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Current knowledge about Post-Polio Syndrome (PPS)

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Abstract

Introduction: PPS appears at least 15 years after polio virus infection, followed by stabilization of the neurological condition. In the course of the disease, there are neurological, musculoskeletal and general symptoms.

The aim of the study: The article focuses on the current knowledge about post-polio syndrome.

Material and method: Standard criteria were used to review the literature data. The search of articles in the PubMed, Google Scholar, ReaserchGate database was carried out using the following keywords: post-polio syndrome, poliovirus, poliomyelitis.

Description: There is no treatment that would cure PPS patients. However, interdisciplinary management focused on symptomatic treatment can significantly improve the quality of life of patients. One of the first solutions proposed to improve the clinical condition of patients with PSS was physical rehabilitation. In the treatment of post-polio syndrome, in addition to the use of non-pharmacological agents, therapy with the use of immunoglobulin infusions, the use of coenzyme Q10 or L-citrulline treatment has been introduced.

Summary: Despite the fact that there is no specific treatment in PPS, it has been proven that non-pharmacological intervention (motor rehabilitation, lifestyle change, orthoses, respiratory assistance) has a beneficial effect on relieving the symptoms of the disease

Keywords: post-polio syndrome, poliovirus, poliomyelitis

INTRODUCTION

First half of the twentieth century consumed many lives, not only by the warfare of the First and Second World Wars, but also due to the widespread Heine-Medina disease at that time. During this time, millions of people had this disease, and the onset and largest extent of the infection was in Europe and United States. The last polio epidemic took place in India in 1988. At the beginning of 2014, the disease was endemic in Nigeria, Afghanistan and Pakistan, and isolated cases were found in Ethiopia, Cameroon, Kenya, Somalia and Syria [1]. The first clinical description of poliomyelitis was made in 1793 by Michael Underwood, and a detailed picture of the disease in their works was provided by German - Jakob Heine in 1840 and the Swede - Karl Oskar Medin in 1890, which contributed to the popularization of the name Heine-Medin disease [2]. The problem of polio spread lasted until 1950, when the Polish virologist Hilary Koprowski drew an effective vaccine against polio [3]. A 99% drop in morbidity recorded in 1988 signaled the immediate elimination of polio virus. However, the elimination of new cases should not mean the end of the consequences of the disease. As many as 20 million people still live with disabilities, which are complications of this infection [4].

This article focuses on the dysfunctions of motor neurons that occur several dozen years after polio disease, which is referred to as post-polio syndrome (PPS). Studies show that the

frequency of PPS ranges from 30% to 80% of patients who have had a polio virus infection [3]. There are several hypotheses regarding the pathogenesis of post-polio syndrome, which will be presented later in this article. The current state of knowledge regarding the effective therapeutic approach used in this group of patients was also discussed.

POLIOMYELITIS ANTERIOR ACUTA

In the description of post-polio syndrome, one cannot omit the polio virus infection itself and the disease it causes. The polio virus belongs to the *Picornaviridae* family, it is a very small virus, whose genetic material is a single strand of RNA. The polio virus genome is enclosed in an icosahedral capsid consisting of 60 protomers formed by structural proteins (VP1, VP2, VP3 and VP4) [5, 6]. The virus is transmitted through the faecal-oral route [7]. After entering the body, polioviruses multiply in the lymphatic tissue of the throat and digestive system [8]. The incubation period generally lasts from 7 to 14 days, but an extension of this time to 35 days has been observed. Most people infected with polio get transient viremia. It further spreads to the tissues of the reticuloendothelial system without any symptoms. In 4-8% of infected people, symptoms appear, referred to as "minor illness", including fever, headache and sore throat (so-called miscarriage) [8, 9].

Two clinical forms of the disease can be distinguished in the course of poliomyelitis [10]:

1. non-paralytic – it concerned the majority of infected people and took three forms:

– asymptomatic (90-95% of cases);

– miscarriage - mentioned above;

– aseptic meningitis.

