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Health Resort Detox Programs Impact on the Body: a Prospective Laboratory Analysis in «Kivach Clinic»

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ABSTRACT

INTRODUCTION. The impact on a human organism of health resort detox programs based on therapeutic governance of lymphatic tissues drainage on human metabolism and a possibility to reduce intoxication and inflammation level has not been evaluated yet.
AIM. To make the first attempt to objectively estimate the influence of health resort body detoxification programs on lipid and carbohydrate metabolism and the processes of intoxication and inflammation.
MATERIAL AND METHODS. The laboratory data were obtained for all the patients treated under the detoxication program in the corresponding date range (89 persons had a venous blood collected on the first day and the day before the departure). The dynamics of the laboratory indicators were calculated.
RESULTS AND DISCUSSION. There is an increase of intoxication markers to the end of the first week and a decrease of inflammation and intoxication markers to the end of the second accompanied by a decrease in total cholesterol level. HOMA decreases in all groups, but other insulin resistance markers remain unaltered.
The decrease in cholesterol confirms the expected effect of lymphatic drainage and bile acid loss. There is a decrease in the hepatic insulin resistance without a significant change of the total one. The process of autointoxication rising during the lymphatic drainage and its further decline below the start values is confirmed.
CONCLUSION. An attempt was made to evaluate the body's detoxification programmes using laboratory markers. Such programs decrease level of total cholesterol, body's intoxication and inflammation level, lower hepatic component of the insulin resistance. This impact is in stages.
KEYWORDS: environmental pollutants, sorption detoxification, health resorts, lipid metabolism, carbohydrate metabolism, inflammation, insulin resistance

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Проспективный анализ влияния санаторно-курортных детокс-программ на организм в «Клинике Кивач» с учетом лабораторных показателей

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РЕЗЮМЕ

ВВЕДЕНИЕ. Не было проведено ни одного исследования влияния на организм человека санаторно-курортных детокс-программ, основанных на терапевтическом управлении дренажем лимфатических тканей, на метаболизм человека и возможность снижения уровня интоксикации и воспаления.

ЦЕЛЬ. Предпринять первую попытку объективной оценки влияния санаторно-курортных программ детоксикации организма на липидный и углеводный обмен, процессы интоксикации и воспаления.
МАТЕРИАЛ И МЕТОДЫ. Лабораторные данные были получены для всех пациентов, проходивших лечение по программе детоксикации в соответствующем диапазоне дат (у 89 человек венозная кровь была взята в первый день и за день до отъезда). Рассчитана динамика лабораторных показателей.
РЕЗУЛЬТАТЫ И ОБСУЖДЕНИЕ. Отмечается повышение маркеров интоксикации к концу первой недели и снижение маркеров воспаления и интоксикации к концу второй, сопровождающееся снижением уровня общего холестерина. Показатель HOMA снижается во всех группах, но другие маркеры инсулинорезистентности остаются неизменными.
Снижение уровня холестерина подтверждает ожидаемый эффект лимфодренажа и потери желчных кислот. Наблюдается снижение печеночной инсулинорезистентности без существенного изменения общей. Подтвержден процесс нарастания аутоинтоксикации во время лимфодренажа и ее дальнейшее снижение ниже исходных значений.
ЗАКЛЮЧЕНИЕ. Предпринята попытка оценить программы детоксикации организма с помощью лабораторных маркеров. Такие программы снижают уровень общего холестерина, уровень интоксикации организма и воспаления, снижают печеночный компонент инсулинорезистентности. Это воздействие происходит поэтапно.
КЛЮЧЕВЫЕ СЛОВА: загрязнители окружающей среды, сорбционная детоксикация, курорты, липидный обмен, углеводный обмен, воспаление, инсулинорезистентность

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INTRODUCTION

In the course of aging processes and through the action of exogenous pollutants unidirectional impairment of intercellular and lymphatic microcirculation occurs [1]. Starting from the adolescence, the lymphoid parenchyma of the lymph nodes is being replaced by connective and adipose tissue. Thus, in old age, the amount of inguinal and axillary lymph nodes is halved [2]. It limits the transport of nutrients and medicines to the intercellular matrix and cells, and removal of the products of cell vital activity. Metabolites accumulating in the body are capable of stimulating phagocytosis and activating lipid peroxidation and coagulation of blood and lymph. An increase in inflammatory and intoxication processes in body tissues, which develops throughout life, resulting in hypoxia and premature aging [1, 3].

