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IMPROVING THE TACTICS OF TREATING CHILDREN WITH SEVERE CEREBRAL PALSY.

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Abstract. This article discusses severe forms of cerebral palsy in children of different ages and the development of anemia in these children, and iron supplements are needed to treat such children (III). The lack of data on this disease and the effect of ferric iron preparations on the course and prognosis of infantile cerebral palsy served as the relevance of the study.

The aim of the study. To evaluate the effectiveness of the use of ferric iron (Emfer) preparations on the course and prognosis of infantile cerebral palsy.

Materials and research methods. To achieve this goal, the results of treatment of 67 sick children with severe cerebral palsy were analyzed. Children age from 2 to 17 years old. All patients were ranked by age groups in accordance with the age classification with the GMFCS scale: up to 2 years old - 9 children (13.43%), 2-3 years old - 11 children (16.4%), 4-6 years old - 18 children (26.8%), 7-12 years old - 15 children (22.38%), 13-17 years old - 14 children (20.9%). The study group was divided into 3 subgroups of motor deficit according to the GMFCS scale: level 3 - 16 children (23.88%), level 4 - 20 children (29.85%), level 5 - 31 children (46.27%). All patients were divided into 2 groups - the main group - 38 children (56.71%, age - 11.04 ± 6.3 years), for whom anemia was corrected using the Emfer preparation based on ferric iron, and the comparison group - 29 children (43.29%, age - 12.06 ± 5.1 years), who were treated without iron supplements.

Research results. As a result of the study, it was found that the following syndromes were: oppression in the study group - 26 (68.23%), neuro-reflex excitability - 5 (15.30%), convulsive - 7 (21.17%). In the comparison group, depression syndrome - 20 (70.77%), neuro-reflex excitability - 5 (16.92%) and convulsive - 4 (12.31%). In both groups, the prevalence of depression syndrome was established in the structure of adaptation disorders. The work confirmed that diseases of the peripheral nervous system are manifested by a syndrome of motor disorders, the most important characteristic of which is muscle tone. Disorders of muscle tone (hypertonicity, hypotonia, dystonus) were observed in most of the studied groups. In patients with cerebral palsy in the self-service category, after the developed rehabilitation measures, it increased 2.3 times, in the category of communication (12 times), play activity (4.5 times), orientation (3.8 times), movement (3.3 times))

Conclusions: The performed complex of rehabilitation measures helps to reduce pathological reflexes, improve anthropometric indicators in the dynamics of observation, which has a beneficial effect on the outcome of the disease in children with neuro-motor disorders.

Keywords: cerebral palsy; scale GMFCS; disability; iron preparations; anemia; rehabilitation measures

Relevance. Cerebral palsy (CP) is one of the leading causes of childhood disability in the pathology of the nervous system. The representation of this group of diseases significantly increases in premature and deeply premature infants. The complication rate in LC is directly proportional to the level of motor deficit [1]. According to foreign studies, pathology of the visual analyzer occurs in 35.8% of children with CP; hearing impairment - in 12.3%; speech disorders - in 60.7%, intellectual disorders - in 48.0 - 60.0%, symptomatic epilepsy - in 31.4 - 40.0% [6]. Motor disturbances in LC are often associated with sensory disturbances, epilepsy, and secondary neuromuscular damage. Among the prenatal risk factors on the part of the mother, there are: a history of miscarriages or stillbirths, the birth of a child weighing less than 2000 g in the history, the birth of a child with delayed motor or speech development in the history, mental retardation, thyroid diseases, convulsive syndromes [2,4,5]. Prenatal risk factors during the current pregnancy include intrauterine growth retardation, clinical presentation of preeclampsia with edema, proteinuria and hypertension, multiple pregnancy, bleeding in the 3rd trimester and male sex of the fetus, intrauterine infections, infections or maternal intoxication, among which the most common infections of the group Toxoplasma, Rubella, Citomegalovirus, Herpesvirus spp. (ToRCH) and influenza infection [3,7-10]. Apgar scores at the 1st and 5th minutes of life are reliable markers of birth asphyxia; a number of studies indicate a relationship between a low score - from 6 to 4 or less points - with an unfavorable outcome of perinatal encephalopathy. Interesting is the fact that only 17% of full-term infants with perinatal encephalopathy have significant neurological deficits in the follow-up. This difference is explained by the polymorphism of genes encoding the synthesis of apolipoprotein E, which determines the susceptibility of the brain to adverse effects [11, 12, 14, 16, 19, 20].

