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NEW APPROACHES TO NEUROPROTECTIVE THERAPY OF ACUTE CEREBROVASCULAR ACCIDENT

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Abstract: Acute cerebrovascular accident (CVA) continues to be one of the leading causes of disability and mortality in the world. Along with the restoration of brain perfusion, the urgent task is to protect neurons from secondary damage. The article discusses modern approaches to neuroprotective therapy, including drugs with proven efficacy, new pharmacological targets, as well as promising areas such as the use of neuropeptides, antioxidants and cellular technologies. Particular attention is paid to multifactorial therapy and individualization of treatment for patients with CVA. The review is based on recent data, including recommendations from international communities.

Keywords: stroke, neuroprotection, CVA, cerebroprotection, antioxidants, recovery, neuroplasticity.

Introduction

Acute cerebrovascular accident (CVA) is not only a medical problem, but also a socio-economic problem due to the high rate of disability and mortality [1]. Despite advances in the development of emergency care methods, including thrombolysis and mechanical thrombectomy, the limited "therapeutic window" and the impossibility of using these methods in most patients make the development of neuroprotective strategies relevant [2].

Neuroprotection in stroke is aimed at preventing secondary neuronal damage resulting from ischemia, reperfusion syndrome, inflammation and oxidative stress. The modern concept of CVA therapy includes not only the restoration of blood flow, but also the protection of neurons, oligodendrocytes, endothelial cells and glial matrix [3].

Modern directions of neuroprotection

Modern approaches to neuroprotective therapy for CVA are aimed at multicomponent intervention in the cascade of pathophysiological processes initiated by ischemia or hemorrhage. The main directions are:

• Decreasing the excitability of the glutamate system - due to NMDA receptor antagonists, such as memantine, which prevents calcium overload of neurons [3];

• Antioxidant protection - drugs that neutralize free radicals (for example, ethylmethylhydroxypyridine succinate) reduce oxidative stress and damage to cell membranes [4];

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• Modulation of apoptosis - the use of agents that affect the expression of anti-apoptotic proteins and mitochondrial function, such as citicoline [5];

• Anti-inflammatory effect - suppression of proinflammatory cytokines and microglia activation (for example, with edarvon or glimepirides) can prevent remote neuronal damage [6];

• Stabilization of the blood-brain barrier - prevention of cerebral edema with osmotic diuretics and steroids can significantly reduce mortality in hemorrhagic strokes [7].

In addition, the role of neurohormonal factors such as erythropoietin, as well as stem cells capable of inducing the restoration of damaged brain structures, is being actively studied.

Clinical data on the effectiveness of new neuroprotectors

In recent years, new drugs with neuroprotective action aimed at improving outcomes in patients with stroke have been actively used and studied in clinical practice. The following drugs have the greatest evidence base in this area:

• Citicoline is a metabolic neuroprotector involved in the synthesis of phosphatidylcholine, a key component of the cell membrane. Multicenter studies, including ICTUS and COBRIT, have demonstrated a moderate but significant improvement in cognitive and motor functions in patients after ischemic stroke with long-term use of citicoline [8].

• Actovegin is a deproteinized hemodialysate of calf blood with antihypoxic and antioxidant effects. It is used in the acute and recovery period of stroke, helping to reduce the severity of neurological deficits [9]. • Semax is a synthetic analogue of adrenocorticotropic hormone, exhibiting neuromodulatory, antioxidant and anti-inflammatory effects. It is used in the complex therapy of ischemic strokes in Russia, showing encouraging results in terms of restoring cognitive function and rehabilitation [10].

• Gliatilin (choline alfoscerate) - improves phospholipid metabolism in neuronal membranes and has a moderate anticholinesterase effect. In combination with rehabilitation measures, it helps to accelerate the restoration of neuropsychological functions [11].

• Mildronate (meldonium) is a drug with a pronounced metabolic effect, improves the energy supply of neurons in ischemic conditions, although its effectiveness in strokes remains a subject of debate [12].

Promising results have also been demonstrated by combination therapy regimens, including the use of antioxidants, nootropics, as well as the use of hypothermia and early rehabilitation methods.

Prognosis and rehabilitation of patients

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The prognosis for stroke directly depends on the timeliness of care, the extent of brain tissue damage, the patient's age and concomitant diseases. Despite advances in neuroprotection, mortality remains high - up to 20-30% for ischemic stroke and over 40% for hemorrhagic stroke [13].

Early and comprehensive rehabilitation in combination with neuroprotective therapy plays a key role in improving outcomes. The main areas of rehabilitation include:

• Physical therapy and kinesitherapy aimed at restoring motor activity;

• Speech therapy correction of speech disorders;

• Psychological and cognitive rehabilitation;

• Neuropsychological support and correction of mood disorders, including treatment of post-stroke depression.

The effectiveness of rehabilitation increases with the use of modern technologies: robotic systems, functional electrical stimulation and telerehabilitation.

Conclusion

Modern neuroprotective therapy for acute cerebrovascular accident is based on a pathogenetically substantiated approach and includes the use of drugs with antioxidant, anti-apoptotic, anti-inflammatory and metabolic effects. Despite the presence of a large number of clinical studies, not all methods have a high evidence base.

Further randomized studies are needed to study the efficacy and safety of neuroprotective drugs in the acute period of stroke, as well as the integration of pharmacotherapy with individualized rehabilitation programs.

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