

MINERAL WATERS AS A PART OF SANATORIUM - RESORT REHABILITATION FOR CHILDREN IN REMISSION OF ONCOLOGICAL DISEASES

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Abstract

The aim: to make clinical and clinical-laboratory assessment of the dynamics of indicators in children after treatment of oncohematological diseases (OHD) and solid tumors (ST) after prescription of general rehabilitation complex (GRC) and rehabilitation complexes (RC 1-5) with addition of mineral waters (MW).

Materials and methods. Sanatorium-resort rehabilitation of 485 children was carried out in the sanatoriums of Ukraine (Odessa and Truskavets). GRC included a gentle motor mode; climatotherapy; dietary food; therapeutic physical training according to the methods in special medical groups for children with various somatic diseases; singlet-oxygen cocktail; baby herbal tea (holosas with ascorbic acid); psychological assistance programs for sick children and their parents. In RC (1-5) mineral waters of different physical and chemical composition ("Aqua-Libra", "Voznesenskaya", "Truskavets-Aqua-Eco", "Morshinskaya", "Maria") were additionally included.

Methods. Clinical, functional (electrocardiography, electroencephalography, echoencephalography, ultrasound Doppler), laboratory (general clinical, biochemical, nonspecific adaptive reactions of the body, indices of hematogenicity ratios, statistical).

Results. Multidirectional positive effects of rehabilitation complexes with mineral water intake have been established. Disappearance or significant reduction of complaints, manifestations of pain, dyspeptic and asthenic syndrome, as well as objective signs of the disease took place. The use of differentiated programs of sanatorium rehabilitation with MW inclusion, taking into account the period of OHD or ST remission and concomitant diseases of the hepatobiliary, cardiovascular and nervous systems, programs of psychological support improves clinical and functional condition of the patients. The necessity of caution regarding the use of biologically active MW and the advantages of low-mineralized MW without specific components and compounds by gentle methods is substantiated.

All human studies were conducted in compliance with the rules of the Helsinki Declaration of the World Medical Association "Ethical principles of medical research with human participation as an object of study". Informed consent was obtained from all participants.

Key words: children, oncohematological diseases, solid tumors, sanatorium rehabilitation, mineral waters, clinical indicators, clinical and laboratory indicators

Introduction

In recent years, the effectiveness of treatment and prognosis in various cancers in children has significantly increased. Successes in treatment with the use of modern programs have increased life expectancy and in 80% of cases to ensure the recovery of sick children. In acute lymphoblastic leukemia, this figure is 90% [1, 15, 16].

According to literature data, more than 6% of the working adult population was diagnosed with cancer in childhood [2-6]. The disease itself and its treatment cause various disorders of the child's physical development, bone, cardiovascular, endocrine, immune systems, is traumatic for the child's and parents' psyche. The normal course of the educational process is disturbed, there is a restriction of contacts with friends and the complexity of interpersonal relationships.

In Ukraine in the early 90's modern protocols of oncological diseases chemotherapy began to introduce. At present, the treatment of oncohematological diseases (OHD) and solid tumors (ST) is standardized in accordance with modern world principles of their diagnosis and treatment. However, polychemotherapy, radiation therapy, especially in children with comorbidities, cause various disorders of nervous, musculoskeletal, cardiovascular, endocrine, immune systems, psycho-emotional sphere.

The use of targeted rehabilitation programs will improve the psychoneurological and general condition of sick children [7].

For the organization of sanatorium-resort rehabilitation (SRR) of sick children the indications and contraindications to sanatorium treatment by appointment of separate physical factors in the general complex, conditions of selection on SRR of children with oncohematological diseases are defined.

The rehabilitation of children after special treatment is aimed at improving the quality of life, but many issues remain unresolved. In particular, only certain natural and preformed physical factors are used in rehabilitation. For example, mineral waters of different physical and chemical composition, which are widely represented in different regions of Ukraine, are insufficiently used due to the lack of proven effectiveness, scientifically

based indications and contraindications for their use in remission children.