The scale of great motor functions (Gross Motor Function Classification System, GMFCS) is used to assess the motor function of a child in everyday life; its use is mandatory when assessing indications for botulinum therapy and dynamic observation of a child during rehabilitation [13].

Considering that severe forms of anemia develop in children with severe cerebral palsy on the GMFCS scale 3-5 due to eating disorders [17], they need nutritional correction with the introduction of injectable iron preparations followed by oral administration.

Given the high importance of the use of iron (III) preparations and the ability of ferric iron to be oxidized to bivalent with subsequent reduction again to ferric and the effect of reduced iron on the nervous system by interacting with tau protein, through the ligand-receptor interaction of transferrin and apolipoprotein [18], it is interest in the use of ferric iron preparations in infantile cerebral palsy, which served as the relevance of the study.

The aim of the study. To evaluate the effectiveness of the use of ferric iron (Emfer) preparations on the course and prognosis of infantile cerebral palsy.

Materials and research methods. To achieve this goal, the results of treatment of 67 sick children with severe cerebral palsy were analyzed. Children age from 2 to 17 years old. All patients were ranked by age groups in accordance with the age classification with the GMFCS scale: up to 2 years old - 9 children (13.43%), 2-3 years old - 11 children (16.4%), 4-6 years old - 18 children (26.8%), 7-12 years old - 15 children (22.38%), 13-17 years old - 14 children (20.9%). The study group was divided into 3 subgroups of motor deficit according to the GMFCS scale: level 3 - 16 children (23.88%), level 4 - 20 children (29.85%), level 5 - 31 children (46.27%).

All patients were divided into 2 groups - the main group - 38 children (56.71%, age - 11.04 ± 6.3 years), for whom anemia was corrected using the Emfer preparation based on ferric iron, and the comparison group - 29 children (43.29%, age - 12.06 ± 5.1 years), who were treated without iron supplements.

The whole complex of clinical and neurological research methods, biochemical research methods was carried out.

Clinical and neurological examination, including interviewing children, their parents or guardians for complaints; analysis of exchange cards from maternity hospitals and medical records of an outpatient and inpatient patient; assessment of nutritional status; neurological examination; examination of related specialists (consultation with an ophthalmologist, pediatrician, orthopedist, speech therapist, medical psychologist).

The parents of all children gave written consent to participate in the experiment.

Statistical processing of the material was carried out using the Student-Fisher test, the nonparametric Mann-Winney test, the Kraskes-Wallis test, and the Wilconson test for indirect samples.

Research results.

67 sick children with severe cerebral palsy - 34 boys and 33 girls were divided into 3 subgroups according to the nosological form of the disease and the characteristics of the clinical manifestation.

The gender and age characteristics are given in table 1.

Table 1. Distribution of sick children by sex and age.

Age group	GMFCS 3		GMFCS 4		GMFCS 5	
	boys	girls	boys	girls	boys	girls
Up to 2	0	1	2	0	0	3

years						
2-3 years	5	2	4	2	7	2
4-6 years old	2	1	5	0	2	4
7-12 years old	2	2	3	3	4	3
13-17 years old	0	1	0	1	3	2
Total	9	7	14	6	16	15

Obstetric and gynecological history of mothers of children with the development of cerebral palsy.

The results of the influence of the age of mothers, previous pregnancies, childbirth and abortions (spontaneous and medical) on the incidence of cerebral palsy and the severity of motor deficits are presented in Table 2.

Table 2. Obstetric and gynecological history of mothers of patients with cerebral palsy (abs;%; M ± m).

Sign	GMFCS 3	GMFCS 4	GMFCS 5	Comparison group (29 children)
Mother's age, years	28,01±1,52	28,76±1,34	29,02±1,68	27,21±0,92
Number of pregnancies, abs (%)	4 (41,7)	5 (43,4)	6 (46,8)	3 (37,5)
Number of abortions, abs (%)	2 (20,85)	2 (17,36)	3 (23,4)	1 (12,5)
Delivery type abs (%)	5 (43,4)	4 (41,7)	3 (37,5)	3 (37,5)

Analysis of the timing of delivery and the main parameters of the newborn shows a significant difference in the indicators of the main and control groups. A statistically significant correlation was established between the Apgar scores at 1 and 5 minutes of a newborn's life and the subsequent level of motor deficit on the GMFCS scale (Table 3).

