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# The role of pharmacotherapy, rehabilitation and nutrition in the treatment of children with West syndrome

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**Abstract**

West syndrome is classified as an epileptic encephalopathy. This syndrome is diagnosed in children aged 4-6 months. Its unsuccessful prognosis and complicated aetiology affects the delay of psychomotor development and cognitive functions of children. Repeated attacks inhibit the realization of next tasks assigned to the children's age. Properly conducted treatment of West syndrome should be interdisciplinary and include pharmacological treatment, diet and rehabilitation. Pharmacological treatment of West syndrome includes: the ACTH hormone, corticosteroids (prednisolone), vigabatrin, valproic acid, nitrazepam, pyridoxine, zonisamide, topiramide. The therapy includes also a ketogenic diet, which assumes changes in the proportion of nutrients. Predominant ingredient in the diet are fats (80-90% of daily intake of nutrients). Further, children with West syndrome require neuropsychological and motor rehabilitation (Vojta therapy, NDT- Bobath therapy).

Cooperation of therapeutic experts with parents of the children makes it possible to achieve therapeutic benefits through improvement of the children's quality of life. Mental disability and cognitive impairment associated with the syndrome result in the loss of skills already acquired by children, therefore motivation and support of the children's parents is a significant task assigned to therapeutic team members.

**Keywords:** West syndrome, children, therapy, treatment

## Introduction

West syndrome is classified as an epileptic encephalopathy, diagnosed usually between 4-6 month of age, however sometimes it can be diagnosed in older children. The patterns of hipsarrhythmia recorded in the electroencephalographic record are a result of aetiology of the disease, the maturity of the children's brain and the influence of antiepileptic medications [1]. The aim of this article is to present West syndrome, that is a drug-resistant epilepsy, the possibilities of pharmacological treatment, diet and rehabilitation in paediatric patients group. Due to the diverse aetiology of the syndrome prognosis is unfavourable and mortality rate is about 10%. Consequences of spasms lead to difficulties in implementation of further development tasks, inhibition of adaptation to the social environment, delay in psychomotor and cognitive functions development [2]. The majority of patients experience intensification

of clinical symptoms and evolution in different epilepsy syndromes, particularly Lennox-Gastuat syndrome. Diagnosis is based on characteristic dysfunctions of central nervous system (changes in neurological or neuroimaging examination), inappropriate mental and motor skills development. Symptomatic type of West syndrome includes cases developed in prenatal, perinatal and postnatal period. The largest percentage of cases (30-45%) constitute prenatal factors. They include hypoxemic and ischemic encephalopathy, brain development disorders, metabolic diseases, phakomatosis and infections. Second most common cause are perinatal factors. Neuroinfections, brain damages, central nervous system tumours, hypoxia and ischemic condition are considered postnatal factors. They are two types of West syndrome: symptomatic and cryptogenic [3]. West syndrome attack is characterized by the occurrence of sudden symmetric flexion /extension of the torso with simultaneous elevation and extension of lower limbs. Attacks usually appear in the form of series of spasms lasting about 10 minutes [4]. Lagaea L. et al conducted the study on a group of 51 infants with West syndrome (mild cramps, hipsarrhythmia), which aim was to establish initial treatment strategies and long-term results. Results of the study illustrate that the basic cerebral functions disorders and short-term periods of contractions are responsible for the later mental development and delay in psychomotor development of children with West syndrome [5].

