DIETARY FIBER IN REDUCING OF ELEVATED BLOOD LEAD CONCENTRATION IN CHILDREN

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Summary

The aim of the study was to evaluate the effectiveness of dietary fiber in reducing elevated blood lead concentration (BLC) of Ukrainian children.

Materials and methods. 80 random children aged 4 to 15 years were examined. The lead content in venous blood was detected by atomic absorption spectrometry with electro-thermal atomizer (ET AAS). Indicators of morphological and biochemical blood tests were determined by generally accepted methods.

Results. About a quarter of the children had BLC ≥ 5μg/dL. They had a higher content of eosinophil cells, an increase of ALT activity in the blood compared to children with lower BLCs. As a nutritional supplement for the rehabilitation of these children, dietary fiber from cereals of 10 g per day was used for 30 days, as an addition to main dishes and salads during lunch. As a result, BLC significantly decreased. At the same time, the number of eosinophils in blood and the activity of ALT significantly decreased. The thiol-disulfide ratio increased. Children tolerated nutritional intervention well. Its safety was also indicated by the absence of changes in indicators of the functional state of the liver. This allows us to recommend this dietary supplement for the improvement of children undergoing environmental lead pressure.

Key words: environment, public health, lead exposure, oxidative stress, rehabilitation.

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1. Introduction

Humans have been using lead (Pb) for a variety of applications since millennia, and concomitant with this use has developed an ancient recognition of the adverse effects of lead on the human body *(Halmo, 2023)*. With the progress of civilization and active processes of urbanization and industrialization, the scale of use of lead, and accordingly its negative impact on public health, only increased. Lead exposure is estimated to account for 21.7 million years lost to disability and death (disability-adjusted life years, or DALYs) worldwide due to long-term effects on health, including 30% of the global burden of idiopathic intellectual disability, 4.6% of the global burden of cardiovascular disease and 3% of the global burden of chronic kidney diseases *(WHO, 2023)*. Human exposure to lead has been linked to different sources of contamination, resulting in high blood lead concentration (BLC) and adverse health implications, primarily in exposed children *(Swaringen, 2022)*. Evidence-based research has shown the efficacy and cost-effectiveness of some public policies to prevent or reduce these exposures in the United States and other developed countries *(Levin, 2021)*.

But there remain well defined neighborhoods where children continue to have toxic lead exposures *(Levin, 2021)*. Those neighborhoods tend to have disproportionate commercial and industrial lead activity; a history of dense traffic; older and deteriorating housing; past and operating landfills, dumps and hazardous waste sites; and often lead contaminated drinking water. The population there tends to be low income *(Levin, 2021)*. Such areas are found even in developed countries. In Ukraine, all these negative factors are joined by such as active combat operations in a large part of the territories for more than a year and a half. Therefore, millions of children continue to be at risk for lead exposure despite a dramatic decline over the past 4 decades in the whole world, and hundreds present annually to emergency departments with lead poisoning *(Nadler, 2022)*. As the 20 and 21 centuries progressed, so did the appreciation for increasingly subtle and even subclinical manifestations of lead toxicity *(Halmo, 2023; Capitão, 2022; Disalvo, 2022; Zhang, 2022; Olufemi, 2022; Zhao, 2023; Awadh, 2023; Halabicky, 2023)*. Therefore, lead poisoning cannot be consigned to history books yet *(Emond, 2022)*.

According to WHO recommendations for clinical management of lead exposure, in all cases, action should be taken to identify the source of lead and stop ongoing exposure, as this will, in itself, reduce the blood lead concentration and improve clinical features of toxicity *(WHO guideline, 2021)*. And to remove the lead that has already accumulated in the child's body, chelator therapy is usually used. But pharmacological chelators themselves are quite toxic. Therefore, according to current WHO recommendations, chelation therapy should be considered for a child (≤ 10 years) with a BLC ≥ 40 μg/dL *(WHO guideline, 2021)*. However, the BLC that should initiate clinical intervention, according to the same recommendations, is ≥ 5 μg/dL *(WHO guideline, 2021)*. Therefore, to accelerate the elimination of lead accumulated in the blood at concentrations of 5 ≤ BLC < 40 μg/dL, an alternative to pharmacological chelators is needed.