2. paralytic – constituting 1-2% of cases in which the virus penetrated the central nervous system where it attacked α-motoneurons of the anterior horns of the spinal cord and motor cortex. There can be distinguish:

– medullary form – most paralyzed cases, involvement of mainly the lower motor neuron, to a lesser extent the upper one with asymmetrical flaccid paralysis of the lower limb skeletal muscles, less often other parts of the body;

– bulbous form –with damage to the vegetative centers of the brain leading to paralysis of the respiratory muscles.

In the course of acute paralytic poliomyelitis, mainly the motor cells of the spinal cord in the cervical and lumbar spine are damaged [11, 12]. Often there is a transition of inflammatory changes from the frontal horns to the adjacent intermediate-lateral or posterior horns. In severe cases, respiratory muscle motoneurons are damaged and cranial nerve nuclei are involved:

trigeminal, facial, glossopharyngeal, vagus at the level of the bulb and pons. In the acute phase we also deal with damage to the neurons of the cerebral cortex - the pre-medial gyrus. Inflammatory changes can also be seen in other parts of the CNS: the hypothalamus, thalamus, cerebellum, sometimes in the dentate nucleus, and autopsy has also shown damage to the reticular activating formation, bridge and midbrain including the suture nucleus [13]. Poliovirus receptors are present on the motor plate as well as in regenerating muscle fibers [14].

PATHOPHYSIOLOGY OF PPS

The etiology of the disease remains elusive. However, there are several hypotheses regarding the mechanisms of post-polio syndrome. Among them we distinguish the following:

Dysfunction of an excessively developed motor unit - it is considered the most probable reason for the development of PPS. As a result of infection, about 95% of the α-motoneurons of the brain stem and spinal cord are damaged, of which about half die. Their function is taken up by other motor neurons, creating new axonal branches innervating nerve fibers that have previously lost their nerve connections. At the same time, a single neuron can supply a maximum of 20 additional fibers [15]. This leads to a significant expansion of motor units. This process occurs constantly and despite the relative muscle performance, subsequent α-motoneurons die, whose function is taken over by subsequent motor neurons. After many years of this phenomenon, there is metabolic exhaustion and gradual progressive degradation of axonal branches [16]. Evidence of this phenomenon can be found in electromyographic records [17, 18].

Neuromuscular junction defect - researchers suggest a functional and / or structural defect of the junction in polio survivors. Damage to postsynaptic neuromuscular transmission may be associated with reduced acetylcholine release. In these cases, a decrease in the diameter of the axonal endings and the number of acetylcholine-containing vesicles were observed in structural studies of the neuromuscular plate [19].

Reactivation of persistent infection - there is no clear evidence to support this theory. Some patients with post-polio syndrome had elevated titers of IgM against polio virus in blood serum, as well as present RNA of virus in the cerebrospinal fluid and blood lymphocytes, suggesting the presence of the virus in the body [20, 21]. To the disadvantage of this theory is the fact that other Coxsackie enteroviruses, for example, can give symptoms similar to poliomyelitis and then PPS. Cosackie RNA was also isolated in patients with PPS symptoms, suggesting a link with the immune response to the presence of enterovirus RNA antigen [22].

Autoimmune mechanisms - post-mortem analysis of spinal cord tissues provides evidence of inflammation there [23]. In vivo studies also show increased inflammatory activity of the body in the course of PPS. An increase in the concentration of pro-inflammatory cytokines in blood serum and cerebrospinal fluid was observed, among others. TNF-α and IFN-γ [24]. The presence of a chronic inflammatory process can be part of a delayed immune response to a primary infection, a complication of a previous infection, or an expression of ongoing inflammation.

The process of premature aging - with age, the nerve tissue undergoes gradual, physiological degradation. This process in people with polio may be strengthened due to previous infection, and the changes may be felt earlier than in healthy people. These patients will experience symptoms related to the aging process earlier and more strongly, such as a decrease in efficiency, weakening of muscular strength [25, 26].