It occurs through an increased entry of toxic substances into the human body from the environment resulting from the anthropogenic impact on it. Human activity leads to drinking water, soil and air pollution, which manifests through an increase in the concentration of toxic substances in the environment above the safe limit. Due to the anthropogenic impact, the environment gets contaminated with nitrates, sulfur dioxide, lead, bisphenol A, phthalates, perfluoroalkyl substances, volatile organic compounds, dioxins, polycyclic aromatic hydrocarbons, dust and smog particles, radon, pesticides etc. [4, 5]. Solid particle contaminants in the air masses (the atmosphere or the indoor air) are inhaled and, if less than 10 μm in diameter, end up in the bloodstream through the respiratory mucosa. Inhaled pollutants are transported through the bloodstream and the lymphatic system causing inflammation in the lymph nodes and spreading to the peripheral organs (the liver, adipose tissue). They have a toxic effect on the body due to their chemical properties, causing systemic inflammation and oxidative stress, neurotoxicity, irritation (and permeability impairment) of the mucosa and the gastrointestinal tract, increasing cardiovascular, respiratory and neurologic morbidity and overall mortality at the population level [4, 6].

The above-mentioned age-related changes in the lymphatic system, which per se contribute to the autointoxication of the body, because of the increased external intoxication burden were specified by Y.M. Levin, who developed the therapeutic rehabilitation program ("Endoecological rehabilitation"), to be the target of the therapeutic intervention [2].

Y.M. Levin developed a concept of therapeutic governance of interstitial humoral transport and lymphatic drainage of tissues and lymph detoxification. The object of the impact is predominantly the lymphatic system, and the main expected outcome is restoration of regulatory, adaptive and protective resources of the human organism through reduction of the intoxication of the body. Lymphatic drainage is a result of a complex impact on the human body, promoting toxin removal via humoral transport, from the intercellular space to the organs of excretion. The novelty of his concept was non-traumatic detoxification of the lymph via intensification of lymph excretion through the capillaries of intestinal villi, along with enhancing the biligenetic and detoxification functions of the liver, the detoxification function of the kidneys and intestinal adsorption in order to prevent reabsorption [2]. The theoretical outlines mentioned above have served as the basis for the "Detox" programs in Kivach Clinic (The Republic of Karelia, Russia). However, the health impact of the programs themselves has not been evaluated yet.

AIM OF THE STUDY

To determine the mean changes in lipid and carbohydrate metabolism and in the level of intoxication and inflammation in patients before and after undergoing a health resort detoxification program based on Y. M. Levin's method through analyzing the dynamics of the laboratory markers.

MATERIAL AND METHODS

A single-center prospective open observational study was conducted from 17/01/2021 till 30/06/2021 at the "Kivach Clinic" (v. Konchezero, The Republic of Karelia, Russia). A total of 89 people, who underwent the "Detox" health resort treatment program were examined. The inclusion criteria for the participants were as follows:

1) aged at least 18 and over;

2) undergoing any of the standard health resort programs provided by the clinic ("Detox Basic", "Detox Premium", "Detox Exclusive");

3) receipt of blood test results performed on the day of the arrival and results of a similar follow-up test performed before the departure (total cholesterol, insulin, glucose, complete blood count with a white blood cell differential and ESR; triglycerides and LDL cholesterol for the second phase).