The purpose of the work was to evaluate the effectiveness of dietary fiber (DF) as a natural alternative to pharmacological chelators in reducing BLC in children.

2. Material and methods of research

80 random children aged 4 to 15 years, who were in a pediatric treatment facility, were examined. The inclusion of children in the study was carried out subject to the informed consent of the parents of the children after providing detailed information about the procedure and purpose of the work. To diagnose, predict the course and evaluate the effectiveness of clinical interventions, we chose those indicators of laboratory examination that could be the most informative and at the same time relatively accessible. According to modern data, these are the blood lead concentration – BLC *(WHO, 2023)*, hematological and biochemical indices *(Capitão, 2022; Rawat, 2021)*, biomarkers of oxidative stress *(Disalvo, 2022; Zhang, 2022)*.

The determination of lead was carried out in heparinized venous blood by atomic absorption spectrometry with electro-thermal atomization (ET AAS). General clinical tests of blood and urine were carried out according to generally accepted methods. A biochemical blood test included separate indicators of the state of the liver to assess the possible negative effects of lead on these parameters, as well as to control the safety of therapy, as shown in the literature. The content of beta-lipoproteins, bilirubin, total protein, the activity of alanine aminotransferase (ALT), an indicator of the thymol test was determined. The activity of lipid peroxidation (POL) processes was judged by the accumulation of primary (diene conjugants – DC) and final (malonic dialdehyde – MDA) lipoperoxidation products in the blood. The state of the antioxidant system was assessed by the activity of glutathione-peroxidase (GPO) and by the content of sulfhydryl and thiol-disulfide groups of blood proteins. The research was conducted according to unified methods. The ratio of group averages SH/SS was also calculated.

Statistical processing of the obtained data was carried out by methods of variational statistics using the Student-Fischer T-criterion.

To establish the dependence of the studied parameters on the BLC, as well as considering the recommendations of the WHO on the feasibility of clinical intervention *(WHO guideline, 2021)*, children were divided into 2 groups: 1) a group with a lead content of up to 4.9 μg/dL, n = 62; 2) a group with a lead level in the range of 5.0–9.9 μg/dL, n = 18. The control in assessing the ecopathogenic effects of lead was the first group of children. In assessing the efficacy and safety of the intervention, indicators at the beginning and end of observation were compared.

It is known that the studied indicators can be influenced not only by the level of lead in the blood, but also by age, by the presence of certain diseases. To establish uniformity according to these factors of the selected groups of children, the criterion χ^2 was calculated. This method, also called "particle and proportions analysis", allows us to prove statistically the uniformity or unevenness of the distribution of certain features in groups. Evaluation of calculations χ^2 showed that by age, by the presence of certain diseases, the groups were homogeneous, so the differences in the indicators of morphological and biochemical studies could be explained in this case only by different levels of lead in the blood.

3. Results of the research and their discussion

3.1. Indicators of morphological and biochemical examination

The results of the study are presented in the table. In the biochemical indicators of the functional state of the liver, there were no significant differences both between groups of children with different levels of lead and between different periods of observation, so they were not included in the table.

Analysis of BLC in children showed that about a quarter of them have a concentration above 5 μg / dL at the start of observation. This concentration is a practical value at which clinical interventions can be started according to the WHO recommendations *(WHO guideline, 2021)*. These were children of the second group.

In children of the second group, a significantly greater 1.7 times relative number of eosinophils was also found than in children of the first group. This is consistent with data from other researchers that a significant increase in the number of eosinophils was associated with Pb exposure in children *(Zheng, 2023)*, and it's observed a strong positive correlation between BLC and eosinophils *(Rawat, 2021)*. And it indicates a possible allergy of the body with an increase in the BLC, which can contribute to the development of allergic diseases such as asthma in children *(Zheng, 2023)*.

Compared with the first group, ALT was increased in the blood of children of the second group. This enzyme is organ-specific for the liver, so an increase in its activity in the blood indicates a violation of the integrity of the membranes of hepatocytes. The reason for this may be lead caused by excessive lipoperoxidation in membranes *(Disalvo, 2022; Zhang, 2022)*. Thus, the content of diene conjugants had a pronounced tendency to increase by 40% in children of the second group. This indicates the activation of lipoperoxidation processes with an increase in the level of lead in the blood.

