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## EFFECTIVENESS OF COMBINED REHABILITATION THERAPY IN KIDS WITH METABOLIC SYNDROME

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### ABSTRACT

The work carried out a multivariate study of the mechanisms of metabolic disorders, closely related to an increase in blood pressure in children with arterial hypertension from 10 to 17 years. For this purpose, 60 children with arterial hypertension and metabolic disorders were examined. 20 children made up the control group. Before and after spa treatment, all children underwent a set of clinical and laboratory examinations, which included daily monitoring of blood pressure, biochemical studies of lipid and carbohydrate profiles, insulin, insulin resistance indices HOMO and CARO, leptin, adiponectin.

Besides the individual hypocaloric diet, the rehabilitation included proper physical activity, school of arterial hypertension, not allowing for a child to sit at the computer or watch TV for a long time (or at all), treatment of foci of chronic infection (including pelotherapy and inhalations), sedative aero-phytotherapy, aero-ionotherapy, exercise therapy in either arterial hypertension or obesity group, classical hand massage of the neck and shoulders, electrosleep therapy. Depending on the treatment received the children with arterial hypertension (n=60) were divided into three groups (using the method of simple randomisation).

The use of balneotherapy and electrosleep therapy in complex spa treatment contributes to the normalization of initially disturbed biochemical carbohydrate and lipid metabolic markers, a decrease in high levels of leptin and insulin, and an increase in initially reduced adiponectin. This allows us to conclude that the combined sanatorium-resort rehabilitation of patients is highly effective, which is expressed in a decrease in blood pressure, body weight, indicators of fat and carbohydrate metabolism. Intensive spa treatment has a beneficial effect on changing the criteria for the development of MS in children with obesity and hypertension. Of course, to achieve the optimal effect in the correction of disorders of carbohydrate and lipid metabolism, a long period of therapeutic measures and observation of patients is required, at least 3-6 months.

**KEYWORDS:** infants; metabolic syndrome, balneotherapy, electrosleep therapy, rehabilitation.

### INTRODUCTION

In recent years, more and more doctors from various specialties have to deal with such a symptom, as the metabolic syndrome (MS). Today, it includes

the following components: insulin resistance with compensatory hyperinsulinemia, diabetes and other disorders of carbohydrate metabolism, abdominal

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obesity, hypertension, atherogenic dyslipidemia, hyperuricemia, violation of the fibrinolytic activity of blood, hyperandrogenism, hyperuricemia, microalbuminuria, fatty steatosis [Welty F et al., 2016; Zimmet P et al., 2018; Chen Y et al., 2018]. Due to the fact that the clinical manifestation of these conditions occurs during childhood, MS starts to be recognized as an urgent pediatric problem. Medical and social significance of the problem associated with chronic, often with asymptomatic hyperglycemic states, hypertension, dyslipidemia, which for a long time does not bother the patient, but at the same time contribute to the accumulation of a pathological process with the development of early and late complications [Inge T et al., 2015; Ogden C et al., 2016; Wu Y et al., 2016; Al-Hamad D, Raman V, 2017; Zuo Y et al., 2022].

Adipose tissue plays a key role in the pathogenesis of insulin resistance and the development of metabolic syndrome due to the production of biologically active metabolites capable of regulating appetite, glucose and lipid metabolism, influencing the action of insulin and inflammation, among which leptin and adiponectin are the most important. Adiponectin has a variety of protective properties against obesity-linked complications, such as hypertension, metabolic dysfunction, atherosclerosis, and ischemic heart disease. However, the relationship between adiponectin and cardiovascular diseases is complex, and the specific mechanism of action is not fully understood [Ohashi K et al., 2011; Barber T et al., 2021; Lei X et al., 2022]. Despite having a well-described role in regulating systemic metabolism and appetite, leptin displays pleiotropic actions, and it may also affect blood pressure and contribute to hypertension through sympathetic activation in the vasculature or at the renal level [Xie D, Bollag W, 2016]. In males, the adipokine leptin highly contributes to obesity-related cardiovascular disease by increasing sympathetic activity. Females secrete 3× to 4× more leptin than males, but do not exhibit high sympathetic tone with obesity, leptin induces hypertension and endothelial dysfunction via aldosterone-dependent mechanisms [Huby A et al., 2016].

