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THE ROLE OF TRANSCRANIAL MAGNETIC STIMULATION IN THE THERAPY OF PATIENTS WITH MULTIPLE SCLEROSIS

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ABSTRACT

The review article provides literature data on the results of studies on the treatment of multiple sclerosis. Modern therapeutic measures are described to improve the quality of life of patients with this pathology.

Scattered multiple sclerosis (MS) — Multiple sclerosis (MS) is an autoimmune disease caused by environmental factors that act on a genetically susceptible host. It consists of three clinical stages: preclinical stage, determined only by MRI [1,2]; the relapsing stage, characterized by episodes of neurological dysfunction followed by resolution; and the progressive stage, which usually develops from the relapse stage. Advances in immune mechanisms that contribute to MS have resulted in more than ten FDA -approved immunotherapies that target effector T cells, regulatory cells, B cells, and cellular transport into the nervous system.

Etiology

The etiology of multiple sclerosis (MS) is likely polygenic and multifactorial, involving genetic, environmental, and immunological factors. Evidence for environmental effects comes from epidemiological studies (Acheson, 1985). People from high- and low-risk areas appear to further reduce their chances of contracting the disease if they move at an early age, and increased risk may be present for those who migrate early from low- and high- risk areas[2,3]. There is also circumstantial evidence that people from high-risk areas may have introduced an infectious agent that caused small epidemics in isolated populations previously free of the disease (Kurtzke, 1986)[4].

Although the exact cause of multiple sclerosis (MS) is still unknown, there is growing evidence that multiple factors can increase the risk of developing the condition. Some of the most common risk factors for multiple sclerosis include :[3,5]

Genetics: Although MS is not a hereditary disease, studies have shown that having close relatives, such as a parent or siblings with MS, can greatly increase the risk of developing the disease.

Various viruses have been found to increase the risk of developing MS. There is growing evidence that some viruses, such as Epstein- Barr virus (EBV) and herpes virus 6 (HHV -6), may be possible co-factors in the development of MS .

Smoking: Studies have shown that smokers are 1.5 times more likely to develop MS than non-smokers. It has been found that cigarette smoking not only increases susceptibility to MS, but can also contribute to the rapid progression of the disease.

Certain Autoimmune Diseases: The prevalence of certain autoimmune diseases, such as systemic lupus erythematosus (SLE), type 1 diabetes, autoimmune thyroid disease, psoriasis, and rheumatoid arthritis (RA), are known to slightly increase the risk of developing MS [5,6].

Age, gender, and race: Demographic factors such as age, gender, and race may increase the risk of developing MS. For example, the risk of developing MS increases with age. In addition, due to genetic changes, women are twice as likely to get sick. In terms of race, MS is more common in people of northern European descent than in people of Asian, African, or Native American ancestry.

Mechanisms of disease development

Role of the immune system

Recent studies have confirmed the mandatory participation of the immune system - primary or secondary - in the pathogenesis of multiple sclerosis. Disturbances in the immune system, as already mentioned, are associated with the peculiarities of the set of genes that control the immune response. In patients with multiple sclerosis of different nationalities and ethnic groups, this genetic identity can determine the features of the onset of the disease, clinical forms, type of treatment, duration and outcome of the disease.

Demyelination and remyelination

The result of the immunopathological reaction is a focus of chronic inflammatory demyelination - plaque of multiple sclerosis. In multiple sclerosis, morphological changes can be recorded not only directly in the foci of demyelination , but also in normal myelin at the cellular and molecular level. [10,12]. Depending on the degree of maturity and time of occurrence in the same patient, several types of plaques can be distinguished: acute (active new foci of demyelination), old (chronic, inactive foci) and old chronic foci with signs of activation, usually along the periphery of the plaque (W. Methews et al ., 1991), which can be regarded as a continuation of plaque growth.

Foci are located in any part of the white matter of the brain and spinal cord. Autoimmune reactions in multiple sclerosis are directed exclusively against myelin proteins, therefore, in the white matter of the brain and spinal cord, the myelin sheath of the conductors of the nervous system is affected, more often in the periventricular space of the cerebral hemispheres, the brain stem, cerebellum, chiasm of the optic nerves, sometimes in the hypothalamus, subcortical formations (O. A. Hondkarian et al., 1987) [3,6,8].

Relapse and progression

Relapses and progression of disability are the main clinical manifestations of multiple sclerosis (MS). Relapses are considered the clinical expression of acute inflammatory demyelination in the central nervous system (CNS), while progression is thought to reflect chronic demyelination, gliosis, and axonal loss. At the onset of the disease, remission of symptoms is likely due to resolution of inflammation, channel redistribution, and

remyelination ; however, after repeated attacks, axonal damage is more likely and axonal loss accumulates. Therefore, the balance between injury and repair likely determines the progression of MS [7].