The exclusion criteria were the contraindications to the health resort treatment established by order of the Ministry of Health of the Russian Federation No. 1029н of September 28, 2020, and aged 65 and over. There was no additional selection of the patients after their check-in and admission to the health resort programs. Venous blood served as a material for the evaluation. It was taken in the medical procedure rooms of the clinic into colour-coded vacuum blood collection tubes. These labeled tubes were prepared in the laboratory of the clinic for the transportation (i.e. centrifuged, barcoded and packed in lockable bags). Then they were transported in thermal bags with necessary quantity of cooling elements with accompanying documents to the "Helix" Laboratory service where all the tests were performed. The results of the tests were received on behalf of the subcontractor.

The study was conducted in two phases. The evaluation of the results of the laboratory tests was performed in every participant on the first day of the program and on the 5th/9th/12th days and on the 7th/10th/14th days of the programs, respectively.

The first phase of the study included the patients, who underwent the "Detox" program during a 14-day period (54 people, 27 men and 27 women, aged between 23 and 64; the median age was 49 years). The following measurements were taken and values were evaluated: total cholesterol, glucose, insulin, white blood cell differential (with blood smear microscopy), ESR. The calculation of the following indices was performed: HOMA-IR (homeostasis model evaluation of insulin resistance), the leukocyte index of intoxication (LII) (J.J. Calf-Calif formula and B.A. Reis' modification), and the hematological index of intoxication by V.S. Vasiliev (HII).

The second phase of the study included the patients, who underwent the "Detox" program during a 7- and 10-day period. The 7-day program group included 22 people (7 men and 15 women, aged between 29 and 63, the median age was 40 years). The 10-day program group included 13 people (6 men and 7 women, aged between 37 and 52, the median age was 44 years). The following measurements were taken and values were evaluated: glucose, insulin, total cholesterol, triglycerides, LDL cholesterol, white blood cell differential (with blood smear microscopy), ESR. The calculation of the following indices was performed: HOMA-IR, TyG (the triglyceride glucose index) and METS-IR (the metabolic score for insulin resistance), the leukocyte index of intoxication (LII) (J.J. Calf-Calif formula and B.A. Reis' modification), the hematological index of intoxication by V. S. Vasiliev (HII).

Each group of the patients received identical treatment within the limits of their health resort program, which included calorie restriction, tubages, intestinal adsorbents, cleansing enemas and monitor bowel cleansing, taking herbal lymph drainage and antiparasitic preparations, medications for restoration of the microflora, hydrotherapy, halotherapy, massage, system magnetic therapy, thermal procedures (Karelian banya, Finnish and infrared sauna, pelotherapy), body wraps (wet and salt body wraps and/or thalassotherapy).

The HOMA-IR was calculated as fasting insulin level (mcIU/mL) x fasting glucose level (mmol / L) / 22,5 and allowed us to evaluate the median values of insulin resistance [7]. METS-IR was calculated as follows: Ln((2x fasting plasma glucose)+ fasting triglycerides)x body mass index)/(Ln(high-density lipoprotein cholesterol)) [8], and TyG – as follows: Ln ((fasting plasma glucose (mg/dL) x fasting triglycerides (mg/dL) / 2), where ln is a natural logarithm [9]. The leukocyte index of intoxication (LII) was established by the formula proposed by J.J. Calf-Calif. LII = ((4xM+3xMet+2xBf+S)x(PC+1)) / (MO+L)x(E+1). M – myelocytes, Met – metamyelocytes, Bf – band forms, S – segmented neutrophils, PC – Plasma cells, MO – monocytes, L – lymphocytes, E – eosinophils [10, 11]. It is believed that the introduction of the numerical coefficients into the formula in order to enhance the significance of some cells is not completely justified: we cannot establish with sufficient reliability the level of significance of each cell in the leukocyte differential, for the plasma cells and the metamyelocytes are present in approximately 0.3–0.5% and 5–7% of cases, respectively. That's why B.A. Reis' modification is often used. (LII (R)): LII (R) = (M+Met+Bf+S)/(MO+L+E) [9]. Also, the hematological index of intoxication by V. S. Vasiliev (HII) serves as an additional determination method. It is calculated as follows: HII = LII x CfL x CfESR, in which LII is the leukocyte index of intoxication, CfL is the leukocytosis correction factor and CfESR is the erythrocyte sedimentation rate correction factor [10].

