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Optimization of Treatment for Stroke Consequences

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Annotation: Stroke is an acute disturbance of the blood supply to the brain , characterized by the sudden (within minutes, hours) appearance of focal and/or cerebral neurological symptoms , which persist for more than 24 hours or lead to the death of the patient in a shorter period of time due to cerebrovascular pathology. This article discusses modern pharmacological drugs for treating the consequences of stroke.

Keywords: stroke, neuroprotection, nootropics, hypothalamic phospholipids.

Stroke is one of the leading causes of morbidity and mortality worldwide. In economically developed countries, stroke ranks third in the structure of morbidity and mortality after cardiovascular and oncological pathologies [4].

Stroke almost always happens unexpectedly; even if a person is at risk, he often does not devote much time to preventing this disease [3, 4].

At the same time, there are a number of therapeutic problems in the treatment of stroke that do not have an effective solution with the help of drugs, regardless of the type of stroke:

1. restoration of the structure and functions of the brain after a stroke;
2. restoration of brain nutrition and blood circulation in the stroke area.

The unresolved problem of neurological recovery after a stroke leads to the inability of a patient with cerebrovascular brain damage (stroke) to lead a full life, work effectively, and adequately perceive and retain information [2].

Recent research into stroke has led to an understanding of the underlying biological mechanisms that cause neuronal death and degeneration in this devastating neurological disease. Convincing evidence has been obtained that transplantation of stem cells, including those obtained from bone marrow, can improve blood supply to the brain, reduce the formation of glial scars and cysts, prevent significant dysfunction of the central nervous system, and also contribute to more complete rehabilitation of patients [1 , 7].

Based on the pathogenetic importance of metabolic disorders in brain tissue during strokes, in recent years it has been considered advisable to prescribe to patients who have suffered cerebrovascular accidents not only drugs that affect hemodynamic parameters, but also drugs that act primarily on cerebral metabolism (neurometabolic cerebroprotectors) [3]. For these purposes, nootropic (Greek " noos " - thinking, mind; " tropos " - direction) drugs are most often used - substances that have a specific positive effect on the higher integrative functions of the brain due to a direct effect on the metabolism of neurons, and also increase stability nervous system to damaging factors.

One of the current trends in pharmaceutical technology is the development of liposomal dosage forms that have a number of advantages. Liposomes with a drug introduced into the body interact with cell membranes, bind to them and transfer the drug to the cell. Incorporation of drugs into liposomes can alter the pharmacokinetics and biodistribution of the drug, leading to increased efficacy [7, 9].

The current development of science and technology, along with the search and synthesis of new drugs, makes it possible to improve the dosage forms of already used drugs, increasing their therapeutic effectiveness and reducing the frequency and degree of adverse reactions. One of these methods of improvement is the creation of lipid-containing systems - liposomes . Liposomes are microscopic fatty

particles filled with liquid, the shell of which consists of molecules of the same natural phospholipids (PL) that are part of cell membranes [8]. According to the classification of lipids, PL belong to the group of water-soluble swelling amphiphiles . The amphiphilicity of PL, due to the presence in the molecule of a hydrophilic part - a phosphorylated alcohol (the so-called “polar head”) and a lipophilic part - a chain of fatty acids (the so-called “ fatty acid tail”), determines their unique properties - the ability to emulsify and disperse in aqueous systems with the formation under certain conditions of membrane structures (lamellas , liposomes , micelles). It is this property of PL that nature took as the basis for the design of all cell membranes without exception. It, with targeted use and special selection, allows the use of PL as a surfactant (surfactant) in the preparation of emulsions or in the form of nanoparticles (liposomes , micelles) as a vehicle for the delivery of medicinal compounds and biologically active substances [10, 12] . Water-soluble (hydrophilic) drugs can be enclosed in the internal water space of liposomes , while fat-soluble (hydrophobic) drugs are included in the lipid bilayer .