Table 3. Dates of gestation and basic indicators of newborns with subsequent development of cerebral palsy (M ± m).

Sign	GMFCS 3	GMFCS 4	GMFCS 5	Comparison group (29 children)
Due date, weeks	32,54±0,63**	32,87±0,71***	33,02±0,76*	33,87±0,35
Birth weight, g	2512,43±234,21**	2301,27±211,17***	2208,65±244,33**	2375,72±238,32
Apgar	5,21±0,32**	4,53±0,45***	5,34±0,67***	6,45±0,22

score at 1 minute of life, points				
Assessment on the Apgar scale at 5 minutes of life, points	6,55±0,21**	5,33±0,63***	6,23±0,34	7,55±0,67

*****-p≤0,05

**-p≤0,01

***-p≤0,001

The assessment of the clinical and neurological status was carried out according to the assessment of its functional status.

The functional status characterization included a description of the child's daily activity according to the GMFCS scale of large motor functions.

The 4th level of GMFCS is critical for the child's mobility - 35.7% of patients cannot move even within their own room, 21.4% can leave the house with support by the hands (1st level FMS). Almost all children with the 5th GMFCS level are immobilized - only 6.3% are able to move independently in the form of crawling.

Severe nutritional deficiency - was observed mainly in tetraplegia (4.3% of children) and diplegia (3.6% of children). Spastic hemiparesis was characterized prognostically most favorably: 83.9% of the subjects had the 3rd level of GMFCS.

The leading spastic phenomena described during the clinical and neurological examination of children with LC were adductor syndrome and hamstring syndrome. Adductor syndrome is a spastic contraction of the adductor longus muscles, adductor brevis, adductor magnus) with adduction of the patient's hips until they touch and cross, which makes it much more difficult to stand and walk without additional support. Increase in GMFCS level is statistically significant ($p \leq 0.001$). Hamstring syndrome, caused by spasticity of the internal flexors of the knee joint (mm. Gracilis, semimembranosus, semitendinosus), is most clearly manifested on palpation of these muscles in the position of the patient with a bent hip and slow extension in the knee joint. Its prevalence is also directly related to the level of motor deficit.

Nutritional disorders prevailed in children with spastic tetraparesis and non-spastic LC. It should be noted that regardless of the CP form, a high percentage of children with swallowing disorders was observed, which potentially creates preconditions for the development of malnutrition.

Syndromes: depression in the main group - 26 (68.23%), neuro-reflex excitability - 5 (15.30%), convulsive - 7 (21.17%). In the comparison group, depression syndrome - 20 (70.77%), neuro-reflex excitability - 5 (16.92%) and convulsive - 4 (12.31%). In both groups, the prevalence of depression syndrome was established in the structure of adaptation disorders. The work confirmed that diseases of the peripheral nervous system are manifested by a syndrome of motor disorders, the most important characteristic of which is muscle tone. Disorders of muscle tone (hypertonicity, hypotonia, dystonus) were observed in most of the studied groups.

An unfavorable prognosis prevailed in patients of the comparison groups (p,00.05). The level of a favorable prognosis decreased in the presence of hypotension and hypertonicity. In the structure of the relatively favorable prognosis of the patients of the main group, the prevalence of muscle hypertonia was established. In the structure of an unfavorable prognosis in patients of the comparison group, the prevalence of muscular hypotension in the history was established.

The study confirmed that the level of favorable and relatively favorable in both groups of subjects depends on the presence and degree of temporal delays in motor development caused by neuropsychiatric deficits.

A decrease in the level of a favorable prognosis was revealed with an increase in the level of a relatively unfavorable and unfavorable one with the formation of social insufficiency (restriction of self-service and movement) in both groups of subjects.