**Pharmacological treatment of children with West syndrome**

According to The American Academy of Neurology 2004 and Child Neurology Society reports, the ACTH hormone is an effective treatment for a short-term flexion attacks. Similar results are achieved with vigabatrin, antiepileptic medicine, used also in West syndrome treatment, irreversible gamma-aminobutyric acid (GABA-T). Vigabatrin causes growth of GABA concentration in central nervous system [6]. Guidelines of American Academy of Neurology from 2012 recommend ACTH hormone and vigabatrin in short term treatment of West syndrome. ACTH hormone and vigabatrin are described as the first-line medicines. Therapy with prednisolone or ACTH hormone in cryptogenic type of West syndrome may replace vigabatrin treatment. The sooner are children treated after the first flexion attack the better are the long term results of the treatment. Short term ACTH hormone therapy through intramuscular injection allows to avoid side effects as a result of prolonged usage of hormonal replacement therapy. The most common side effects of ACTH hormone therapy are: increased appetite, irritability, increased body mass, hypokalemia, arterial hypertension. ACTH hormone treatment and long term intake of glicocorticosteroid are connected with

decrease in mineral bone density, which requires calcium supplementation, regular exercises and vitamin D level control. In case of glicocorticosteroid usage children should be observed in the direction of immunosuppression occurrence [7]. Study conducted by Lux AL. et al presented that a short-term hormonal therapy with ACTH hormone was effective in 60-80% of cases of infants with West syndrome [8]. According to the guidelines, vigabatrin treatment regarding infants may be continued for 6-9 months if ophthalmologic care is provided, therapy risk is assessed regularly, and the therapy is beneficial for the patient [7]. Vigabatrin treatment requires periodic ophthalmic screening because of its toxic effect on retina [6]. Vigabatrin is taken orally. Initial ophthalmologic assessment should be carried out no later than 4 weeks after the start of treatment, subsequent visits should be preformed once in every 3 months. Moreover, control examination is required 3-6 months after the treatment is completed [7]. Furthermore, valproic acid, nitrazepam and pyridoxine are used to treat West syndrome. Attempts were also made to use ketogenic diet, intravenous immunoglobulin, topiramate and zonisamide. In order to determine optimal treatment for paediatric patients with flexion attacks, it is necessary to conduct more prospective randomized trials, to determine short and long-term benefits of medication. Before starting the treatment, it is appropriate to assess children's mental and motor development to observe benefits of treatment and to determine the long-term consequences of the disease progression [6]. In the medical literature, West syndrome treatment guidelines are limited, most of the research is retrospective, and there are few prospective studies. Hormonal ACTH treatment, using corticosteroids (prednisolone) and vigabatrin is the most supported treatment of spasms in infants. As a second-line of treatment, it is recommended to use ketogenic diet, topiramide, zonisamide, pyridoxine. The treatment of West syndrome in older children depends on the cause of its occurrence. Identification of causes of West syndrome enables the selection of the right method of treatment. It is recommended to treat cryptogenic West syndrome through the use of ACTH hormone or prednisone. The symptomatic form of the syndrome caused by tuberous sclerosis should be treated with the use of vigabatrin, while the remaining causes by selecting one of the three medicines (ACTH, prednisone, vigabatrin) [9].

**The role of neuropsychological and physical rehabilitation in the treatment of children with West syndrome**

The rehabilitation of children with West syndrome is multitasking. It should lead to the quality of life improvement, optimize cognitive functions and give opportunities for social

