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## **POSSIBILITIES OF REHABILITATION TREATMENT OF CHILDREN WITH LYMPHOBLASTIC LEUKEMIA (LITERARY REVIEW)**

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**Ключевые слова:** дети, лимфобластный лейкоз, реабилитация

**Abstract. Possibilities of rehabilitation treatment of children with lymphoblastic leukemia (literary review).** Lukashchuk S.V., Lemko O.I. According to nowadays protocols of acute lymphoblastic leukemia (ALL) treatment, the percentage of recovering patients has increased significantly. This determines the necessity for complex long-term rehabilitation, as chemotherapeutic drugs are highly toxic and contribute to the development of comorbid diseases of the gastrointestinal tract, nervous and musculoskeletal systems. The purpose of the study was to review and analyze data from foreign and domestic literature concerning possibilities for rehabilitative treatment of children with ALL and to reveal informative methods assessing the effectiveness of rehabilitation. Important elements of rehabilitation goals and assessment of its effectiveness are the International Classification of Functioning, Disability and Health of Children and Adolescents, and the Quality of Children's Life. Rehabilitation begins at the hospital and includes psychological support for the child with the involvement of psychotherapists and family, as well as the performance of certain physical exercises lasting for 15-30 minutes, which are selected individually, taking into account the functional capabilities and motivation of the child. After the acute period, physical activity is carried out in accordance with an individual plan, which takes into account the peculiarities of the disease and includes active video games, cycling and other activities. Rehabilitation treatment on the basis of sanatorium-resort institutions with the participation of a multidisciplinary team is actual. Such treatment, in addition to physical exercises, includes the use of natural and preformed physical factors in order to influence the manifestations of comorbid pathology, and also contributes to an increase of the social activity and independence of the child. However, the number of such studies is limited, which determines the necessity to develop clear practical recommendations regarding methods of exposure, their duration and intensity.

**Реферат. Возможности реабилитационного лечения детей с лимфобластным лейкозом (обзор литературы).** Лукашук С.В., Лемко О.И. Благодаря современным протоколам лечения острого лимфобластного лейкоза (ОЛЛ) процент выздоравливающих пациентов значительно возрос, что определяет необходимость комплексной длительной реабилитации, поскольку химиотерапевтические препараты обладают высокой токсичностью, что способствует развитию коморбидных заболеваний желудочно-кишечного тракта, нервной системы и опорно-двигательного аппарата. Цель работы – сбор и анализ данных зарубежной и отечественной литературы о возможностях восстановительного лечения детей с ОЛЛ и поиск информативных методов оценки эффективности реабилитации. Важными элементами постановки целей и оценки эффективности реабилитации являются Международная классификация функционирования, ограничения жизнедеятельности и здоровья детей и подростков, а также качество жизни детей. Реабилитация начинается на госпитальном этапе и включает психологическую поддержку ребенка с привлечением психотерапевтов и семьи, а также выполнение определенных физических упражнений, которые подбираются индивидуально, продолжительностью 15-30 минут, с учетом функциональных возможностей и мотивации ребенка. После завершения острого периода физические нагрузки проводятся согласно индивидуальному плану, который учитывает особенности течения болезни и включает активные видеоигры, катание на велосипеде и другие занятия. Актуальным является реабилитационное лечение на базе санаторно-курортных учреждений с привлечением мультидисциплинарной команды. Такое лечение, кроме физических упражнений, предусматривает использование природных и преформированных физических факторов с целью воздействия на проявления коморбидной патологии, а также способствует повышению социальной активности и самостоятельности ребенка. Однако количество таких исследований ограничено, что определяет необходимость разработки четких практических рекомендаций относительно методов воздействия, их продолжительности и интенсивности.

Acute lymphoblastic leukemia (ALL) is one of the most common cancers in children. However, in recent years, thanks to the development of international protocols, the results of treatment of patients with this pathology have improved significantly.

The purpose of the work is to collect and analyze data from foreign and domestic literature on the possibilities of rehabilitative treatment of children with ALL and search for informative methods for assessing the effectiveness of rehabilitation.