The study was approved by the Ethics committee of the "Kivach Clinic": The study was approved by the Ethics committee of the "Kivach Clinic" (Certificate of approval No. 1 issued on 11.01.2021).

The statistical data analysis was performed in Microsoft Excel 2019 with the help of the built-in tools. The medians were evaluated as the averages in all cases with Excel inbuild "mediana" function applied on a column of numeric values. The dynamics of values was evaluated as $(x_2-x_1)/x_1$ * 100% where x_1 – is the first meaning of an indicator and x_2 – is the second one. An interquartile range (Table 1, see Appendix) was evaluated to estimate a statistic dispersion of the groups as q3-q1 where q1 and q3 are 25-th and 75-th percentiles of the data respectively. They were calculated with Excel inbuilt "procentile.inc" function.

RESULTS AND DISCUSSION

The findings are shown in Table 1 (in appendix). We observe the decline of median values of total cholesterol levels from the initial values in the range of 5.36-5.48 mmol/l (above the reference level) to the range of 4.95-5.16 (below the reference level). Clinically, a significant decline of cholesterol values was in the 10 and 14-day program groups (-11.94% and -10.43% respectively). In the largest control group, which underwent the 14-day program, the total cholesterol levels returned to the reference range in 54% of people with hypercholesterolemia (<5.2 mmol/l) by the time of their check-out. HOMA index of insulin resistance demonstrated a decrease for all groups with reducing amplitude of decline as far as the longitude of the programs growths. HOMA decrease was the most prominent from 1.14 to 0.7 in "Detox 7" group and minimal from 2.14 to 2.08 in "Detox 14" group. The METS-IR and TyG indices did not demonstrate a shift and maximal changes of their median values is below 4%. The leucocyte indices (the Calf-Calif leucocyte index of intoxication, the Reis index of intoxication, the hematological index of intoxication by Vasiliev) had different literature data regarding their reference and target ranges, so the dynamics of the indices were evaluated. Two of these indices demonstrated growth in the 7-days treatment program group of patients up to 16.08% for hematological index of intoxication. The negative dynamics of values was presented in the 10- and 14-day groups for all three indices in both groups ranging from 11.48% to 29.92%. ESR absolute median values did not change significantly and remained within the reference range mostly. But its relative values notably changed up to 50% in "Detox 7" group, up to 25% in "Detox 10" group and became 15.04% less than the start point in "Detox 14" group. We observed an increase of white blood cell count in "Detox 7" group (+8.63%) and less notable rise in "Detox 10" group with a 10.62% decrease of white blood cell count in "Detox 14" group. No adverse events were observed.