In the course of our work, manifestations of vegetative-visceral, dysthymic, dyssomnic and combined disorders were documented at the age from 1 to 5 years in all children of the studied groups. These clinical signs persisted at the age of 6-9 years in the majority of patients - in 7 (87.05%) of the main group and 7 (81.54%) of the comparison group and were accompanied by maladjustment caused by pain and paroxysmal disorders (vegetative crises, affective-respiratory seizures, fainting, episyndrome and sleep disturbance) in 3 (36.47%) of the main and 3 (41.54%) comparison groups. There was a significant predominance of these deviations in patients of the comparison groups ($p<0.05$). The persistence of signs of liquorodynamic disorders noted from 1 year to 5 years and in the age period from 5 to 9 years was documented in 17 (78.82%) children of the main group and 11 (63%) of the comparison group.

With dynamic examination 6 months after the start of the complex of rehabilitation measures, the increase in height in children with cerebral palsy ranged from 1.0 to 7.5 cm (Δ height + 2.4 cm), in children with muscle dysfunction syndrome the increase was from 1.6 up to 8.7 cm (Δ growth +2.8 cm), in children with hydrocephalus, the increase in height was from 0.8 to 6.5 cm (Δ growth +2.2 cm), in children with polyneuropathy of various origins the increase was from 1.2 to 7.8 cm (Δ growth + 2.4 cm). Consequently, the growth rate varied from 1.6 to 2.3 cm per year. It should be noted that all indicators characterizing the dynamics of growth in patients with movement disorders syndrome were higher than in other patients with pathology (Table 4)

Table 4. Anthropometric indicators 6 months after the course of rehabilitation measures.

Sign	Basic group	Comparison group
Height, cm	115,6	120,8
SDS growth	-0,7	-1,3
Δ growth	3,1*	2,2
ΔSDS growth	0,1*	0,01
Growth rate	8,0*	4,3
SDS growth rate	2,0*	-1.4*

*-$p\leq0,05$

In the patients of the comparison group, no significant difference in anthropometric indicators was observed.

In the main group, children with severe forms of cerebral palsy took iron (III) Emfer, which is characterized by the fact that ferric iron is converted into bivalent in the body with the help of special enzymes (ferrum reductase) and transported as part of the iron carrier proteins of special transporters (DMP1) on the membrane of the apical cell of macrophages, where, through complex biochemical transformations, bivalent iron is formed, which is necessary for the transport of oxygen and carbon dioxide, it also combines with haptoglobin and hemoglobin and, through apolipoprotein B, is transformed into bilirubin and biliverdin. The drug Emfer significantly improves the indicators of the clinical and neurological status due to the described mechanism, and it also increases the body's resistance to infectious agents, as the body's nonspecific resistance increases. By influencing tau proteins, trivalent iron is able to activate a complex consisting of a receptor-ligand-mediated mechanism, which is based on a decrease in the content of matrix metalloproteinases, which determine the degree of depletion, since their increased level leads to an increase in susceptibility to infection and causes the occurrence iron deficiency anemia. Since the human organism must very precisely regulate the iron content in the body, the concentration of ferric iron contained in the Emfer preparation is quite sufficient to reduce the degree of anemia at the cellular level.

In the hemiparatic form of cerebral palsy, motor functions in the lower extremities were restored at the beginning of treatment: muscle spasticity decreased, children dragged their leg less, walked longer, and tried to jump. The vocabulary has also increased, the possibility of social communication has expanded. Subsequently, active movements in the hand increased: children more often took toys, more manipulated them in the game. During the subsequent rehabilitation, intellectual capabilities improved: memory, attention, thinking, an interest in learning and communication with peers appeared.

The lowest results were noted in children with hydrocephalus. In such children, at the beginning of rehabilitation measures, it was possible to achieve some reduction in spasticity, better fixation of the head, and understanding of the addressed speech. The range of movements in the hands gradually increased, the children reached for the toys, grabbed them. During the further course of rehabilitation, many of the children tried to sit, stand, walk with support, that is, they restored gross motor skills.

In patients with cerebral palsy in the self-service category, after the developed rehabilitation measures, it increased 2.3 times, in the category of communication (12 times), play activity (4.5 times), orientation (3.8 times), movement (3.3 times)) - Fig. 1 and Fig. 2.