Predisposition to degenerative changes of α-motoneurons, as a manifestation of blood supply disorders and glial damage secondary to ongoing inflammation, as well as genetic predisposition seem to be insignificant or have little impact on the development of this disease.

SYMPTOMS AND DIAGNOSTICS OF PPS

PPS appears at least 15 years after polio virus infection, followed by stabilization of the neurological condition [27]. In the course of the disease, there are neurological, musculoskeletal and general symptoms. Among the neurological symptoms, new, slowly progressive muscle weakness, paraesthesia, and over time muscle atrophy, dysphagia, dysphonia and respiratory failure can be observed. Musculoskeletal symptoms include joint and muscle pain as well as spondylosis and scoliosis. General symptoms include progressive fatigue, a decrease in physical performance, cold intolerance, sleep disorders and neuro-psychological deficits (cognitive impairment, depression, dysthymia) [28]. Generalized fatigue resulting from the disease is further compounded by weight gain, which often occurs in this group of patients, impaired breathing, hyposomia and polypharmaceuticals and leads to a significant deterioration of physical and mental activity, therefore it is considered one of the most worrying symptoms of PPS [3]. Patients observed in the clinics, in addition to significant generalized weakness, most often complain of severe muscle and joint pain. They also report difficulties in carrying out daily activities such as walking or climbing stairs.

To make a diagnosis of PPS, the following criteria, created by the European Federation of Neurological Societies (EFNS) [29], must be met:

1. confirmed history of poliomyelitis

2. partial / complete remission of the neurological and functional state after acute polio infection
3. a period of neurological and functional stability lasting at least 15 years
4. at least 2 new symptoms from the following: excessive muscle fatigue, muscle aches and / or conditions, muscle atrophy, cold intolerance
5. exclusion of other medical causes of ailments [30].

THERAPEUTIC STRATEGIES

There is no treatment that would cure PPS patients [31]. However, interdisciplinary management focused on symptomatic treatment can significantly improve the quality of life of patients [32].

Training programs

One of the first solutions proposed to improve the clinical condition of patients with PSS was physical rehabilitation [28]. Appropriate physical exercise has been proven to improve muscle strength, cardio-pulmonary fitness and reduce the severity of generalized fatigue [33]. JL. Kriz et al. showed that 16-week upper limb aerobic training in patients with PPS resulted in a significant improvement in VO_2max, minute ventilation (VE) and exercise power and time [30]. Other similar studies have also shown positive results from aerobic exercise without causing adverse events [34, 35]. When adding exercises, it is important to properly adjust the intensity of the training so that there is no overloading of the muscles - the intensity of the exercise should be set at 70-75% of maximum heart rate. Resting between interval exercises for sufficient recovery is also mandatory, and workouts should last no more than 20-30 minutes. Creating such an exercise program allows avoiding excessive muscle overload in patients, which could lead to a deterioration of muscle function [36].

The literature provides conflicting information regarding the impact of strength training on the clinical picture of PPS. In the MJ. Fillyaw et al. study, no difference in muscle endurance was observed between the 2-year group and the control group [37]. Whereas KM. Chan et al. in a study published in 2003, they found that moderate strength training used in 10 patients with PPS resulted in a significant improvement in muscle strength [38].

A good alternative for patients with PPS are training in warm water. Dynamic water exercises reduce the load on joints, improve the circulatory and respiratory condition, relieve pain and improve subjective well-being [39].

Therefore, physical rehabilitation should be seen as an important element in the patient's overall therapeutic program.

Respiratory aid

Respiratory disorders, which are associated with a significant risk of mortality in post-polio patients, are extremely common in PPS [40, 41].

