The role of micronutrients and vitamins in the prevention and remote treatment of heart failure

El papel de los micronutrientes y las vitaminas en la prevención y el tratamiento remoto de la insuficiencia cardíaca.

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Abstract

The purpose of this study is to study the role of vitamins and trace elements in the prevention of cardiovascular diseases (arrhythmias) in children. In 2015-2019, 300 children of the experimental group, 141 girls and 159 boys with diseases associated with heart dysfunctions were examined. The average age of children is 11.2±1.2 years, the interval is from 6 to 16 years. The second, control group included 150 healthy children, 81 boys and 69 girls, the average age of the child in this group was 11.6±1.2 years. Children from the control and experimental groups lived in the same city (Orenburg, Russia; Grozny, Russia), in identical climatic (environmental) conditions. The concentration of trace elements in the hair and the level of vitamin D, B9 and B12 in the blood was determined using the method of atomic emission spectrometry and the immunochemical method, respectively. A 1.4-fold higher frequency of occurrence of vitamin D deficiency or deficiency was found in the experimental group ($p \leq 0.001$). As for the deficiency of vitamins from group B, it was detected exclusively in patients with impaired heart function. Calcium deficiency was found in 267 children from the experimental group (89%) with cardiac abnormalities compared with 60 children from the control group (40%, at $p \leq 0.001$). A similar trend was recorded for magnesium: deficiency was found in 270 children (90%) from the experimental group with a deficiency of vitamin D compared with 51 (34%) children from the control. ($p \leq 0.001$). The values of Pearson correlations (at $p \leq 0.05$) between the deficiency of vitamin D and the low concentration of the chemical elements, in particular, calcium (0.95), magnesium (0.92), manganese (0.89), phosphorus (0.87), zinc (0.84), were obtained. For four elements, the dependences were obtained between a low concentration of vitamin D and an increased concentration of these elements: lead (0.89), strontium (0.83), nickel (0.84), and aluminum (0.79). In children with cardiac abnormalities, the concentration of vitamins is 1.5–2 times or more significantly lower compared to the control group. For the risk of disturbances in the heart, a concentration of vitamin D at a level of 21.8 ng/ml is sufficient, which slightly exceeds the minimum permissible concentration of this vitamin. Since most of the chemical elements we studied are somehow related to the concentration of vitamin D, the determination of the critical concentration of this vitamin seemed extremely important. Children with vitamins D, B9 and B12 deficiency, have heart problems more often than the healthy children of the same age and living in similar conditions. For a third (5 out of 18) of the studied chemical elements there is a direct correlation between their low concentration and low concentration of vitamin D in the blood plasma. For 4 elements, a high concentration was established in conditions of a lack of vitamin D (lead, nickel, strontium, aluminum). A high risk of arrhythmia may be associated with a concentration of vitamin D not exceeding 21.8 ng/ml.

Key words: vitamins, minerals, concentration, deficiency, arrhythmia.

Resumen

El propósito de este estudio es estudiar el papel de las vitaminas y oligoelementos en la prevención de enfermedades cardiovasculares (arritmias) en niños. En 2015-2019, se examinaron 300 niños del grupo experimental, 141 niñas y 159 niños con enfermedades asociadas con disfunciones cardíacas. La edad promedio de los niños es de 11.2 ± 1.2 años, el intervalo es de 6 a 16 años. El segundo grupo de control incluyó 150 niños sanos, 81 niños y 69 niñas, la edad promedio del niño en este grupo fue de 11.6 ± 1.2 años. Los niños de los grupos de control y experimentales vivían en la misma ciudad (Orenburg, Rusia; Grozny, Rusia), en idénticas condiciones climáticas (ambientales). La concentración de oligoelementos en el cabello y el nivel de vitamina D, B9 y B12 en la sangre se determinaron utilizando el método de espectrometría de emisión atómica y el método inmunoquímico, respectivamente. Se encontró una frecuencia 1,4 veces mayor de aparición de deficiencia o deficiencia de vitamina D en el grupo experimental ($p \leq 0{,}001$). En cuanto a la deficiencia de vitaminas del grupo B, se detectó exclusivamente en pacientes con insuficiencia cardíaca. Se encontró deficiencia de calcio en 267 niños del grupo experimental (89%) con anomalías cardíacas en comparación con 60 niños del grupo control (40%, a $p \leq 0.001$). Se registró una tendencia similar para el magnesio: se encontró deficiencia en 270 niños (90%) del grupo experimental con una deficiencia de vitamina D en comparación con 51 (34%) niños del control. ($p \leq 0.001$). Los valores de las correlaciones de Pearson (en $p \leq 0.05$) entre la deficiencia de vitamina D y la baja concentración de los elementos químicos, en particular, calcio (0.95), magnesio (0.92), manganeso (0.89), fósforo (0.87), zinc (0,84), se obtuvieron. Para cuatro elementos, las dependencias se obtuvieron entre una baja concentración de vitamina D y una mayor concentración de estos elementos: plomo (0.89), estroncio (0.83), níquel (0.84) y aluminio (0.79). En niños con anomalías cardíacas, la concentración de vitaminas es 1.5-2 veces o más significativamente menor en comparación con el grupo control. Para el riesgo de alteraciones en el corazón, una concentración de vitamina D a un nivel de 21.8 ng / ml es suficiente, lo que excede ligeramente la concentración mínima permitida de esta vitamina. Dado que la mayoría de los elementos químicos que estudiamos están de alguna manera relacionados con la concentración de vitamina D, la determinación de la concentración crítica de esta vitamina parecía extremadamente importante. Los niños con deficiencia de vitaminas D, B9 y B12 tienen problemas cardíacos con mayor frecuencia que los niños sanos de la misma edad y que viven en condiciones similares. Para un tercio (5 de 18) de los elementos químicos estudiados existe una correlación directa entre su baja concentración y baja concentración de vitamina D en el plasma sanguíneo. Para 4 elementos, se estableció una alta concentración en condiciones de falta de vitamina D (plomo, níquel, estroncio, aluminio). Un alto riesgo de arritmia puede estar asociado con una concentración de vitamina D que no exceda de 21.8 ng / ml.