adaptation. Psychokinetic stimulation is based on brain plasticity. Comprehensive, intensive, long-term rehabilitation of children creates the possibility of their best development. In the cognitive functions therapy it is significant to implement previously assigned aims and to arrange short- term planning rehabilitation activities. Diagnostic aims are based on monitoring course of the disease, brain damage localization, cerebral hemisphere dominance and the level of intelligence. Psychological rehabilitation is multilateral, its main aim is to improve the quality of life, social adjustment and cognitive functions optimization. The most common parents' mistake is setting goals that are impossible to achieve. Therapeutic aims impossible for children to achieve result from the diverse clinical course of the syndrome. The psychological aims should be individual, adapted to the children's developmental and social possibilities. Neuropsychological therapy should take the form of a dynamic interaction of all mentioned factors. Learning process is the main neuropsychological mechanism. Neuropsychological method includes a specific pedagogical and neurolinguistic approach, attempting to improve children's language skills. The therapeutic process has a long-term nature and requires cooperation of neurologists, physiotherapists and psychologists. Physical rehabilitation of children with West syndrome is crucial. Its aim is a maximal development the children's motor skills, especially regarding mobility. Before starting rehabilitation it is necessary to conduct physiotherapeutic diagnostics during which the behaviour and neurological development of paediatric patients should be assessed. Popular method used in the rehabilitation of children with West syndrome is Vojta therapy. This method is successfully used in children with various neurological syndromes, genetic defects, asymmetric body positioning or asymmetrical tension. The main component of the rehabilitation is preceded by the analysis of the body position and the definition of the motion initiation zone. The essence of exercises in Vojta method is to perform repetitive exercises of a specific parts of the body with dysfunctions through their stimulation [10]. Vojta therapy is performed by the children's parents after prior physiotherapist instructions. It serves to build and improve emotional connection between children and parents performing therapy. It is important that therapist's actions should not cause pain to children during exercises. Inadequate technique of treatment and the release of pain receptors makes it impossible to reach the appropriate stimuli from the deep sensory receptors and the lack of therapy effects [11]. During Vojta therapy children receive information via muscles and joints receptors through central nervous system stimulation. Receptors are activated in accordance with the correct movement pattern. Therapy allows in space body control, control of body posture,

stimulates psychomotor development, develops proper posture and movement patterns, which improves spontaneous motor skills. It forms the correct movement pattern, affects the respiratory system, tongue efficiency, speech development, stimulates peripheral circulation, supports the sucking and swallowing reflex, improves vegetative functions. Exercises should be performed regularly 3-4 times a day. It should last a few to thirty minutes, depending on the patients' needs and their age. Therapeutic program should be selected individually for each child next to observing and diagnosing children [12]. The basis of Vojta method is stimulation of coordination fields, in central nervous system, based on spatial and temporal summation. Through stimulation of several spheres of children's body arranged in the so-called activation position, the correct movement patterns are unlocked. Stimulation is carried out through a stimulus (pressure that is exerted by the thumb, two fingers or the edge of the palm). The stimulus triggers a strictly defined reaction. The earliest possible introduction of properly selected rehabilitation allows to prevent the fixation of pathological postural patterns [13]. Another method successfully used in treatment of children with West syndrome is Bobath method (NDT or NDT-Bobath). The creators of the method, Karel and Berta Bobath, combined the importance of the plasticity of the nervous system, sensory disorders and sensor motor sensation. The Bobath therapy should be carried out 7 days a week, 24 hours a day. It should be started as soon as possible after the diagnosis of children's disorder, to avoid pathological changes in the area of tension, sensation, perception and body movement. The therapy aims at physiological behaviours fixation and counteracting pathological behaviours. Conducted therapy teaches children new motor skills, including physiological reflexes, progressive developmental changes, neuroplastic possibilities of the nervous system, the rate of reflexes development and the reaction which aim is to stimulate proprioceptors. It uses the interaction between person, environment and functional task. In the Bobath method the therapist shows and supervises children's parents, participating in the therapy. Toys are a complementary therapeutic tool used in neurological rehabilitation [14]. The main purpose of Bobath method is to help children to achieve independence to the greatest possible extent. The therapy should be adjusted to physiological capabilities of children, their personality, and pace of development. Movement patterns should not be repeated very often. The active form of movement allows to achieve the right experiences as a result of stimulation. An important role is assigned to parents, their involvement, which favours achieving good results in the process of improving the children's development [13]. According to Bobath method, early introduction of kinesitherapy should be consistent with their developmental process, during

which the children gradually learn the movement, combines their sensory and motor experiences in cognitive schemes. Nervous system shows high plasticity and dynamic development, especially to the second year of age. The component of the development of the nervous system is an active development of neurons in the cerebral cortex and myelination of the cortico-spinal pathways. Kinesitherapy exercises help children to improve. Many different factors influence the achievement of positive results. The knowledge of those factors helps to set achievable goals and foresee further development of children. Effects of kinesitherapy consist of the number of exercises, its duration and the children's abilities determined by the disease [15].