Table 1

Indicators of morphological and biochemical examination of blood in children of different groups, M±m

Indicators	At the beginning of the observation		At the end of the observation	
	BLC ≤ 4.9 μg/dL	BLC 5.0–9.9 μg/dL	BLC ≤ 4,9 μg/dL	BLC ≤ 4.9 μg/dL
Lead, μg/dL	3.21±0.23	8.61±0.22*	3.14±0.21	5.16±0.27**
Hemoglobin, g/l	126.54±1.46	126.39±2.70	127.84±1.53	130.72±2.24
Erythrocytes, T/l	4.00±0.05	4.04±0.09	3.99±0.05	4.06±0.09
Eosinophils, %	1.65±0.24	2.83±0.54*	1.77±0.23	1.17±0.28**
ALT, μmol/l/s	0.42±0.01	0.47±0.02*	0.41±0.01	0.38±0.01**
DC, μmol/l	22.18±1.50	31.38±3.29	24.00±1.51	26.44±2.77
MDA, μmol/l	182.11±5.11	184.61±12.91	169.19±5.90	149.99±12.11
GPO, μmol/l/sec	8.38±0.50	8.54±0.82	9.36±0.63	10.64±1.56
SH-groups, μmol/l	1.11±0.08	1.47±0.24	1.04±0.08	1.25±0.15
S-S-links, μmol/l	0.45±0.06	0.64±0.21	0.40±0.05	0.44±0.06
SH/SS index	2.50	2.29	2.60	2.82

Note. * – The difference is reliable ($p < 0.05$) with the indicator of the first group, ** – the difference is reliable ($p < 0.05$) between the indicators at the beginning and at the end of the observation in each group.

At the same time, the state of antioxidant protection in children of the second group tended to weaken. Although the values of both indicators of the thiol-disulfide system increased, the increase in the number of SH-groups (by 30%) somewhat lagged the increase in the number of S-S-bonds (by 40%). As a result, the ratio of SH/SS decreased (2.50 in the first group and 2.29 in the second), which indicates depletion of reserves of antioxidant protection of the child's body with an increase in lead concentration.

It is known that impaired prooxidant-antioxidant homeostasis may be the primary mechanism associated with lead toxicity *(Zhang, 2022)*. Therefore, it is important to apply therapeutic intervention to this link in the pathogenesis to prevent the development of lead-induced pathology.

3.2. Justification of the use of dietary fiber

When choosing a medical intervention, we relied on the current recommendations of the WHO guideline, 2021. We informed parents about the need to identify and eliminate sources of lead in their child's body and take the necessary measures to reduce and stop exposure.

To remove from the body of children the lead that has already accumulated, we chose dietary fiber from cereals. The basis was the following considerations. The conventional techniques employed for the elimination of heavy metals are deemed inadequate when the concentration is relatively low *(Abd Elnabi, 2023)*. In our study, the second group of children had such relatively low BLCs (≥ 5 μg/dL, but < 40 μg/dL). In addition, conventional methods exhibit certain limitations, including the production of secondary pollutants, a high demand for energy and chemicals, and reduced cost-effectiveness *(Abd Elnabi, 2023)*. Therefore, there are more and more toxicological studies aimed at identifying natural products applied to the prevention or treatment of Pb poisoning by chelating and decreasing Pb bioaccumulation *(Destro, 2023)*.

Dietary fiber can be such a natural chelator. It is known that lead is largely accumulated in edible parts and fruits of plants growing in lead-contaminated areas *(Knez, 2022; Zhou, 2022; Proshad, 2023; Du, 2023)*. This has led researchers to believe that treated fibrous plant-based food wastes could be excellent sorbents for eliminating several detrimental and poisonous compounds, such as heavy metals, from wastewater and aqueous solutions *(Karim, 2023)*. It is a renewable and ecologically benign strategy based on a "circular bioeconomy" and "green chemistry" *(Karim, 2023)*. DF's role is also assessed as safe and non-toxic antimicrobial agents to manage chronic lead poisoning in humans *(Yao, 2022)*.