Palabras clave: vitaminas, minerales, concentración, deficiencia, arritmia.

Introduction

As it is generally recognized, cardiovascular diseases are among the most widespread ones, with a high mortality rate (Fiaccadori et al., 2009). In particular, in the Russian Federation they are leading in the number of deaths, accounting for up to 48% of the total number of deaths, according to official statistics (Health in Russia, 2017). This significantly exceeds the world average - 30% (WHO, 2017), or about 17 million people per year. One of the current trends in the prevention of cardiovascular diseases remains the study of the role of a lack of micro- and macroelements, as well as vitamins in the dynamics of the development of diseases of the cardiovascular system (Fivez et al., 2016). Studies in this direction are mainly devoted to the concentration of vitamins, micro and macro elements in the blood and tissues of organs, and their role (Kidney Disease: Improving Global Outcomes Acute Kidney Injury Work Group, 2012; Kyle et al., 2013). Some trace elements affect the oxidation processes in cells; a lack of trace elements can lead to a violation of the morphological and physiological properties of cell membranes. The result of this is damage not to individual cells, but to tissues (Lopez-Herce et al., 2006). Vitamin D affects not only gene expression, but also plays a key role in the full functioning of the cardiovascular system (Anderson et al., 2010). Some data indicate an inverse relationship between the number of cases of diseases of the cardiovascular system and the presence of calcium and magnesium in drinking water (Martinez & Mehta, 2016). In such regions, the number of cases increases by a third compared to areas where the water contains a normal, rather than low, concentration of calcium and magnesium. With magnesium deficiency, metabolic changes occur in the body, leading to disruption of the cardiovascular system, and then to the development of the corresponding pathology (Mehta et al., 2009; Martinez & Mehta, 2016; Ozer, 2018).

At the same time, all these data are fragmented and most often are devoted to the study of the role of any one trace element or vitamin (Mehta et al., 2015). This implies the need to create a common database, which will include trace elements and vitamins, taking into account their mutual influence and comprehensive prevention of cardiovascular diseases.

Children are at particular risk (Mehta et al., 2012). This study is devoted to the role of vitamins and microelements in the prevention of arrhythmias in childhood, since further arrhythmia can develop into more serious diseases in adulthood, including heart failure. Among the consequences that arrhythmia and other types of cardiac arrhythmias in childhood can lead to syncope, heart failure (acute and chronic), and sudden death (as a result of a heart attack). Thus, the prevention of cardiovascular disease should begin as early as childhood. One of the simplest methods of prevention is therapy using diets (or drugs) containing the required amount of trace elements and vitamins (Sethi et al., 2017; Ghalandari et al, 2018).

The purpose of this study is to study the role of vitamins and trace elements in the prevention of cardiovascular diseases (arrhythmias) in children. The research objectives included: a) a comparative analysis of vitamins B9, B12 and D concentrations in children with arrhythmias and healthy children; b) assessment of the critical level of concentration of vitamins in children, starting from which a risk of occurrence and development of cardiac abnormalities is possible; c) conduct a similar comparative analysis of the concentration of trace elements in healthy and sick children with arrhythmia.