Figure: 1. The state of life of sick children after a course of rehabilitation therapy (main group)

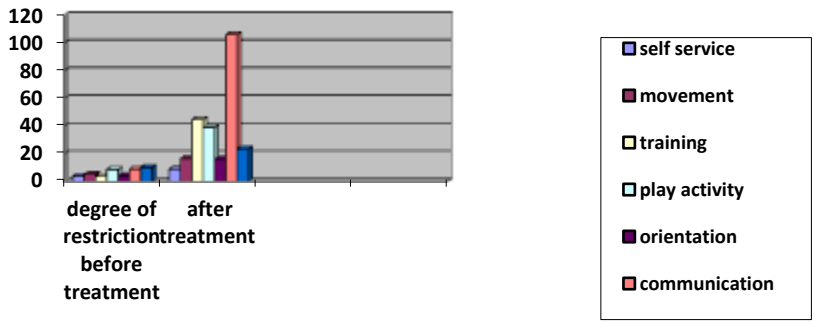
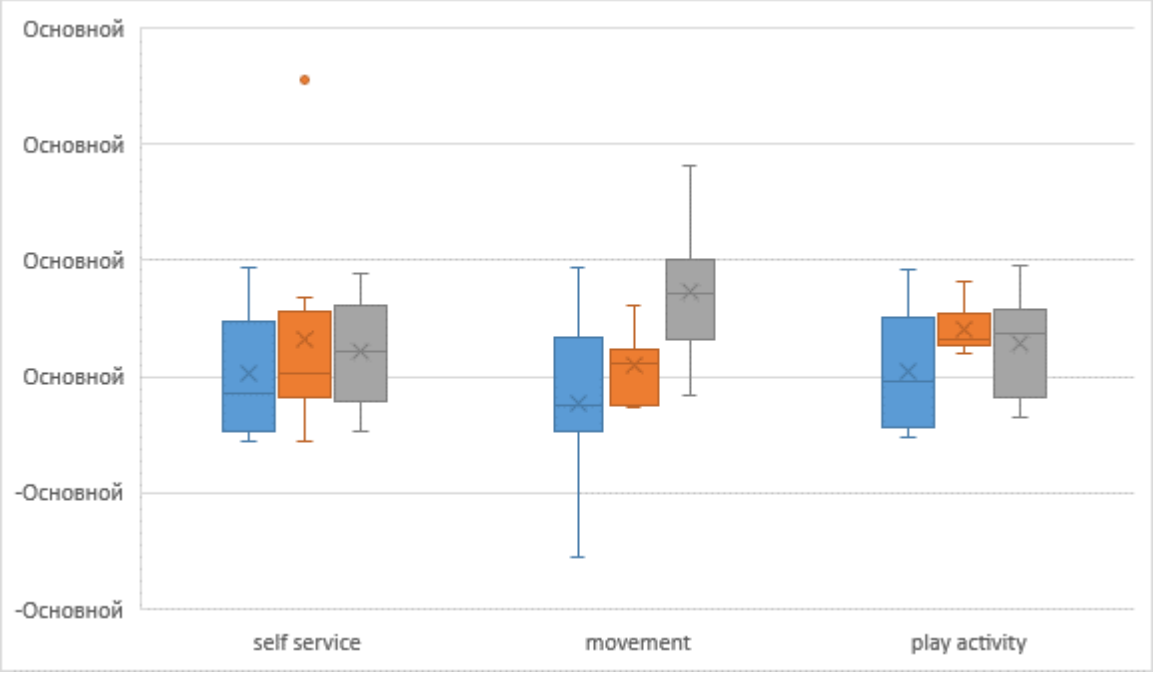


Figure: 2. The state of life of sick children after the course of rehabilitation therapy (comparison group) (Kraskes-Wallis criterion)



At the same time, the need for a disabled child suffering from diseases of the neuro-motor sphere for special equipment and aids before and after the rehabilitation measures had a marked difference. Thus, there was a positive trend in reducing the needs of sick children for special equipment already at the first stages of rehabilitation (Fig. 3 and Fig. 4).