Treatment of patients with ALL is based on the use of chemotherapeutic drugs that have high toxicity. Adverse effects include cardiotoxicity, hepatotoxicity, nephrotoxicity, development of osteonecrosis, pan-

creatitis, thrombosis, psychosis, patients often experience flu-like symptoms, fatigue, pain, nausea, vomiting, hair loss, possible lesions of the bronchopulmonary system. [14, 18]. Special attention should be paid to neurotoxicity, which has various clinical manifestations, ranging from acute neurological disorders (paresthesia, ptosis, paresis of the vocal cords, etc.) to seizures or chronic encephalopathy. Neurological symptoms regress very slowly, and in some cases do not disappear at all [31]. Complications from the oral cavity – from mycosis of the mucous membrane to necrosis of the maxilla are possible [19]. Therefore, it is important not to forget about improving oral hygiene and educating parents and children on this

issue [17]. Among the difficulties that worsen the quality of life, children and parents also note problems with weight, eating, dyspepsia and difficulty moving [20]. About half of patients report a decrease in the volume of movements in large joints, a decrease in muscle strength, especially the back muscles [4].

It is known that 6 months after the end of ALL treatment, most patients are dissatisfied with their physical and psychological condition [28]. Even a year after treatment, such children have higher mean heart rate during normal exercise, may have difficulty walking, running, etc. [11]. 2 years after the end of therapy in children with ALL, compared with healthy children, reduced indicators of physical well-being, emotional well-being and social interaction are noted [9].

The vast majority of patients only 3 years after intensive chemotherapy restores their physical capabilities and emotional state, gets rid of fatigue, which indicates an improvement in quality of life. However, performance remains low [21]. Some authors point out that even 5 or more years after chemotherapy and radiation therapy, children may experience maladaptation, delay or impairment of neuropsychological and physical development [5]. All of the above is long-lasting and significantly worsens the quality of life of children with ALL and their families, reduces their motivation for daily life.

Thus, undoubtedly leukemia patients need long-term rehabilitation to improve their quality of life, with special emphasis on psycho-emotional state, improvement of physical activity, as well as correction of comorbid conditions.

The International Classification of Functioning, Restriction of Life and Health of Children and Adolescents (ICF-CA), which has been implemented in Ukraine since 2018, is a universal tool for formulating goals and evaluating the outcome of an individual rehabilitation program in this group of patients. This classification includes more than 1,400 evaluation categories. The main sets of codes (ICF Core Set) for certain pathologies have been developed.

Darcy L. et al. [15] formulated 52 questions divided into four groups: "body and emotions of the child", "daily life of the child", "the child's need for support" and "contacts of the child with medical services" which are reflected in the ICF-CA.

An important indicator of the effectiveness of the rehabilitation process, in addition to the ICF, is the quality of life, for which a special KINDL-R questionnaire has been developed, which assesses the quality of life of young patients related to health. Three versions of self-assessment of quality of life for children of different ages (4-6 years, 7-13 years and 14-17 years) and two versions for parents of children

(3-6 years and 7-17 years) were developed. KINDL-R includes 24 items covering six aspects of life (physical well-being, psychological well-being, self-esteem, family, friends and school) and six additional points about the disease [27].

To objectify rehabilitation, it is proposed to use various special scales and tests to assess muscle endurance and strength, flexibility, level of daily activity, capabilities of the cardiorespiratory system, etc. [26]. However, the only unified criteria that would be convenient to use in everyday practice are not yet agreed. Too many different indicators make it difficult to use them.

An important part of the rehabilitation process is the psycho-emotional state of the child, a psychologist's support throughout the treatment is recommended. It is important for patients to understand the changes in their body caused by the disease, the need for further treatment. Good relationships between children and staff encourage the child's participation in treatment [16]. At the stage of inpatient treatment, communication with family and friends can also be a good way to solve psychological problems [28].