Clinical manifestations:

PC manifests itself in the form of symptoms and syndromes caused by inflammatory foci in the CNS. They can be identified by careful history taking and clinical examination. Symptoms associated with an exacerbation of MS typically develop within 24 to 48 hours and last for at least 24 hours, often disappearing gradually over the following days and weeks. Although "key" areas, such as the spinal cord, optic nerves, and brain stem, are most often symptomatic, the spectrum of symptoms associated with demyelination is quite wide. These may include paralysis of any cranial nerve, facial myokymia (twitching of facial muscles), trigeminal or glossopharyngeal neuralgia, specific spinal syndromes (eg, sensitive paresis and Brown-Séquard syndrome) , and seizures6. However, only a small proportion of new lesions (about 1 in 10) located deep in the white matter of the brain manifest themselves clinically [10,12].

The risk of exacerbation can be increased by almost a factor after recent urinary or respiratory tract infections, other viral infections that should be documented. These exacerbations should be differentiated from physiological pseudoexacerbations , which may occur against the background of a fever caused by an infection. A history of prior vaccination may also be related to this, although prospective studies have not found a correlation between routine vaccinations, such as those against influenza or hepatitis B, and an exacerbation of MS.

Loss of visual acuity or color perception often develops due to inflammatory demyelination in the anterior visual pathways. Optic neuritis, which in almost 2/3 of cases has a retrobulbar localization, leads to a decrease in visual acuity, accompanied by pain during eye movements. Visual field defects are also detected, usually of a paracentral nature (although any other variant can be observed) and an abnormal pupillary reaction to light (relative afferent pupillary defect). Rarely, anterior optic neuritis results in visible swelling of its disc (papillitis), but increasing swelling should suggest another cause. In most patients, vision is restored in an average of 8 weeks . The optic disc turns pale after many weeks, which indicates the loss of axons and their replacement by glia, as well as the loss of small capillaries that feed the nerve.

Internuclear ophthalmoplegia is a characteristic but not pathognomonic symptom of MS caused by a focus located in the ipsilateral fibers of the medial longitudinal fasciculus in the brain stem. Internuclear ophthalmoplegia is often asymptomatic, but patients may complain of diplopia or blurred vision when looking to the side. A careful study of the saccadic eye movement reveals insufficiency of the adductor muscles on the side of the lesion and adjusting nystagmus of the opposite eye Discoordination . Lesions affecting the brainstem and cerebellum pathways are common in patients with MS and can lead to impaired coordination. This is expressed in atactic gait, dysarthria or dysmetria .

Gait disorders. Individuals with MS may present with a spasmodic gait, an ataxic gait, or both , depending on the primary location of the pathology. Usually the balance suffers. Gait disorders can be caused by cerebellar, visual, motor and sensory dysfunctions.

Speech and difficulty in swallowing. Patients may complain of slurred speech. Most often this is associated with damage to the cerebellum and / or stem connections. Difficulty swallowing

solid and/or liquid food is possible at any time, although this is more typical in the later stages of the disease.

Spasticity occurs due to the loss of inhibitory impulses coming from the brain to the spinal cord, which leads to a contraction of the muscles of agonists and antagonists. This can manifest as painful spasms, cramps, stiffness, and clonus. Both weakness and spasticity lead to disability.

Other disorders of gait and voluntary movements. Paroxysmal short-term (<60 s) disturbances in gait or voluntary movements (choreoathetoid/dystonic) may be a sign of the appearance of ephaptic discharges (crossover), often originating from the brainstem. They should be differentiated from epileptic discharges, although both can be treated with anticonvulsants.

Paresis (motor disorders). Patients may complain of weakness of the upper or lower extremities, more often the lower. Weakness is usually pyramidal in nature, resulting in greater weakness in the extensor muscles of the upper extremities and the flexor muscles of the lower extremities.

Sensitivity disorders. Patients may complain of numbness, paresthesia, and dysesthesia . A burning sensation and painful hypersensitivity to touch (allodynia) or temperature exposure often occurs with demyelination in the spinothalamic pathways.

Pain. Paroxysmal pain, such as trigeminal or glossopharyngeal neuralgia, is quite common. Trigeminal neuralgia in MS may not clinically differ from idiopathic trigeminal neuralgia, but occurs rather as a result of inflammatory demyelination in the exit zone of the root of the fifth pair of cranial nerves than irritation of the peripheral (extrapontine) portion of the nerve. Girdle or torso pain, often referred to as "MS hug", is caused by damage to the spinal cord. MS patients often present with neuropathic pain that can be mistaken for a peripheral neuropathic compression syndrome (eg, carpal tunnel syndrome or lumbosacral radiculopathy).