Material

Material base of research

The studies were conducted in 2015-2019 in Orenburg, Kazan, Moscow and in Grozny (i.e., at the Orenburg State Medical University, at the Kazan State Medical University, at the V.I. Vernadsky Institute of Geochemistry and Analytical Chemistry and at the Chechen State University). Blood samples were taken from children divided in two groups, experimental and control, and the trace elements were analyzed. All analyzes were carried out with the written consent of the parents of the children and verbally with the children.

Object of study

The samples are randomized. 300 children were examined, of which 141 were girls and 159 were boys. The average age of children is 11.2±1.2 years, the interval is from 6 to 16 years. No age differences were found between boys and girls: 11.4±1.0 years on average for boys and 11.0±1.4 years for girls. All children were undergoing the inpatient pediatric cardiac surgery in the Russian Academy of Sciences, Orenburg, and inpatient hematology in the Glinka Children's Republican Clinical Hospital, Grozny, during the period from 2015 to 2019. In parallel, the control group consisting of 150 healthy children who had no problems with the cardiovascular system was examined. Of these, 81 are boys and 69 girls, the average age of the child in this group is 11.6±1.2 years, girls 11.4±1.0 years, boys 11.8±1.4 years. In the control group, no significant differences in age were found within the group and with the experimental group. Children in these groups were recruited in the same healthcare facilities as children from the experimental group.

Inclusion Criteria

Various disorders of the rhythm of cardiac activity: supraventricular and ventricular localization, tachycardia of a chronic nonparoxysmal type, tachycardia of a paroxysmal type of ventricular localization, the presence of weak sinus node syndrome. This also included children with conduction disorders, in particular with Wolf-Parkinson-White syndrome, as well as with atrio-vetricular blockade of 2-3 degrees. Children in the first group can be divided into 2 subgroups: children with organic changes in the heart (191 people) and children with manifestations of autonomic dysfunction (109). Details of the distribution of each disease are presented in Table 1.

Table 1. The distribution of the experimental group by types of disorders of the heart

Illness	Patient number
Congenital heart disease with the appearance of arrhythmia (at different times after surgery)	111
Wolf-Parkinson-White syndrome (or congenital malformations in the cardiac conduction system)	42
Primary dilated cardiomyopathy	12
Hypertrophic cardiomyopathy	26
Arrhythmia as a result of autonomic dysfunction	109

Exclusion Criteria

The absence of problems with the cardiovascular system, or diseases that are not in the list of inclusion criteria.

Children from the control and experimental groups lived in the same settlement (Orenburg, Russia; Grozny, Russia), in identical climatic (environmental) conditions.

Research methods

Examining children, we used generally accepted standard methods of clinical examination, as well as laboratory and instrumental methods. These methods included determining vitamins D, B9, B12 concentrations in the blood. The concentration was determined using the immunochemical method, using electrochemiluminescent detection. The results were analyzed based on the recommendations of the International Society of Endocrinologists. According to the recommendations, the vitamin D below 20 ng/ml, (10^{-12} kg) per 1 ml, or about 50*10-9 mmol/l, means deficiency. The vitamin D range 21-29 ng/ml (or 50-75*10^{-9} mol/l) indicates a lack of vitamin D; 30-100 ng/ml (or 76-250*10^{-9} mol/l) is the normal vitamin D concentration. The vitamin B9 deficiency was identified at the concentration of 4.60 ng/ml, and the vitamin B12 deficiency at the concentration of less than 190 pg/ml (1 pg = 10^{-9} in 1 g) (Holick et al., 2011).

All hair samples taken from children were examined by the multielement spectral method, which allows for the high-quality chemical analysis. In total, 18 trace elements were identified: calcium, magnesium, potassium, sodium, sulfur, phosphorus, chromium, iron, copper, iodine, manganese, cobalt, molybdenum, zinc, selenium, boron, vanadium, silicon. Microelement concentrations were determined in hair samples using inductively coupled plasma atomic emission spectrometry and absorption spectrometry. All analyzes on the trace element composition were performed on an ICPE-9000 Plasma Atomic Emission Spectrometry mass spectrometer (Shimadzu, Japan).

Statistical analysis

Statistical processing of the data was carried out using the program Past v. 3.0, as well as the Microsoft Excel 2010 statistics package. The data were checked for normal distribution using the Shapiro-Wilk method as well as the chi-square method. Since the obtained data corresponded to a sample with a normal distribution, we used the methods of parametric statistics in the subsequent analysis. The tables give the arithmetic mean±standard error of the mean, the quantitative parameters were compared using the t-criteria. The difference in the concentration averages and other variables between different groups was examined using the Scheffé's method. To assess the presence of connections between the variables, the Pearson correlations were calculated.