At the stage of maintenance treatment and outpatient therapy of patients with ALL, a positive effect is obtained in children's visual communication with animals and tactile (biosensory) contact with them, in particular with dogs. Such contacts, due to a number of biochemical reactions with the release of hormones and cytokines, increase the feeling of satisfaction and relaxation in children, help reduce irritation, pain, anxiety and stress. Forming emotional bonds with animals can alleviate the problem of distance from relatives, friends, school, and other social relationships. Research has shown that even in the hospital (acute) stage of rehabilitation, animal therapy can divert attention from the disease more effectively than other leisure activities, including reading and interacting with volunteers [30].

Psychological state of the child is directly correlated with the motivation for daily functioning and performance of physical activity, which contributes to improving the quality of life. There are many studies in the foreign literature that prove the importance of physical therapy as a component of the rehabilitation program of children with oncohematological pathology. Physical therapy involves physical activity, therapeutic exercises and active play to restore strength, balance, flexibility and coordination. Patients can be referred to the rehabilitation department after the first course of chemotherapy, especially if they complain of physical weakness. In case the patient is at high risk of infection, bleeding or shock, the physical therapist

can conduct a rehabilitation program at the patient's bedside [12].

There are studies that indicate the safety of physical rehabilitation even in children with thrombocytopenia after stem cell transplantation, as no correlation was found between the intensity of exercise, on the one hand, and bleeding and platelet count, on the other [29].

In the first, hospital stage, the duration of classes can be 30 minutes daily, except weekends, with a gradual increase in the program to the highest functional level. Training should consist of stretching and strengthening the joints and muscles of the upper and lower extremities. To assess the effectiveness of early rehabilitation, a simple mobility scale (DEMMI) which includes 15 points can be used: from No. 1 – movements in bed to No. 15 – jumps [12]. The functional level is assessed by a doctor once a week. In any case, the intensity of physical activity is selected individually based on a detailed analysis of physical status [4]. The program of individual training can be adjusted daily, based on the functional needs and medical status of the patient, ensuring the prevention of falls and injuries during therapy [29].

As noted, the negative effects of ALL are more often associated with the musculoskeletal system and nervous system. On the other hand, limited physical activity is a risk factor for long-term persistence of symptoms and side effects after chemotherapy. The use of therapeutic (physical) exercises can significantly reduce the negative consequences of treatment in cancer survivors [24].

Braam K. et al. (2016) [25] conducted a thorough review of the literature on the effectiveness of physical exercises in children during the first five years after ALL diagnosis. The positive effect of therapeutic exercises to prevent movement disorders, improve cardiorespiratory endurance, flexibility, increase muscle strength and range of motion, reduce fatigue is shown. All this is reflected in the restoration of quality of life [31].

During the period of maintenance (second stage) treatment, most authors recommend classes lasting from 15 minutes to 60 minutes for such categories of children. Period – from 4 weeks to two years. Preference is given to combined training regimes with the inclusion of aerobic and anaerobic exercises, swimming, cycling, etc. Classes can be held anywhere: in the hospital, in the physical therapy center, at home. At first it is better to use classes according to the individual program, later it is possible to attend group ones [13, 23]. It is very important to control the observance of regular physical activity.

To date, therapeutic exercises are considered a safe intervention, which gives positive results for patients with leukemia. However, there are no clear practical recommendations for specific parameters of therapeutic exercises according to different levels of ICF and the optimal exercise program for children with ALL [25].

In our country, a comprehensive approach to the rehabilitation of children with leukemia is carried out on the basis of sanatoriums. Such recovery is the third stage of rehabilitation, the purpose of which is to improve the functional state of the body's systems as a whole, increase tolerance to physical activity, improve psychological status, reduce drug load [5].

Until recently, oncological pathology was an absolute contraindication to physiotherapy. However, modern ideas about the pathological process allow differentiated use of physical factors in the complex of rehabilitation treatment. Sufficient facts have been accumulated about the effectiveness of spa treatment of children who had cancer, in particular in order to influence comorbid conditions and comorbidities. It should be noted that in this category of patients, even with increasing remission, the percentage of comorbidities increases. Among children aged 6-15 years who had acute leukemia, the structure of concomitant pathologies is dominated by diseases of the digestive system, upper respiratory tract, central and peripheral nervous system, musculoskeletal system, cardiovascular system [6]. Based on a comprehensive examination of the child, an individual program is formed using the possibilities of natural and formed physical factors, therapeutic exercise, reflexology and psychotherapy [1, 5].