Violations of the genitourinary system. Symptoms associated with bladder dysfunction include frequent urination, urgency, urinary incontinence, incomplete bladder emptying or urinary retention, and recurrent urinary tract infections. These symptoms must first be examined with an ultrasound of the bladder before and after emptying, in order to assess the residual volume of urine and, accordingly, determine the correct treatment tactics.

Bladder disorders include:

- inability to hold a normal amount of urine;
- incomplete emptying;
- discrepancy between emptying and accumulation.

Frequent urination, urgency, and urinary incontinence reflect detrusor overactivity , which is usually due to impaired voluntary and supraspinal control of urination due to spinal cord pathology localized above the lumbar and sacral segments. Normally, the detrusor stretch reflex is activated, signaling the need to urinate when the bladder contains 300-400 ml of urine. In patients with detrusor overactivity , as early as 50-100 ml can activate bladder contractions.

Bowel dysfunction. In the later stages of the disease, constipation often becomes such a violation. It usually serves as a manifestation of spinal cord injury and is exacerbated by

certain drugs, as well as by the patient's low mobility. Drugs that depress intestinal motility include antispasmodics, tricyclic antidepressants, anticholinergics , and apioids.

Cognitive impairment is often observed in long-term MS , but in some patients they can begin even at the stage of early exacerbations and play a significant role in the loss of work and daily activities. Patients with MS are particularly prone to developing "subcortical" deficits in information processing and spatial memory. Recent studies in the field of histopathology have demonstrated a serious involvement of the gray matter of the cortex and deep structures of the brain in PC, even at the stage of CIS. Brain volume measurement using MRI, which shows atrophy in both the cortex and deep structures of the brain, in combination with other modern methods, in particular the magnetization transfer method, confirmed the deep relationship between gray matter damage and cognitive impairment.

It is very important to assess and monitor the state of cognitive abilities from the moment of diagnosis; for this purpose, practical methods applicable in clinical practice should be developed. [12,13].

Types of course of multiple sclerosis:

Relapsing-remitting MS: Most (about 85% percent) of patients are initially diagnosed with relapsing- remitting MS. This type of multiple sclerosis is characterized by alternating periods of exacerbations and remissions (a period of complete or partial recovery). The duration of remissions with this type of course of the disease can be several months or years.

Secondary Progressive MS: Approximately 50% of patients diagnosed with relapsing-remitting MS develop secondary progressive MS within about 10 years, and symptoms steadily worsen. However, I note right away that these statistics are given without taking into account the use of immunomodulatory therapy, monoclonal antibody therapy. The results of clinical studies and the experience of practitioners suggest that the percentage of people in whom relapsing- remitting multiple sclerosis turns into secondary progressive MS will steadily decrease.

Primary progressive MS: Approximately 15% of patients are diagnosed with primary progressive MS, a type of disease in which there are no relapses and remissions, and the symptoms are steadily progressing.

Progressive-relapsing MS: Only 6-10% of patients are diagnosed with this type of MS course. As with primary progressive MS, the disease progresses steadily, but acute relapses occur as symptoms progress .[14,15]

Treatment :

In the treatment of multiple sclerosis, an integrated approach is very important, so the following **non-drug** procedures are of great importance:

physical therapy helps to compensate for the consequences of impaired motor ability. However, to achieve the greatest effect and, more importantly, eliminate the risk of harming yourself, you should contact a specialist for the development of a set of exercises;

the same applies to biomechanotherapy , i.e. physical exercises with the help of mechanical simulators. Studies have shown the effectiveness of this method with the right choice of load;

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if the patient has a weak muscle tone and pain syndromes, then you can resort to medical massage. However, remember that massage in some cases can worsen the condition,

increasing spasms. Therefore, it is necessary to resort to the help of a highly specialized specialist with experience in working with patients with multiple sclerosis;

BFB (biofeedback) consists in tracking and managing the physiological processes occurring in the body using the latest multimedia devices;

problems with the spine will help solve its traction traction. A beneficial effect of the procedure is the reduction of pain and training of the joints and vertebrae;

psychotherapy is a very important way to improve the patient's condition. The fact is that negative emotions can aggravate the disease, being a stimulus for additional disturbances in the work of the central nervous system.

Transcranial magnetic stimulation (TMS) is a method based on the principles of electromagnetic induction. It uses pulses of magnetic radiation that penetrate the brain. tissue, and it is a non-invasive, painless and virtually harmless procedure. Previous research supports the therapeutic potential of TMS in several neurodegenerative and psychiatric processes, both in animal models and in human studies.

Therefore, extrapolation of these TMS leads to the aforementioned neurodegenerative disease to other entities with etiopathogenetic and clinical analogy may increase the relevance and possibility of its use in multiple sclerosis (MS). The overall goal will be to demonstrate the effectiveness of TMS in terms of safety and clinical improvement, as well as how to observe molecular changes in relation to treatment.

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