The available therapeutic strategies for Insulin resistance are mainly exercise and dietary habit improvement, and chemotherapy based on biguanides [Zhao X et al., 2023]. The main role in the treatment

of MS in childhood is given to non-medicated treatments, aimed at reducing body weight, change stereotypes of nutrition, escape from bad habits and increase physical activity. Pharmacologic drugs -are only a compliment, not an alternative for these activities, while a specter of medical drugs, used for correction of disorders of carbohydrate and lipid metabolism in children is very limited. In recent years, much attention is paid to the development of new therapeutic approaches in accordance with modern concepts of the etiopathogenesis of MS. As you know, a common pathogenetic mechanism of formation of the basic components of MS is insulin resistance – recession in bad habits and increase of physical activity, during which glucose transport into cells decreases. There comes a condition where the cells live with energy shortage as a result of violations of the synthesis ATP and NADP H<sub>2</sub>, providing energy functions and plastic processes in the body. Violation of cellular energy can rapidly decompensate due to the various diseases and complicate the course of the latter. Thus, for the treatment of MS is necessary to use methods with multiple mechanisms of influence on the metabolism and blood flow [Kelley E et al., 2018; Chambers J et al., 2019; Bull F et al., 2020].

Through its holistic approach, cardiovascular rehabilitation is increasingly needed to compensate for the inevitable and increasing hyper-specialization of acute primary care. Cardiovascular rehabilitation may represent a model of development for many chronic diseases managed by physical medicine departments, as it combines specific functional explorations, personalized rehabilitation techniques and the implementation of therapeutic education [Gremeaux V, Casillas J, 2017]. Cardiac rehabilitation, consisting of prescribed exercise and counseling for risk modification, has proven benefits for patients with cardiovascular disease [Simon M, et al., 2018]. Spa treatment affects all links in the pathogenesis of the formation of arterial hypertension and metabolic syndrome in children [Rasumov A, 2022]. However, comprehensive sanatorium-resort rehabilitation of children with arterial hypertension and, in particular, with metabolic syndrome is not sufficiently developed.

**The purpose of this study** was to evaluate the effectiveness of sanatorium rehabilitation complex in the treatment of children with MS.

## MATERIALS AND METHODS

Totally 60 children with MS signs at the age of 10 to 17 years ( $13.39 \pm 0.14$ ) (42 boys and 18 girls) were examined. Only the children with arterial hypertension having at the same time signs of metabolic syndrome were included into the research. The diagnostic criteria for MS were the criteria by International Diabetes Federation (2007) according to which MS is characterized by central obesity, arterial hypertension, hyperglycemia, reduced high-density lipoprotein concentration, elevated triglycerides in the blood serum.

The standard clinical, laboratory and instrumental methods of examination were used before and after the course of treatment.

Taking history of the child, members of his/her family and close relatives (paying special attention to signs and complications of diabetes mellitus, arterial hypertension and obesity);

Anthropometry (measuring the height and body weight, waist circumference, hip circumference, waist-hip ratio, body mass index). Body mass index (BMI) was counted according to the formula:  $BMI = \text{weight (kg)} / \text{height (m)}^2$ . Assessment of the waist circumference was made on basis of the summary table of the range of indices for children taking into account recommendations by International Diabetes Federation 2007 [Zimmet P et al., 2007].

Electrocardiogram, Holter Electrocardiogram monitoring with determination of the average daily heart rate 24-hour arterial pressure monitoring. While analyzing the 24-hour profile of arterial pressure the following indices were used: mean time indices of systolic arterial pressure and diastolic arterial pressure for 24 hours, a day and a night. The mean time indices give the main idea about the level of arterial pressure. They were assessed according to percentile table of arterial pressure depending on the height, sex and age of a child.

To determine the level of leptin, insulin and adiponectin DRG Leptin ELISA, DRG® Insulin и Adiponectin ELISA Kit (Germany) were used.

Besides the individual hypocaloric diet, the rehabilitation included proper physical activity, school of arterial hypertension, not allowing for a child to sit at the computer or watch TV for a long time (or at all), treatment of foci of chronic infection (including pelotherapy and inhalations), sedative aero-phytotherapy, aero-ionotherapy, exercise

therapy in either arterial hypertension or obesity group, classical hand massage of the neck and shoulders, electrosleep therapy.