Weakness of the respiratory muscles can cause insidiously developing respiratory failure, which is most often diagnosed when complications in the form of upper respiratory tract infections occur [40]. Early use of non-invasive methods to support breathing can significantly reduce the risk of acute respiratory failure and the need for a tracheotomy. JR. Bach et al. have shown that the use of non-invasive intermittent hypertensive ventilation (IPPV) resulted in SaO_2 increasing from 87.5 +/- 9.1% in patients to 96.2 ± 2.0% [42]. Good results are also brought by the use of mechanical inspiration-expiration (MI-E) and non-invasive blood gas monitoring, which can usually be done at home [40]. Respiratory muscle training is also useful, also for patients who already use non-invasive breathing assistance [43].

Dysphagia and dysphonia therapy

In the clinical picture of PPS, bulbar symptoms appear in the form of dysphagia and dysphonia, but they appear relatively rarely [44]. In such situations, rehabilitation of swallowing disorders, voice exercises and the use of voice support devices become useful [45].

Cognitive-behavioral therapy

Some researchers have suggested that generalized fatigue, which often occurs in PPS, may improve after cognitive behavioral therapy (CBT). However, the results of two independent papers published by M. Baller et al. and FS. Koopman showed that CBT did not reduce fatigue in patients with PPS [46, 47].

Intravenous immunoglobulin infusion

The discovery of an increase in pro-inflammatory cytokines in the cerebrospinal fluid, and thus the existence of an inflammatory process, suggested that intravenous immunoglobulin (IvIg) infusion would prove to be a good therapeutic option in PPS [48, 49]. H. Gonzalez et al. as the first to conduct a study assessing the effects of using an immunoglobulin infusion (30g / day for 3 days, repeated after 3 months) in patients with PPS. 142 patients took part in the study. It was observed that the treatment group, unlike the placebo group, showed an improvement in muscle strength (by 8.3% between the two groups at the end of the study in favor of the treated group) [48]. A similar study was carried out by G. Kaponides et al. They evaluated 14 patients with PPS receiving 30g / day of Ivig for 3 days. However, no significant increase in muscle strength or physical performance was found. However, there was a statistically significant improvement in the quality of life of patients assessed on the SF-36 scale [50]. E. Farbu et al. used a higher dose of Ivig in 20 patients with PPS (2g / kg bw). Also, they did not observe

changes in muscle strength and fatigue, but it was noted that patients receiving treatment reported a significant reduction in visual analog scale (VAS) pain after 3 months of treatment [49]. Similar results were obtained by L. Werhagen et al. in a study published in 2011. 31 out of 45 subjects with PPS (69%) experienced a reduction in perceived pain assessed in VAS. The effect of treatment did not differ in terms of age, sex and severity of disability [51].

Coenzyme Q10

A study by K. Mizuno et al. suggests that CoQ10 supplementation affects muscle energy metabolism. The mechanism of this effect is the stimulating effect of CoQ10 on mitochondrial respiratory chain enzymes [52]. This postulate was used by Australian scientists who conducted a study involving 103 patients with PPS. 54 participants were assigned to the CoQ10 group at 100mg for 60 days, while 49 people were assigned to the placebo group. The difference in perceived fatigue was not statistically significant between the two groups. Therefore, it was found that coenzyme q10 does not alleviate the clinical symptoms of PPS [53].

L-citrulline

Because L-citrulline changes muscle metabolism in such a way that it increases nitric oxide (NO) levels and increases protein synthesis, it has been assumed that L-citrulline will positively affect muscle function and increase muscle energy production in patients with PPS. This initiated the creation of an ongoing clinical trial in Switzerland. 30 patients with PPS will be randomly assigned to the treatment or control group. The primary endpoint is the change in a 6-minute walk test. Secondary endpoints include measurement of motor function, quantitative muscle strength, quantitative magnetic resonance imaging and magnetic resonance spectroscopy [54].

CONCLUSIONS

Despite the fact that there is no specific treatment in PPS, it has been proven that non-pharmacological intervention (motor rehabilitation, lifestyle change, orthoses, respiratory assistance) has a beneficial effect on relieving the symptoms of the disease. Among the studies on pharmacological methods, the most promising results were obtained by IvIg. However, more research is needed to discover long-term effects of treatment for the medicine to be used on a larger scale.

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