**The use of ketogenic diet in West syndrome treatment**

Ketogenic diet assumes change in the proportion of consumed nutrients (proteins, fats, carbohydrates). The most important ingredient in the ketogenic diet are fats (80-90% of daily intake of nutrients). The percentage of consumed proteins and carbohydrates ranges from 10-20%. Increasing the amount of fat in diet at the expense of carbohydrates causes ketosis. An increase of glucose in the diet causes ketosis reduction. Ketosis is believed to have neuroprotective and anticonvulsive effects. High level of glucose in blood may increase the occurrence of spasms. Carbohydrate intake is a cause of the loss of neuroprotective effect of ketogenic diet. The basis of ketogenic diet is a high-fat diet with a reduction of glucose. The amount of protein in the diet is sufficient to ensure the proper growth and development of the body. Neuroprotective effect of the diet is obtained after 2 weeks of adhering to the diet. The effect is complex and multidirectional. It involves the change in gene expression, enzyme activity and mitochondrial proliferation. It induces biochemical and metabolic changes in the body [16]. Ketogenic diet affects the modulation of neurotransmitters, the level of biogenic monoamines and the antioxidant mechanism of neurons. Further, it involves pH changes, which provoke a direct effect on ion channels and neurotransmitter receptors. It modifies the tricarboxylic acid cycle to increase the synthesis of GABA in the brain. In addition, it regulates genes related to energy metabolism and affects the mitochondrial biogenesis. It reduces the production of reactive oxygen forms. It protects mitochondrial DNA against oxidative stress. It also improves the stability of the mitochondrial cell membrane, stimulates the production of ATP and minimizes oxidative stress associated with mitochondrial dysfunction. Epileptic seizures stimulate the production of free oxygen radicals, contributing to mitochondrial dysfunction. Reactive oxygen forms cause chronic redox status, changes in

neurons and increased susceptibility to spasms [17]. Prolonged ketogenic diet in children may provoke side effects, such as: nausea, vomiting, dehydration, constipation, loss of appetite, hypoglycaemia, hypercholesterolemia, delayed puberty, lower growth, overweight, reduction in bone density. Although in medical literature there are many studies on anticonvulsive and neuroprotective influences of ketosis, the phenomenon has not been fully discovered. Experimental reports encourage its use to delay the neurodegenerative effect of drug-resistant epilepsy [16]. Ketogenic diet has found its application in the treatment of West syndrome in infants as a part of therapy along with pharmacological treatment. According to a study by Kossoff E.H et al, on a group of 23 children (aged 5 months-2 years), the use of ketogenic diet gives a better results when it is used for a longer period of time. After 12 months of use of ketogenic diet, 46% of patients using the diet improved the level of 90%, and 3 patients experienced a period without spasms [18]. Another study confirming beneficial effect of ketogenic diet is the study conducted by Hong A.M. et al. This study examined group of 104 children (71% of children used vigabatrin or corticosteroids), confirms the benefits of ketogenic diet. More than 50% of spasms attacks improved in 64% after 6 months and 77% after 1-2 years. Spasms were not observed in 37% of patients. In 33% of patients side effects of therapy were reported. More than 50% of paediatric patients achieved improvement. Ketogenic diet is an effective therapy in 2/3 of patients. The study confirms that the effects of its usage may be stronger with simultaneous use of vigabatrin and corticosteroids [19].

**Conclusions**

Regular and targeted rehabilitation, pharmacotherapy, proper diet and care of children with West Syndrome give a chance for better functioning and achieving children's maximum potential. The task of both parents and members of the therapeutic team taking care of children with West syndrome is to create possibilities for optimal development in order to achieve the best therapeutic benefits by stimulating mental and psychomotor development.

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