Fig. 3. The need for a disabled child suffering from diseases of the neuro-motor sphere for special equipment and aids (main group)

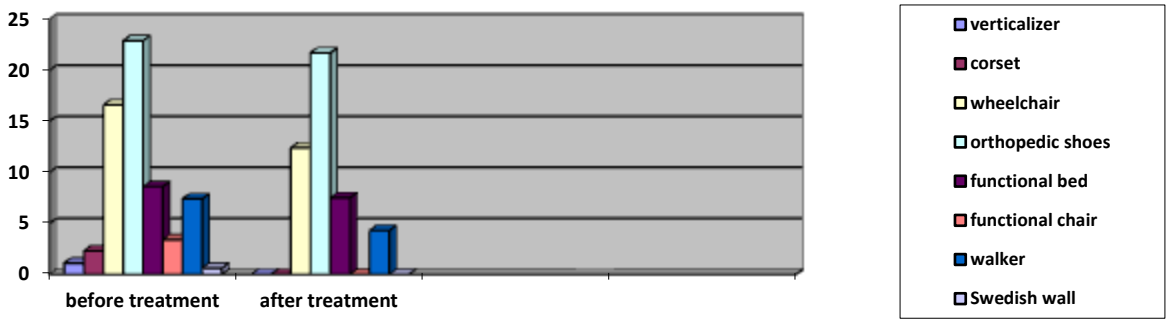
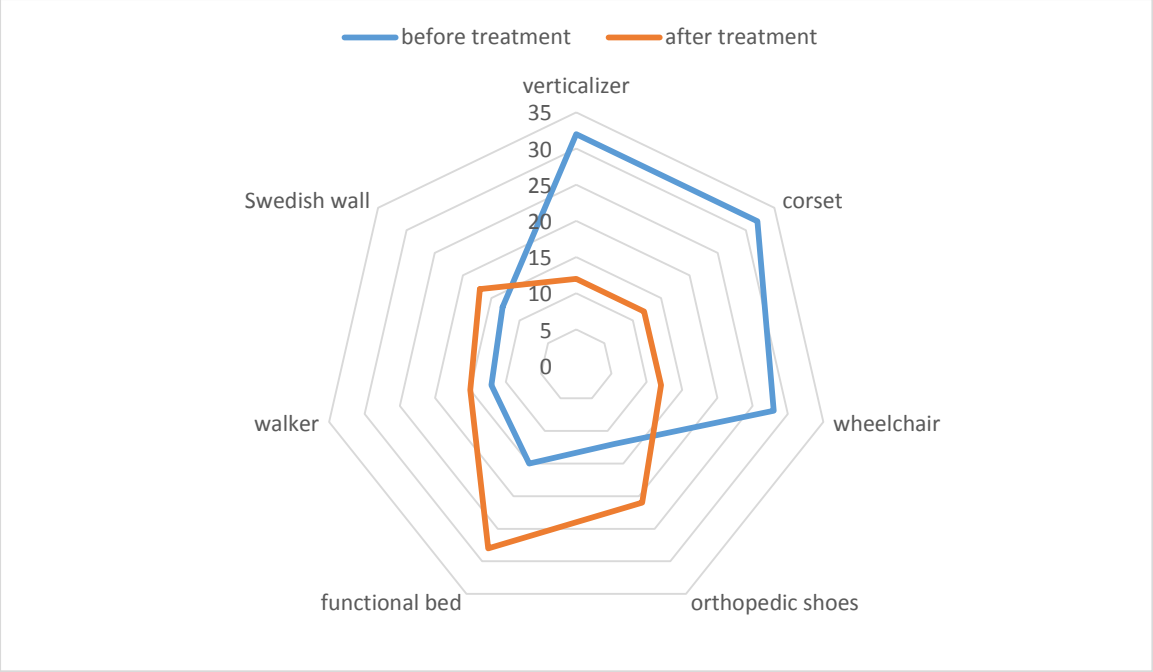


Figure: 4. The need for a disabled child suffering from diseases of the neuro-motor sphere for special equipment and aids (control group). (Wilconson test for indirect samples)



Conclusions: Children with neuro-motor diseases are statistically more likely to have very low physical development than controls. In patients with diseases of the neuro-motor sphere, disharmony of physical development occurs with a very high frequency and is caused by a lack of body weight. The complex of rehabilitation measures carried out helps to reduce pathological reflexes, improve anthropometric indicators in the dynamics of observation, which favorably affects the outcome of the disease in children with disorders of the neuro-motor sphere.

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