The aim. To assess changes in clinical, functional and psychosomatic state of children during SRR programs with the use of drinking courses of mineral waters of different physical and chemical composition ("Voznesenskaya", "Truskavets Aqua-Eco", "Aqua Libra", "Morshinskaya", "Maria").

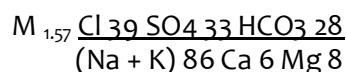
Methods

485 children with OHD and ST underwent SRR in sanatoriums of Odessa and Truskavets (Ukraine). Mineral waters (MW) of different physical and chemical composition of Odessa, Voznesensky, Truskavets, Morshyn deposits (packed), Truskavets deposit (pump-room) were prescribed.

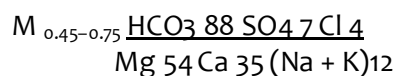
The general complex of rehabilitation for children with oncological diseases included gentle motor mode; climatotherapy; dietary food; therapeutic physical training according to the methods in special medical groups for children with various somatic diseases; singlet-oxygen cocktail; baby herbal tea (holosas with ascorbic acid); psychological assistance programs for sick children and their parents.

In addition to the general complex, 5 medical complexes included MW drinking.

Rehabilitation complex № 1 was prescribed for 48 children with concomitant diseases of hepatobiliary system in remission of OHD (30 patients) and ST (18 patients). The complex additionally included mineral natural medical table water "Voznesenskaya" of sodium bicarbonate-sulfate-chloride content:



Rehabilitation complex № 2 was developed for 26 children with concomitant diseases of hepatobiliary system after treatment of ST. Additionally mineral natural table water "Truskavets-Aqua-Eco" of hydrocarbonate-magnesium-calcium content was prescribed:



Rehabilitation complex № 3 was used in the group of 74 children with concomitant diseases of hepatobiliary system in OHD remission (42 patients) and ST (32 patients). For them mineral therapeutic

table water "Aqua-Libra" sodium bicarbonate-sulfate-chloride:

M_{1.0-1.3} Cl 30-50 SO₄ 25-40 HCO₃ 20-35
(Na + K) 75

was additionally prescribed.

Mineral waters for children with concomitant diseases of hepatobiliary system or with functional dyspepsia in medical complexes № 1-3 were prescribed 4-3 times a day, T₃₀₋₃₅ °C at the rate of 3 mg / kg of body weight per reception, for 30-40 min before meals.

Rehabilitation complex № 4 was prescribed for children in OHD remission (18 patients) and ST (10 patients). It included a differentiated drinking intake of mineral natural table water "Morshinskaya" slightly mineralized without specific components of hydrocarbonate sodium-calcium:

M_{0.14-0.18} HCO₃ 70-80 Cl 11-16 SO₄ 8-14
Ca 34-54 (Na + K) 33-46 Mg 9-22

MW "Morshinskaya" drinking course was prescribed at the rate of 3 ml / kg of body weight per dose, 30 minutes before meals, thrice a day, water temperature 28-35 °C.

Rehabilitation complex № 5 prescribed for 48 children in the period of OHD remission (26 patients) and ST (22 patients) at the conditions of children's sanatorium "Dzherelo" (Truskavets). The complex mentioned included differentiated drinking reception of pump-room mineral natural medical table water "Maria" sulfate-calcium-magnesium with a high content of organic matter

M_{0.6-0.8} HCO₃ 65-96
Ca 35-66 Mg 21-50

Drinking course of MW "Maria" was prescribed at the rate of 3 ml / kg of body weight for a single intake, 30 minutes before meals 3 times a day, at a water temperature of 28-35 °C. 2).

Research methods. Clinical, functional (electrocardiography - ECG, electroencephalography - EEG, echoencephalography - EchoEG, ultrasonic Doppler examination - UDE), laboratory (general clinical, biochemical, nonspecific adaptive reactions of the body - NARB, indices of hematogenicity ratios for estimation of non-specific reactivity and endogenous intoxication level), statistical (method of variation statistics for averages - Student's coefficient, non-parametric Pearson's criterion χ^2) [8-11].