Lipid metabolism

According to the estimation made by Y. Levin, if there is an increase in the concentration of cholesterol and atherogenic lipids in blood, then stimulation of lymphatic drainage reduces accumulation of cholesterol in the human body tissues and lipid plaque formation in the artery walls simultaneously improving the oxygen uptake rate. It occurs due to the natural function of the lymph capillaries: in the absence of vasa vasorum in 2/3 of the artery walls it is the capillaries that undertake the task of removing the lipids and their metabolites. The stimulation of the lymphatic drainage in the natural way leads to antiatherogenic protection of the artery walls [2]. Moreover, the deliberate impact on the enterohepatic circulation of bile acids is carried out, which is the distinctive feature of the "Detox" program. Under normal circumstances, 90-95% of bile acids are being reabsorbed back [12, 13]. Targeted inhibition of this process through performing the bowel cleansing procedures and administering intestinal adsorbents (enterosorbents) is supposed to intensify bile acid loss and increase the level of their synthesis in the hepatocytes (which cannot, however, exceed 5 mg per day). The stimulation of bile acid synthesis reduces the cholesterol level in the liver and enhances its synthesis de novo. A decrease in the concentration of bile acids in the intestines should also lead to the reduction of fat absorption. Furthermore, cholesterol is a primary component of forming bile and its conversion into bile acids and excretion with the feces is the only way of elimination cholesterol from the body (and this path is enforced via conducting the choleretic procedures) [12, 13]. The results demonstrated a decrease in cholesterol levels and are in line with the theoretical expectations.

Carbohydrate metabolism

There are many mechanisms which contribute to insulin resistance. In the adipose tissue the density of insulin receptors mostly decreases. Also, the adipokine secretion changes. The tyrosine kinase activity in the muscle tissue is reduced, which leads to a decrease in the glucose uptake, the antilipolytic effect of insulin is suppressed and glycogenolysis and gluconeogenesis are activated. Hepatic insulin resistance results from the fact that insulin has no inhibitory effect on gluconeogenesis and causes increased glucose production by hepatocytes [14, 15].

HOMA-IR is used to evaluate insulin resistance in patients with type 2 diabetes and pre-diabetes, as well as in presumably healthy people. Regardless of the duration of the programs a decrease in the measured values was observed (with the most substantial decline on the 7-day programs). The notable dynamics can be explained by the fact that HOMA-IR, as supposed, mostly reflects hepatic, and not peripheral, insulin resistance [16] – and the maximum effect on the liver and gastrointestinal tract is achieved during the first days of any Detox program.

At the same time, this index takes into account only two markers that are subject to marked variability. A low-protein diet is known to lower the basal insulin levels in obese people [17]; all the patients had their protein intake restricted for the first 5 days. This might have caused a decrease in insulin and HOMA-IR values, which did not reflect the real dynamics of the insulin resistance. The second phase of the study evaluated new indices of the insulin resistance that do not require insulin for their calculation: METS-IR and TyG.

The results of their insignificant changes suggest that the Detox program has no global impact on the insulin resistance during a short period of time (up to 10 days), although it significantly reduces the manifestation of the hepatic component of the insulin resistance, which could be viewed by HOMA-IR.

Intoxication and inflammation

To measure endogenous intoxication, white blood cell differentials were used. It is known that healthy people have their white blood cells in the homeostatic balance. An increase in the intoxication level through the action of pathogens and inflammatory factors stimulates leukocytosis, causing immature blood cells to enter the bloodstream. It represents a ratio of the level of cells increased during the inflammatory and purulent processes (neutrophils and immature cells) to the level of cells that may be decreased in these processes (lymphocytes, monocytes, eosinophils) and allow to measure the tissue degradation processes and the level of endogenous intoxication [10].

The prognostic value of these indices, their interaction with the treatment effect and correlation with the prognosis of the inflammatory, traumatic and paraneoplastic processes were dealt with in a number of studies [10, 11, 18-22]. At the same time, the reference range given for the indices differs in a variety of sources. Therefore, the dynamics of the values of these indices were evaluated in every individual patient.

An increase in the values of the 2nd and 3rd index of intoxication by the end of the 7-day program, with a trend towards their further decrease in the 10-day program and the 14-day program is interpreted as a transient intensification of inflammatory and intoxication processes by the end of the first week due to increased lymphatic drainage of the metabolites from the body tissues. It is enabled by the choleretic and cleansing procedures, fasting (resulting in the elimination of the opportunistic flora), herbal infusions for promoting lymphatic drainage, body wraps and thermal procedures in order to enhance the detoxification function of the skin and by other methods. Subsequently, there is elimination of endotoxins and followed by the improvement of the values of indices reflecting the reduction of intoxication below the baseline in patients. It is confirmed by an increment in ESR and a trend towards leukocytosis in the beginning (in the 7-day program group) with a later decrease below the baseline (in the 14-day program group) (Table 1).

