory functions from the first days after a stroke. The earlier rehabilitation begins, the more effective the outcome will be. Even patients with a severe stroke should already be attempted to be upright in the intensive care unit.

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