Results

Under the influence of SRR with the use of MW "Voznesenskaya" (RC 1) in the vast majority of children pain disappeared or decreased its manifestations. The frequency of hepatic pain decreased by 5.3 ($p < 0.001$), stomach pain - by 4.0 ($p < 0.05$), intestine one - by 4.0 times. The frequency of dyspeptic syndrome also decreased significantly (depending on the manifestations by 2-5.1 times).

A similar trend was observed in asthenic syndrome, the frequency of which in most patients decreased or disappeared. Thus, the frequency of weakness decreased by 3.3 ($p < 0.05$), fatigue - by 4.0 ($p < 0.01$), irritability - by 2.6 ($p < 0.05$), headache frequency decreased thrice ($p < 0.05$).

The data of the objective examination and its dynamics also testified to the positive effect of the complex with the use of sulfate-containing MW "Voznesenskaya", first of all, in children with digestive system concomitant diseases. In most children, the incidence of pain at the Kerr point decreased from (36.7 ± 8.8) to (3.9 ± 3.5)%, $p < 0.05$, Ortner's symptom - from (30.0 ± 8.4) to (7.8 ± 4.9)%, $p < 0.05$, Murphy's symptom at the end of SRR was not registered, the frequency of normal liver size increased by 2.3 times ($p < 0.05$). The data obtained testify to the positive influence of the complex with the inclusion of MW "Voznesenskaya" on the clinical course of the disease, the disappearance or significant reduction of complaints, pain, dyspeptic and asthenic syndromes, as well as objective signs of the disease.

In the process of SRR according to medical complex with MW "Voznesenskaya" the improvement of, first of all, the indicators of the functional state of the liver was established. This was confirmed by a significant decrease in ALT activity from (54.28 ± 3.85) to (29.03 ± 3) u / l, $p < 0.001$ (at the rate of 32-41 u / l), AST from (44.39 ± 2.34) to (33.82 ± 1.86) u / l, $p < 0.01$ (at a rate of 31-37 u / l), as well as cholesterol levels from (5.28 ± 0.1) to (4.56 ± 0.25) mmol / l, $p < 0.05$ (at a rate of up to 5.2 mmol / l). The dynamics of other biochemical parameters at the end of SRR was insignificant. A decrease in the frequency of adaptation voltage of the IV degree due to an increase in the frequency of the adaptation voltage of 0-2 degrees was established. Under the influence of SRR with the use

of MW "Voznesenskaya" there was a positive dynamics of hemoglobin increase from (129.67 ± 1.89) to (138.68 ± 1.69) g / l, $p < 0.01$ and leukocytes - from (5.64 ± 0.25) to $(7.18 \pm 0.05) \times 10^9 / l$, $p < 0.001$. Changes in the content of the latter are associated with an increase in the number of mature neutrophils and a decrease in the number of lymphocytes from (35.06 ± 2.19) to $(29.00 \pm 2.12)\%$ $p < 0.05$. Thus, the activity of the phagocytic system improved and susceptibility to inflammatory processes decreased in the children under examination.

In ST children after the use of RC with the inclusion of MW "Voznesenskaya" there were positive changes in the manifestations of asthenic syndrome, undue tiredness was halved, anxiety tripled, dizziness disappeared, headache was 2.6 times less, irritability and emotional lability decreased 2.5 times.

At the same time, the pain in the epigastrium and right hypochondrium decreased 6-7 times, and intestinal pain disappeared in all subjects. The functional activity of the gastrointestinal tract improved, as evidenced by positive changes in appetite ($p < 0,001$), almost complete disappearance of bitterness in the mouth ($p < 0,001$), three times less nausea ($p < 0,05$) and intestinal disorders (constipation, diarrhea) occurred 5-8 times ($p < 0,001$) less frequently.