CONCLUSION

This study evaluated, for the first time, the impact of spa treatment programmes on the human body. Simple laboratory calculation indices for evaluation of changes in the human body have been selected and tested. The results of the study confirm the effect of the performed treatment on a decrease in the intoxication and inflammation levels, total cholesterol level reduction and reduction of hepatic insulin resistance. Indirect confirmation of certain provisions of J.M. Lewin's concept (management of lymphatic tissues through complex spa treatment) have been received. A stage-like pattern of the dynamics of the measured values after performing the detoxification treatment complex has been identified: clear positive tendencies are formed starting from the 10th day. Such scenarios can be used to interpret laboratory data obtained from patients during and after the programme, to select additional therapies to support a patient during and after the programme.

ADDITIONAL INFORMATION

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Authors' contribution:
All authors confirm their authorship according to the ICMJE criteria (all authors contributed significantly to the conception, study design and preparation of the article, read and approved the final version before publication).
Special contribution:
Isaev F.I. – concept and design of the study, collection of material and execution of the textual part of the work;
Moskalev A.A. – checking the essential concept of the article, scientific editing.

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Ethics Approval:
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Consent for Publication:
Consent of patients (their representatives) to the processing and publication of non-personalized data was obtained.

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APPENDIX

Table 1. *Dynamics of the index values in the patient groups*

	Group "Detox-7", n=22			Group "Detox-10", n=13			Group "Detox-14", n=54		
	Apparture	**Departure**	**Dynamics**	**Apparture**	**Departure**	**Dynamics**	**Apparture**	**Departure**	**Dynamics**
Total cholesterol, mmol/l	5,36 (1,11)	5,16 (1,33)	-0,24%	5,36 (1,7)	4,9 (1,14)	-11,94%	5,48 (0.98)	4,97 (1.18)	-10,43%
HOMA index	1,34 (1,345)	0,7 (1.12)	-60,21%	1,34 (1,19)	1,12 (0,44)	-19,60%	2,14 (2.22)	2,08 (1.69)	-15,48%
TyG index	4,43 (0,4)	4,44 (0,28)	-1,77%	8,23 (0,69)	8,15 (0,5)	-0,11%	Was not evaluated		
METS-IR index	26,82 (11.19)	26,91 (10.18)	+0,30%	27,57 (7,93)	29,7 (6,74)	+4,00%	Was not evaluated		
Kalf-Kalif intoxication index	0,34 (0,25)	0,32 (0,67)	+12,66%	0,41 (0,37)	0,34 (0,48)	-11,48%	0,36 (0,4)	0,25 (0,31)	-29,92%
Reis intoxication index	1,02 (0,24)	1,01 (0,29)	-8,22%	1,47 (0,64)	0,98 (0,69)	-23,63%	1,09 (0,54)	0,88 (0,39)	-26,91%
Intoxication indicator	0,34 (0,24)	0,32 (0,66)	+16,08%	0,4 (0,46)	0,34 (0,48)	-26,23%	0,39 (0,4)	0,25 (0,31)	-29,92%
ESR, mm/hour	3,0 (4,75)	5,0 (5.75)	+50,00%	6 (6,5)	5 (4,25)	+25,00%	8,5 (9.25)	8,0 (9.0)	-15,04%
WBC count, *10^9/l	5,91 (1,43)	6,22 (1.89)	+8,63%	5,5 (2,12)	5,39 (1,44)	+4,38%	6,24 (2.03)	5,65 (2.02)	-10,62%

Note: *The table presents the median averages for each group of the measures at the arrival and before the check-out (the interquartile range of the values is shown in the parentheses)*