Depending on the treatment received the children with arterial hypertension ( $n=60$ ) were divided into three groups (using the method of simple randomization): group 1 ( $n=20$ ) received routine rehabilitation treatment (RRT); group 2 ( $n=20$ ) received RRT plus electrosleep therapy; group 3 ( $n=20$ ) received RRT plus balneotherapy and the control group ( $n=20$ ). The studied groups of the children with arterial hypertension were representative in age and clinical characteristics. The social background for all children was homogenous.

The following statistical analysis was being conducted by means of SPSS computer software of data processing, during the process the following main statistic features were determined: medium (M), error of medium (m) and standard deviation, reliable results were considered only if  $p < 0.05$ . Hypothesis testing regarding the equality of the two mediums was conducted by the usage of distribution-free statistic methods (Wilcoxon paired calculation and Mann-Whitney U-test). For the evaluation of the degrees of correlation, the correlation analysis was conducted by the calculation of Spearman's correlation coefficient pair (r).

The analysis of the history findings showed that for two thirds of the children the development of obesity was the natural process predetermined by certain eating habits in the family. At that in 73.75% of the examined children 1 to 4 close relatives suffered from obesity (most often, mother (in 26.26%)), 23.75% had diabetes mellitus, 85% having arterial hypertension. The average age when the body weight started to increase considerably ( $4 \pm 1.5$  kg a year) was approximately  $10.5 \pm 2.25$  years of age. Assessing the level of lack of motion, we revealed that almost half of the children watch TV for more than 2 hours a day, 43.75% sat at the computer for more than 2 hours a day, only 35% do some exercises at least sometimes (mostly dances, football, more often for boys), 25% do morning exercises, 90% of children speak about non-motivated taking in of sweets, energy drinks, increased appetite and hypercaloric snacks.

The most frequent complaints were headache and unstable arterial pressure (90%), from 1 to several times a month, of moderate and severe in-



tensity, 1-4 to 5-9 hours of duration. Heaviness in the head for several times a month mentioned half of the patients. 1/3 of children with arterial hypertension registered dizziness, and 7.5% had fainting. 66.25% patients felt pulsation in the head, 48.75% felt tinnitus, 1/4 had "dark spots" before eyes. 43.75% children experienced unstable pulse, heartbeat and irregular heart rhythm of mild intensity from several times a week to several times a month. Half of the patients complained of unpleasant sensations in the heart area. Perspiration, facial hyperaemia were characteristic of 1/3 of the children. Almost all of them had dyspnoea and fatigue on physical exertion; the not enough air feeling at rest had only 1/3 of them. Nose bleedings were revealed in 16.26% of patients.

Complaints about high blood pressure, associated with emotional and/or physical activity presented nine children. Arterial blood pressure in the group was as follows: systolic arterial pressure - ( $129.8 \pm 1.8$ ) mm Hg. Art., diastolic arterial pressure - ( $79.0 \pm 1.7$ ) mm Hg. Art. Labile arterial hypertension was diagnosed in 26 children; stable hypertension was recorded in 34 children.

The basis for rehabilitation was the diet formed based on the principles of the Dietary Approaches to Stop Hypertension program. The main components were porridges and dishes from vegetables. The sense of being sated was ensured thanks to low-fat meat, fish, fresh vegetables and others, the need for sweets thanks to berries and fruit. The diet also contained low-fat dairy products (1% milk and kefir, skimmed cottage cheese and yogurts), skimmed cheeses. Fast absorbing carbohydrates (chocolate, ice-cream, buns, lemonade, etc.), as well as products with 'hidden' fats (sausages, all kinds of canned food, etc.) were excluded. The last meal was 3 hours before going to bed; additional hypercaloric food like sandwiches, chips, crackers, etc. was also excluded. All data on the nature of power were recorded in a food diary.

Even a monthly course of diet, conducted against the background of rehabilitation course, has allowed to achieve certain results.