The first application of liposomes in scientific research was in modeling cell membranes. With their help, the basic patterns of transport of substances through the membrane were established, the important role of phase transitions in the functioning of membranes was shown, the molecular parameters of the lipid bilayer and its dynamic characteristics were determined, the processes of membrane fusion were studied, individual membrane proteins and entire protein ensembles were characterized in the reconstructed systems [1 , 13].

From the point of view of biological compatibility, liposomes are ideal as drug carriers. They are made from naturally occurring lipids and are therefore non-toxic, do not cause unwanted immune reactions, and are biodegradable , meaning they are broken down by enzymes present in the body. However, liposomes are not stable enough in blood and tissues. Rapidly captured and excreted by the reticuloendelial system. For the same reason, liposomal carriers usually cannot be directed precisely to those organs and tissues where the pathological process occurs. However, the attractiveness of the idea of liposomal therapy was so great that the listed complications stimulated numerous and intensive studies, as a result of which original and sometimes ingenious solutions were found for many problems.

Thus, the natural targeting of liposomes by macrophages can be used to activate them, which is very useful for combating viral, bacterial and fungal infections, especially in the skin [13, 14]. The fact that liposomes are not retained by organs such as the heart, kidneys, brain, as well as cells of the nervous system, allows, through the use of liposomal dosage forms, to significantly reduce the cardiotoxicity , nephrotoxicity and neurotoxicity of expensive drugs used for anticancer therapy [14]. In addition, the attachment of molecules specific to target cells (for example, immunoglobulins) to the surface of liposomes is in some cases effective for the targeted delivery of appropriate drugs.

All these techniques have been proposed for conventional liposomes , the residence time of which in the bloodstream is short (from several minutes to several hours). And therefore, they did not solve the general problem of overcoming the natural barriers to liposomes in the body, the main one of which is the liver. The problem was solved by increasing hydrophilicity using a covalently linked synthetic polymer of polyethylene glycol [2, 15]. As a result, the lifetime of liposomes in the bloodstream exceeded two days. But, more importantly, such liposomes gradually accumulated in places where blood vessels were fenestrated , had increased permeability, or were generally poorly developed, which is usually characteristic of tumors and surrounding tissues, as well as in infectious and inflammatory processes.

Liposome Forte is a drug for the treatment of diseases of the nervous system, a psychostimulant , and a nootropic agent.

Pharmacological properties. Parenteral administration of hypothalamic phospholipids can activate hypothalamic metabolism by increasing the turnover of dopamine, tyrosine hydroxylase and adenylate cyclase with subsequent accumulation of cyclic AMP.

This pharmacological effect is reflected especially on the functions of the hypothalamic-pituitary system. By influencing the physicochemical properties of neuronal membranes, hypothalamic phospholipids alter the adaptation of central neuron receptors to treatment.

Pharmacokinetics . Metabolic processes administered parenterally were studied both in terms of assessing total radioactivity and at the cellular level.

Research data shows that the molecules are stable in the blood and reach brain cells.

Liposome Forte can be administered simultaneously with other pharmaceutical products and, in particular, with antipsychotics, with drugs against hyperprolactinemia , with tricyclic antidepressants (reduces the delay of action and increases efficiency) and with cardiac drugs.

In the mid-60s, few people knew what the word " liposomes " meant. Now we are witnessing an unprecedented flowering of a virtually new science and its active penetration into many areas of human activity. This assessment is not the result of bias or deliberate exaggeration of existing achievements. Rather, on the contrary, for a long time only specialists knew about the real successes of this science. And what we see now means that the birth of this field of knowledge was an objective necessity, when the seeds of the new fall on fertile soil prepared for their perception [4, 14].

Conclusions. The versatility of liposomes allows us to count on their successful inclusion in drug treatment regimens used for infusion therapy in the clinic. The lack of industrial production of liposomal drugs, especially for intravenous administration, is caused by the peculiarities and difficulties of the technology for their production. The creation of liposomal drugs for intravenous administration for wide clinical use is an urgent task for domestic medicine.

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