After SRR with the reception of pump-room MW "Voznesenskaya" in ST children, the body's response according to NARB was accompanied by incredible changes in the frequency of low-level reactions from 44.4 to 58.3%, increased and excessive activation. That is, the level of reactivity in children did not change and there was a tendency to increase the degree of tension (II-IV level from 83.3 to 91.6%). The types of adaptive reactions also changed. At the end of the base course, the stress response (25.0%) appeared and the over-activation response disappeared. As for the reactions of other types, their prevalence in the contingent was somewhat reduced.

MW "Truskavets-Aqua-Eco" (RC 2) was used in children after treatment of ST. There was a positive dynamics of pain, dyspepsia, asthenic syndromes and objective signs of the disease.

After SRR with the intake of mineral natural table water "Truskavets-Aqua-Eco" no changes in the

frequency of low-level reactions were registered. Stress frequency and excessive activation statistically decreased (from 19.2% to 0%), $p < 0.05$ and (from 15, 4% to 0%), $p < 0.05$, correspondingly.

A comparative assessment of NARB by the number of lymphocytes in the leukocyte formula after ST treatment with the inclusion of MW "Truskavets Aqua-Eco" and "Voznesenskaya" showed that in the first case the frequency of reactions of increased and excessive activation decreased and there were no signs of stress. In the second case, MW "Voznesenskaya", on the contrary, did not affect the frequency of increased and excessive reactions, but was accompanied by the appearance of stress response. This offers the opportunity for differentiated use of these MW.

Thus, it is advisable to prescribe a course of MW of "Voznesenskaya" or "Truskavetskaya Aqua-Eco" type to children after ST treatment if an adaptive reaction of increased and excessive activation of low level was detected before the beginning of SRR. Children with stress signs before rehabilitation, calm activation or training reaction against the background of a low level of reactivity before rehabilitation should be prescribed a course of MW "Truskavets Aqua-Eco".

Changes in most biochemical parameters under the influence of SRR with the use of MW "Voznesenskaya" and "Truskavets Aqua-Eco" remained within physiological parameters with a tendency to approach the upper limits of these indicators. However, against this background, there is a preservation of the increased content of MDA (5.5 ± 0.4) mmol / l, at the rate of $(2.2-4.8)$ mmol / l) and reduced catalase activity ($59.8 \pm 5, 8$)%, at the rate of $(73.8-77.4)\%$, i. e. the membrane-damaging effect of lipid peroxidation remains, which negatively affects the processes of cell life.

Under the SRR influence with the use of MW "Aqua Libra" in children with OHD disappeared or decreased manifestations of pain in most cases. The frequency of hepatic pain decreased by 6.7 ($p < 0.001$), stomach pain decreased by 6.4 ($p < 0.001$), and the pain in the intestine decreased by 3.0 times. The frequency of dyspeptic syndrome decreased significantly (depending on the manifestations by 5 to 5.5 times), and such symptoms as heartburn, bitter taste in the mouth, constipation, diarrhea at the end of SRR were not registered.

A similar positive dynamics was observed in the asthenic syndrome, the frequency of which at the end of rehabilitation with the use of MW "Aqua Libra" decreased significantly. Thus, the frequency of manifestations of weakness decreased by 4 ($p < 0.001$), emotional lability - by 2 (with < 0.05), irritability - by 2.1 ($p < 0.01$), headache - by 1.4 times.

The dynamics of the objective examination data showed a positive effect of the complex with the use of MV "Aqua Libra" (RC 3). In most OHD children the incidence of pain at Kerr's point decreased from (42.85 ± 7.6) to (7.14 ± 4.0)%, $p < 0.001$, Other's symptom decreased from (45.23 ± 7.7) to (7.14 ± 4.0)%, $p < 0.001$, the frequency of normal liver size increased 2.9 times ($p < 0.001$). Under the influence of RC 3 in OHD children the positive dynamics regarding the activity of AST and ALT was the most significant. AST activity decreased from (35.04 ± 1.87) to (25.99 ± 1.99) u / l, $p < 0.01$ (at a rate of 31-37 u / l), ALT - from (30.8 ± 1.33) to (26.70 ± 1.90) u / l, $0.05 < p < 0.1$ (at a rate of 32-41 u / l). In addition, there was a positive dynamics of the thymol test growth - from (1.51 ± 0.29) to (4.14 ± 0.40) units, $p < 0.001$ (normally up to 4 units), and also total protein from ($72,45 \pm 1,5$) to ($79,07 \pm 2,83$) g / l, $p < 0,05$. These data indicate liver functional state improvement.