Introduction

We found that the minimum concentrations of vitamin D, as well as B9 and B12, corresponding to a deficiency or deficiency, were found in children suffering from various forms of cardiac dysfunction (Table 2).

Comparison of the experimental and control groups showed a reliable, 1.4 times higher incidence of vitamin D deficiency in the experimental group. As for the deficiency of vitamins from group B, it was detected exclusively in patients with impaired heart function. Out of 63 children from the experimental group, vitamin B9 deficiency was found in 45 in combination with vitamin D deficiency. For vitamin B12, a similar trend was found - only with an even higher frequency of occurrence with vitamin D deficiency (Table 2).

Vitamin D deficiency is also associated with low concentrations of some of the trace elements. Thus, calcium deficiency was found in 267 children from the experimental group (89%) with cardiac abnormalities compared with 60 children from the control group (40%, at p≤0.001). A similar trend was recorded for magnesium: its deficiency was found in 270 children (90%) from the experimental group with a deficiency of vitamin D compared with 51 (34%) children from the control. (p≤0.001). Similar indicators were obtained for manganese (256 children, 85% in the experimental group with a lack of vitamin D versus 43 (or 28%) in the control, p≤0.001). For zinc, vitamin D concentration in case of deficiency in the experimental group is lower than normal compared to the control group (189 children or 63% versus 23 children or 35% in the control, p≤0.002). The same dependence is present in the case of phosphorus: in the experimental group in children with vitamin D deficiency, phosphorus deficiency was detected in 219 children (73%) against 33 (22%) from the control group (p≤0.01).

About half of children with vitamin D deficiency (49% or 147 children) from the experimental group showed an excess of such a toxic element as lead. This is more than 2 times higher than in the control group (30 children or 20%, p≤0.001). According to the family history, the parents (mothers) of children from the experimental group during pregnancy smoked two-thirds of the mothers of children with heart problems compared to one-third of the mothers of children from the control group (75% versus 23%, p≤0.001).

We also recorded an excess in the group of children with cardiac abnormalities and vitamin D deficiency in the concentration of elements such as strontium (114 or 38% versus 18 or 12%, p≤0.01), nickel (87 or 29% against 18 children or 12%, p≤0.01) and aluminum (recorded exclusively in the experimental group in children with vitamin D deficiency, 21 children or 7%, p≤0.001).

We obtained reliable values of Pearson correlations (at p≤0.05) between vitamin D deficiency and low concentration of the chemical elements studied by us, in particular, calcium (0.95), magnesium (0.92), manganese (0.89), phosphorus (0.87), zinc (0.84). For four elements, the dependences were obtained between a low concentration of vitamin D and an increased concentration of these elements: lead (0.89), strontium (0.83), nickel (0.84), and aluminum (0.79).

Based on the obtained data on a reduced concentration of vitamins D, B9 and B12 in children from the experimental group and children from the control, the corresponding concentration values of these vitamins were obtained (Table 3).

As can be seen from the data table. 3, in children with cardiac abnormalities, the concentration of vitamins is 1.5–2 times or more significantly lower compared to the control group. Based on the analysis, we were able to establish the level of concentration of vitamin D and vitamins from group B, which can determine the development of disorders of the heart (table 4).

We were able to establish that for the risk of disturbances in the heart, a concentration of vitamin D at a level of 21.8 ng/ml is sufficient, which slightly exceeds the minimum permissible concentration of this vitamin.

Table 2. Children with a deficiency or deficiency of vitamins D, B9 and B12				
Vitamin or Vitamin Combination	Total number of children examined in two groups (total 450, 100%)	Number of children in the experimental group (total 300, 100%)	Number of children in the control group (total 150, 100%)	Significance Levels (p≤)
D	342 (76%)	243 (81%)	84 (56%)	0.01
B9	72 (16%)	63 (21%)	0	0.001
B12	135 (30%)	117 (39%)	0	0.001
D, B9, B12	18 (4%)	15 (5%)	0	0.01
D & B9	54 (12%)	45 (15%)	0	0.001
D & B12	117 (26%)	102 (34%)	00.01	0.001

Table 3. The values of the average concentration of vitamins D, B9 and B12 in children from the control and experimental groups				
Vitamin	Valid concentration values (ng/ml, for B12 - pg/ml)	Values of average concentration, experimental group	Values of average concentration, control group	Significance Levels (p≤)
D	30-100	15.30±2.4*	35.3±4.5	0.029
B9	4.5-18.5	4.35±0.2*	9.23±0.52	0.038
B12	190.0-660.0	185.2±7.2*	230.2±7.21	0.045

* - differences are significant at p≤0.05 between experiment and control.