Given the polymorphism of complaints, among which the manifestations of astheno-neurotic, dyspeptic and pain syndromes, are predominant it is recommended to include hydrotherapy (baths, showers), electrotherapy, magnetic therapy into the basic rehabilitation complex [6]. Thus, the use of low-frequency magnetic field is justified in concomitant diseases of the nervous system to increase the speed of impulses through nerve fibers, reduce perineural edema, etc. [7]. Acupressure with the involvement of special points, as one of the methods of reflexology, can reduce pain and improve general well-being in children with oncopathology [8].

There are studies that indicate that general massage sessions (20-30 minutes, 6 procedures) can reduce the intensity of pain in children aged 10-18 years who have been treated for cancer, including ALL [10]. However, most authors consider the positive effects of massage to be clinically insignificant both to reduce pain and to reduce physical fatigue,

anxiety and improve quality of life, which was shown in a systematic review [22]. The unfounded fear of health professionals about the correlation between massage and the risk of metastases and the closedness of such patients to research negatively impacts for the creation of sufficient evidence to support this practice [10, 22].

Staying at the resort allows the child to quickly break free of a stressful situation, to distract from the disease. An important component of spa treatment is hydrotherapy, in particular in the form of baths. Sodium chloride and oxygen baths of indifferent temperature for 5-10 minutes every other day, a course of 8 procedures can improve the well-being of the child, increase his efficiency. In such children, in order to normalize the processes of lipid peroxidation and antioxidant protection and indirect immunocorrection, singlet oxygen therapy is prescribed [2].

Climatotherapy involves walking in the fresh air, air baths with a cold load, sea bathing at a water temperature of not less than 21°, which increases the adaptive capacity of the child [2].

Due to the fact that lymphoblastic leukemia, as noted above, is accompanied by the development of comorbid pathology and the formation of metabolic disorders, the use of balneotherapy is promising. The antitoxic, alkalizing, adaptogenic properties of natural mineral waters are proved, which determines the expediency of their use in the complex treatment of patients as adjuvant therapy. Drinking mineral water can help reduce side effects and neutralize the toxic effects of drug therapy for leukemia [20].

One of the possible complications of leukemia may be iron deficiency anemia. The experience of using natural ferrous mineral waters of the Soimy resort (Zakarpattia region), with a specialized rehabilitation department, is described. Long-term observations show the effectiveness of compensation for iron deficiency in the use of these waters. Favorable influence on the functional state of the digestive system, positive dynamics of clinical and

laboratory indicators of iron metabolism have been revealed. At the same time, a significant increase in the levels of iron, calcium and magnesium (by 46-52%) in the hair of patients indicates the high bioavailability of elements and their inclusion in active metabolism [3]. However, no such studies have been performed in children with ALL.

At the same time, it should be emphasized that the medical complex in rehabilitation should be sparing for the weakened body, not to cause sharp changes in the functioning of systems, so as not to lead to failure of remission. All loads must be distributed evenly, with the obligatory observance of rest time after procedures.

Thus, a number of authors have shown the effectiveness of spa treatment in patients with ALL. The complete absence of physiotherapy is unjustified, but a set of physical factors must have a proven lack of negative impact on the underlying disease in children [1].

## CONCLUSIONS

1. Thus, modern programs for the management of patients with ALL, considering the severity of the underlying pathology and significant side effects of chemotherapy, which are accompanied by the development of a number of comorbid conditions, should include special comprehensive rehabilitation measures, beginning with the acute period and especially later, in the period of convalescence.

2. Such long-term comprehensive programs require an individual approach, taking into account the peculiarities of the disease and the psycho-emotional and physical condition of the child.

3. It is expedient to carry out the third stage of rehabilitation in the form of spa treatment with the involvement of a multidisciplinary team and the use of both natural and preformed physical factors.

Conflict of interest. The authors declare no conflict of interest.

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