As a result of treatment in all groups of ill children with arterial hypertension there was positive dynamics of the complaints, most marked in Group 2 (use of electrosleep therapy). Absolute majority of the children noted less number of elevations of

arterial pressure, headaches. However, in the group of children only 2 children still had complaints on elevated arterial pressure during the month and all the children denied having headache at the end of the treatment. Almost all children mentioned considerably improved capacity to work and resistance to intellectual loads, rarer episodes of dizziness, heaviness in the head, fatigue, dyspnea and palpitation even on mild physical exertion. 90% patients noted considerably reduced appetite, less number of sudden attacks of hunger and wish 'to have a snack'.

Reduced complaints of irritability (scale Quality of Life Questionnaire) recorded in 24 children of 28, anxiety and difficulty of falling asleep, sleepiness during the day, poor sleep improved in 14 children of 18 (use of the electrosleep therapy), decrease in sweating was observed in 18 children out of 20 (2 and 3 group).

As a result of the therapy, weight stabilization was observed in 8 children, while weight reduction was noted in 52 children. In the patients, receiving electrosleep therapy the reduction in the body weight (7%) was in all the children of the group and was more marked ( $p < 0.001$ ) than in the 1 groups (3.2%) or 3 groups (4.8%) ( $p < 0.05$ ). Reduction in the waist to hip ratio was due to waist size which is the evidence of the less visceral fat and correct direction of treatment of metabolic disorders. As a result of the treatment, waist to hip ratio appeared to be 0.80 in the first group, 0.83 ( $p < 0.05$ ) in the second group, and 0.81 in the third group ( $p < 0.05$ ). In the group with use balneotherapy changes were more marked due to the regulation of lipid metabolism (Table 1).

At the end of the treatment all the patients of Group 2 achieved the target level of arterial pressure; the effective control over AP was achieved in 80% of the patients from the 1 group and in 90% of

**TABLE 1**  
Dynamics of anthropometric indices  
in children with MS

Index	Before treatment	After treatment
BMI ( $kg/m^2$ )	$27.60 \pm 1.21$	$25.4 \pm 1.22^*$
Waist (sm)	$86.4 \pm 2.0$	$82.7 \pm 1.4^*$
<b>NOTES:</b> * - $p < 0.05$ - reliability of differences in the dynamics of treatment		

the children in the 3 group.

After 3 weeks of observation in the group receiving electrosleep therapy AP reduced on average from  $131.4 \pm 1.18 / 81.3 \pm 1.34$  mmHg to  $120.0 \pm 2.07 / 72.0 \pm 2.4$  mmHg ( $p < 0.001$ ) in the group of balneotherapy from  $129.5 \pm 1.35 / 78.4 \pm 1.73$  mmHg to  $121.0 \pm 2.32 / 74.42 \pm 1.3$  mmHg ( $p < 0.05$ ); in the group receiving RRT from  $128.3 \pm 2.02 / 79.0 \pm 2.9$  mmHg to  $124.2 \pm 1.4 / 74.4 \pm 3.2$  mmHg ( $p < 0.05$ ).

The obtained results of the study of lipid profile before and after treatment are presented in table 2.

The most positive dynamics in the restoration of lipid profile observed in the group of children with the use of the balneotherapy. Normalization of biochemical parameters was observed in 88% of children in Group 3. However, with the positive dynamics of appetite hormones in group 3 ( $p < 0.05$ ), a significant improvement in the levels of leptin and adiponectin ( $p < 0.001$ ) was observed in the group with the use of electrosleep therapy (level of leptin was reduced by 23% and Adiponectin raised reliably by 2 times). Thus, for the normalization of lipid profile in children with metabolic syndrome in the future, we propose to combine electrosleep therapy and balneotherapy.

The study of carbohydrate metabolism in children with hypertension and metabolic disturbances revealed no significant differences in the level of glucose in capillary and venous blood with healthy children. Oral glucose tolerance test was significantly ( $p < 0.05$ ) increased in comparison with healthy children in 15.25%. However, excess

TABLE 2

Dynamics of lipid profile in children with MS (M±m)