Table 4. The concentration levels of vitamins D, B9 and B12, determining the possibility of disturbances in the work of the heart				
Vitamin	Values of concentration in blood serum (ng/ml, for B12 - pg/ml)	Sensitivity Level, %	Specificity Level, %	Significance Levels (p≤)
D	21.8	77	75	0.029
B9	4.10	71	55	0.431
B12	160.0	59	65	0.540

Discussion

Vitamin D is a prohormone that affects gene expression, which determines its significant role. It is known that vitamin D plays a regulatory role in the cardiovascular system, and that its deficiency can increase the risk of developing cardiovascular diseases. This relationship may be direct in nature, as has been shown in some studies (Anderson et al., 2010).

Trace elements can play a decisive role in metabolic processes occurring both in the body as a whole and in the heart muscle in particular. So, calcium, located in cardiomyocytes, causes the appearance of an electric charge and the general electric potential of the entire heart muscle. Calcium deficiency negatively affects the work of the whole heart, at the level of physiological processes (Sabatino et al., 2015; Sgambat & Moudgil, 2016).

Magnesium is known to be an integral part of more than 300 enzymes in the body. The impaired enzyme activity can cause the blood vessel dysfunction and problems with the energy production doe to the breakdown of ATP. Enzymes also act on cardiomyocytes and the heart muscle, triggering the relaxation processes. Overall, the effect of reduced magnesium is manifested in the spasmodic vasoconstriction and heart rhythm disturbances (Mehta et al., 2013).

Manganese is directly related to calcium and its role is also considerable. The mechanism of calcium intake by the heart muscle cells depends on the concentration of manganese. For instance, a low concentration of this element can cause the circulatory dysfunction as well as the ventricular fibrillation. For phosphorus and zinc, a direct relationship has been established between the level of their concentration in the heart and the level of ejection in the left ventricle (Kazi et al, 2008).

The ways in which lead enters the body are diverse. Lead is used in glass and ceramic paints and even in the alcoholic beverage coloring products. Lead that enters the human body can also come from breathing in the products of gasoline (motor vehicles) and coal combustion, which may also contain a high concentration of this element (Wei et al., 2008; Storelli et al., 2010). High concentrations of lead are also recorded for tobacco smoke. During pregnancy, in the first trimester, lead easily enters the body of the baby through the placenta, and in infants it passes along with breast milk (Hulst et al., 2004; Gundacker et al., 2010). Thus, smoking can expose a child to lead intoxication. This is shown by us - most of the children from the experimental group had smoking mothers. Among the consequences of lead intoxication for a child are such as abnormalities in the development of internal organs (trachea, kidneys, heart), cerebral palsy, and underdevelopment of limbs (Storelli et al., 2010). For strontium, vanadium, lead, and aluminum, it is known that they determine the possibility of calcium entering inside cardiomyocytes, but in high concentrations can lead to consequences such as impaired coronary circulation and ventricular fibrillation (Prozialeck et al., 2006).

The above confirms the thesis that trace elements play a decisive role in most known enzymatic reactions associated with various metabolic processes. In the human body, these chemical elements form bonds, reacting with each other, with an imbalance of elements fatal consequences are possible, for example, atherosclerotic changes in blood vessels (Castillo et al., 2012). Since most of the chemical elements we studied are somehow related to the concentration of vitamin D, the determination of the critical concentration of this vitamin seemed extremely important. A lack of vitamin D, with a certain concentration, as shown by our data, can trigger a cascade of reactions - a lack of certain trace elements and an excess of others, which ultimately increases the likelihood of diseases of the cardiovascular system. A balanced diet, as well as moderate use of drugs containing vitamins D, B9, B12, as well as trace elements, will allow for the implementation of primary prevention of cardiovascular diseases in childhood (Phan et al., 2006; Zappitelli et al., 2008, 2009; Alkandari et al., 2011; Mitting et al., 2015).

Conclusions

Children with a deficiency of vitamin D, B9 and B12, more often healthy children of the same age and living in similar conditions, have heart problems. It was found that for a third (5 out of 18) of the studied chemical elements there is a direct correlation between their low concentration and low concentration of vitamin D in the blood plasma. For 4 elements, a high concentration was established in conditions of a lack of vitamin D (lead, nickel, strontium, aluminum). It was revealed that a high risk of arrhythmia may be associated with a concentration of vitamin D not exceeding 21.8 ng/ml.

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