Only insignificant (from (2.06 ± 0.18) to (1.95 ± 0.17) RU) reduction of the increased degree of tension and practically invariable resistance index testified to the stable preservation of adaptation disorders in children who underwent rehabilitation with inclusion of MW "Aqua Libra".

Under influence of RC 3 in OHD children there was a positive dynamics of increase in hemoglobin from (129.00 ± 1.71) to (139.21 ± 3.08) g / l, $p < 0.01$ and leukocytes - from ($6, 06 \pm 0.36$) to (7.11 ± 0.26) $\times 10^9$ / l, $p < 0.05$.

After completion of rehabilitation with the use of MW "Aqua Libra" in ST children, the following changed took place. The frequency of pain decreased in 43.8% of children, dyspepsia disappeared in 53.1% of them, asthenia disappeared in 15.6% of children. In addition, there was a positive trend in the objective signs of the disease. In most children, the incidence of pain at Kerr's point decreased from (45.8 ± 8.8) to (6.3 ± 4.3)%, $p < 0.001$, Other's symptom decreased from (46.9 ± 8.8) to (

6.3 ± 4.3)%, $p < 0.001$, normal liver size increased by 2.8 times ($p < 0.01$).

Response reactions on the signs of stress in leukocyte formula were manifested by its decrease by 3.3 times and reactions of increased activation by 3.2 times with a tendency to increase training reactions by 1.6 times and quiet activation by 1.6 times. At the same time, no significant changes in the NARB manifestations of low and high stress levels were observed. There was also a significant decrease in the frequency of elevated LII from (18.8 ± 6.9) to (3.1 ± 3.1)% ($p < 0.05$), decreased LII indexes tended to decrease (from ($25, 0 \pm 7.7$) to (12.5 ± 5.8)%).

Evaluation of some biochemical parameters changes in children after ST treatment under influence of RC 3 showed a decrease in urea content from (4.5 ± 0.3) to (3.8 ± 0.2) mmol / l ($0.1 > g > 0.05$) and a significant decrease in cholesterol levels from (5.2 ± 0.4) to (4.3 ± 0.1) mmol / l ($p < 0.05$).

At the end of the rehabilitation course with the use of MW "Morshinskaya" (RC 4), according to the assessment of the functional status of the children with OHD remission, 50.0% of them noted a decrease of fatigue intensity, 27.8% - a decreased irritability, and 27.8% of children under examination noted improvement of appetite, 22.2% noted reduction of flatulence. The right hypochondrium pain disappeared in 16.7% of children, and in 33.3% of them noted epigastric pain disappearance.

The number of low level of nonspecific adaptive reactions decreased 1.3 times, and the number of III - IV stress levels reactions decreased twice, none of stress reactions were registered after SRR. The reactions of training and increased activation doubled. The frequency of high levels of nonspecific adaptive reactions of the first degree of stress has increased.

Under the influence of RC 4 in 44.4% of children the ratio of activity of humoral and cellular immune response improved (LII). There is a tendency to regulate affective and effector parts of the immune response (index of leukocytes-monocytes ratio), the ratio of specific and nonspecific protection normalized in one third of patients, normalization of LII took place in 33.3% of children and this indicates endogenous bacterial intoxication decrease.

In addition, there was a 30.0% decrease of low-level NARB, a 33.3% increase of reactions of high and

medium levels and stress decrease from II to 0.I degree in 20.0% of children.