Index	Before treatment	After treatment
Total cholesterol (mmol/l)	$4.14 \pm 0.12$	$3.52 \pm 0.12^*$
Triglycerides (mmol/l)	$1.28 \pm 0.08$	$0.9 \pm 0.06^*$
High-density lipoprotein (mmol/l)	$1.24 \pm 0.04$	$1.42 \pm 0.07^*$
Low-density lipoprotein (mmol/l)	$2.25 \pm 0.11$	$1.57 \pm 0.09^*$
Very-low-density lipoprotein (mmol/l)	$0.58 \pm 0.03$	$0.44 \pm 0.03^*$
Atherogenic factors	$2.34 \pm 0.16$	$1.47 \pm 0.12^{**}$
Adiponectin (ng/ml)	$6.10 \pm 0.77$	$10.33 \pm 1.44^{**}$
Leptin (ng/ml)	$26.22 \pm 3.27$	$14.32 \pm 1.29^{**}$

NOTES: \* -  $p < 0.05$ , \*\*\*-  $p < 0.001$  - reliability of differences in the dynamics of treatment

TABLE 3

Dynamics of carbohydrate metabolism in children with MS (M ± m)

Index	Before treatment	After treatment
Glucose (mmol/l)	$4.3 \pm 0.2$	$4.00 \pm 0.15$
Oral glucose tolerance test (mmol/l)	$4.69 \pm 0.26$	$4.1 \pm 0.19^*$
Venous blood glucose (mmol/l)	$4.7 \pm 0.2$	$4.69 \pm 0.26$
Insulin (mkME/ml)	$16.41 \pm 1.1$	$12.4 \pm 1.22^{**}$
Index Caro	$0.29 \pm 0.07$	$0.37 \pm 0.019^{**}$
Index Homo	$3.43 \pm 0.43$	$2.58 \pm 0.27^{**}$

NOTE: \* -  $p < 0.05$ , \*\*\*-  $p < 0.001$  - reliability of differences in the dynamics of treatment

weight found in only 7 children. Frequency of hyperinsulinemia occurred in 11 children. Insulin resistance of varying severity in terms of Caro and Homo registered more than half subjects.

In the dynamics of research (Table 3) note the tendency to reduce blood glucose. Indices of insulin resistance normalized by the end of treatment in 83.3% of cases. The most pronounced effect was observed in the groups with the use of balneotherapy and electrosleep therapy, where pathological changes remain only in 2 of the 40 people, due to hemodynamic balance, trophic and enzymatic processes. This allows us to recommend these methods for the regulation of carbohydrate metabolism in the complex treatment of MS in children. At the end of the treatment all the patients of Group 2 achieved the target level of arterial pressure; the effective control over AP was achieved in 90% of the patients from the 3 group and in 80% of the children in the 1 group.

After 3 weeks of observation in the group receiving electrosleep therapy arterial pressure reduced on average from  $131.4 \pm 1.18 / 81.3 \pm 1.34$  mmHg to  $120.0 \pm 2.07 / 72.0 \pm 2.4$  mmHg ( $p < 0.001$ ), in the group of balneotherapy from  $129.5 \pm 1.35 / 78.4 \pm 1.73$  mmHg to  $121.0 \pm 2.32 / 74.42 \pm 1.3$  mmHg ( $p < 0.05$ ); in the group receiving RRT from  $128.3 \pm 2.02 / 79.0 \pm 2.9$  mmHg to  $124.2 \pm 1.4 / 74.4 \pm 3.2$  mmHg ( $p < 0.05$ ).

Unfortunately, the small number of observations and possibly brief period of observation does not allow us to represent statistically grounded conclusions. Of course, for optimal effect in the correction of carbohydrate and lipid metabolism requires a long, at least 3-6 months, the period of

observation and treatment measures for patients. Required to gradually adapt the child to low-calorie diet that limits foods that can cause depressive mood changes, not being too traumatic.

### CONCLUSION

The data presented demonstrate the promise of sanatorium treatment of metabolic syndrome in children.

The continuation of scientific and applied research aimed at developing advanced algorithms for treatment with balneotherapy and electrosleep therapy, the development of optimal schemes for use of the methods with the definition of long-term

use and dose for the correction of carbohydrate and lipid metabolism in children at different ages is required.

The use of balneotherapy recommended in the case lipid metabolism disorders, the effect of electrosleep therapy is more pronounced in the treatment of disorders of carbohydrate.

Electrosleep therapy is an effective method for treatment of MS pathogenesis in children and can be used as a neuroprotective and metabolic treatment of the main disease.

Recommended the combined use of sanatorium methods in the rehabilitation of MS for the normalization of the pathogenesis.

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