Dietary fibers include non-digestible plant carbohydrates, lignin and resistant starch *(Salvatore, 2023)*. It has long been known that bulking fiber is required as a stool-bulking agent to promote gut motility, bowel movement and removal of unwanted toxins *(Hojsak, 2022)*. It has been established that there is an association between reduced dietary fiber intake and increased accumulation of lead in the body *(Ooi, 2022)*.

Given all these data, as well as the fact that today population-level intakes of dietary fiber are low and needs to increase intake *(Mathers, 2023)*, given the lack of contraindications for fiber in children requiring nutritional support *(Hojsak, 2022)*, we used dietary fiber as a sorbent to remove lead from the body of children.

When choosing a source of dietary fiber, we paid attention to the fact that there is a risk of previous lead contamination of the food additive itself. This risk is greater for vegetables than for cereals *(Knez, 2022; Proshad, 2023; Du, 2023)*. Therefore, we settled on dietary fiber from wheat.

It was also necessary to determine the dose of nutritive supplement. In pediatric practice, concerns exist over tolerance of dietary fiber which may lead to unnecessary restrictions, especially for children receiving nutritional support *(Hojsak, 2022)*. It is still believed that the exact amount and characteristics of the fiber requirement in infants and children need to be further established *(Salvatore, 2023)*. On the one hand, the low intake of fibers has been associated with constipation. On the other hand, the intake of excessive fibers is not recommended as it may cause flatulence and abdominal discomfort *(Salvatore, 2023)*. Current recommendations suggest a daily amount of fiber in the region of 10 g/day for young children increasing to around 20 g/day for adolescents *(Hojsak, 2022)*.

So, as a nutritional supplement for children of the second group, dietary fiber from cereals of 10 g per day was used for 30 days, as an addition to main dishes and salads during lunch.

3.3. Effect of dietary fiber in children

As a result of the use of dietary fiber in children, their BLC has significantly decreased by 1.7 times (see Table). This confirms the data on the sorption properties of dietary fiber *(Karim, 2023)*.

At the same time, those studied indicators that at the beginning of the observation had differences with control were also subjected to correction. The relative number of eosinophils significantly decreased by 2,4 times. This effect may be associated with the positive effect of dietary fiber on the intestinal microbiota *(Mathers, 2023; Puhlmann, 2022)*, which in turn is involved in the formation of the immune response *(Gebrayel, 2022)*. A lack of fiber in the diet has been associated with several disorders in children including allergies *(Hojsak, 2022)*. Historical changes in fiber intake may be contributing to the increase of allergic and hypersensitivity disorders as fiber-derived metabolites are evolutionarily hardwired into the molecular circuitry governing immune cell decision-making processes *(Venter, 2022)*. It is well established that diets with a high fiber content promote a microbiota that has beneficial effect on intestinal health by stimulating intestinal mucus barrier function and promoting immune tolerance over inflammation *(Suriano, 2022)*. Including, obviously, inflammation, which was caused by lead. This is confirmed by a review *(Yao, 2022)*. This review highlights the role of DF and its metabolic products in alleviating lead-induced neuroinflammation by inducing changes in the species and quantity of gut microbiota and regulating the immune system, providing a potential dietary protective strategy for lead-induced disease *(Yao, 2022)*.

In addition, the activity of organ-specific enzyme for the liver – ALT – normalized in the blood of children who received dietary fiber in our study. Presumably, this happened because of strengthening the membranes of hepatocytes by reducing excess lipoperoxidation in them and improving antioxidant defense. The tendency to increase the level of diene conjugants, which was observed before the intervention, after the course of dietary fiber was eliminated. The thiol-disulfide ratio increased by 23%. This is consistent with the conclusion of a systematic review performed according to PRISMA guidelines, about a positive impact of plant extracts on redox metabolism upon lead exposure *(Destro, 2023)*.

Children tolerated nutritional intervention well. Its safety was also indicated by the absence of changes in indicators of the functional state of the liver.

4. Conclusions

Dietary fibers showed sorbing properties, contributed to the removal of lead from the body. This nutritional supplement has also helped improve metabolic status in children with elevated BLC. This allows us to recommend dietary fibers for the rehabilitation of children undergoing environmental lead pressure. However, additional investigation is needed.

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