The ratio of nonspecific and specific protection according to index of neutrophils-leukocytes ratio at the end of treatment was normalized in 40.0% of children. In all 40.0% of children with elevated LI / ESR after the use of RK 4 autointoxication decreased, in 30% of them LII decreased.

Thus, under the influence of the rehabilitation complex with inclusion of MW "Morshinskaya" in ST remission children their well-being, functional activity, NARB decrease, leveling stress response, regulating the ratio of cellular and humoral links of immunity, decrease of autointoxication took place.

The use of MW "Maria" (RK 5) in OHD remission children led to a decrease of fatigue in 2.2 times, pain in the gastroduodenal area and in the right hypochondrium by 3.0 times, headache by 5 times, improved appetite was noted in 19.2% of children.

At the end of SRR, the frequency of low-level NARB decreased from 46.2 to 30.8% and the frequency of III-IV degree of stress ($p < 0.01$) decreased from 46.2 to 0% with a significant increase in I-II stress degree, while maintaining in 92.3% of children manifestations of quiet activation reactions. After SRR with the use of RC 5 suppression of the effector link of the immune response and macrophage activity of the immune response remained at the level before SRR beginning.

At the same time, the hypersensitivity of the instant type decreased by 1.4 times (decrease of index of leukocytes-eosinophils ratio), LII decreased by 2.5 times, the manifestations of bacterial intoxication decreased by 1.2 times (LI/ESR). This indicates the activation of detoxification processes and reduce of endogenous intoxication in OHD remission children.

The changes in children's biochemical parameters in OHD remission under RC 5 influence occurred within the limits of physiological values, both in 5 years and more prolonged remission.

The level of erythrocytes increased from (3.9 ± 0.2) to $(4.7 \pm 0.18) \cdot 10^{12} / l$, ($p < 0,01$) which suggests positive changes.

In remission children, received a complex with MW "Maria" at the beginning of rehabilitation there were violations of immunological reactivity, which was manifested by suppression of the effector

immune response, autointoxication, suppression of macrophage activity, increased hypersensitivity, LII changes.

At the end of SRR in ST remission children there was no positive dynamics of immunological reactivity. The frequency of instantaneous hypersensitivity indicators as a possible reaction to intercurrent acute respiratory diseases that occurred in children during their stay in the sanatorium increased from 45.5 to 59.1%. An increase from 54.5 to 86.4% of nonspecific adaptive reactions of low level of functioning, II degree of stress was established. Excessive activation reactions occurred in 4.5% of children.

The changes in biochemical parameters in this group of children occurred within physiological values in remission up to 5 and more than 5 years.

The results obtained results confirm the need for caution regarding the use of biologically active MW. Preference should be given to low-mineralized MW without specific components and compounds according to gentle methods.

In [12] it was noted that in children who received drinking treatment with low-mineralized MW for a month, there is a more positive dynamics ($P > 0.05$) of a number of biochemical parameters, which are close to those observed in the control group only after 6 months after RT. This indicates the acceleration of functional activity normalization rate in a number of organs and systems in OHD children, when therapeutic-table waters are included in the early rehabilitation treatment. According to [12], the internal use of MW in early rehabilitation treatment of OHD children at the stage of completion of supporting therapy is advisable.

The authors [13] believe that mineral low-mineralized therapeutic-table MW (both pump - room and packaged) should be recommended for widespread use not only under condition of a resort, but also in out-of-resort practice - in inpatient, outpatient stages of OHD rehabilitation, as well as for prevention and treatment of a variety of comorbidities.

Conclusions

The use MW allows to restore the functional state of the digestive glands, motility of the gastrointestinal tract, normalize the adaptation mechanisms, the activity of the nervous, endocrine

and immune systems. Availability, cost-effectiveness, lack of side effects inherent in drug therapy, as well as the ecological purity of mineral waters of Ukraine, determines their use in the treatment of oncohematological pathology in children [14].

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The authors declare that there are no conflicts of interest.

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