

Correlation between the presence of metals with potential for intoxication, omega 3 deficiency, increased omega 6: omega 3 ratio and their associated symptoms

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ABSTRACT

Objectives. The study aims to determine the correlation between the presence of heavy metals with intoxication potential (mercury, aluminum, arsenic), increasing the values for the omega 6: omega 3 ratio, decreasing the concentration of omega 3 and its impact on health. Another objective of this study is the use of an integrated protocol, developed by an interdisciplinary team, based on a customized alignment program and a treatment plan.

Materials and methods. We evaluated in a retrospective observational study, 77 patients who came to the Nutribalance Clinic between September 2017 and December 2019, with specific symptoms of intoxication with toxic metals, especially mercury, aluminum, arsenic and omega 3 deficiencies. The manifested symptoms required a complete set of blood tests for each subject in the study group, tests that showed the presence of one, two and three toxic metals in the case of all 77 subjects.

The interdisciplinary team developed a personalized treatment and diet plan, monitoring the evolution on the symptoms initially manifested by each subject.

Outcomes. The results of this study shows the beneficial impact of the personalized diet plan and supplements used on the decrease in omega 6: omega 3 ratio, the significant increases in omega 3 which support the detoxification process of heavy metals and a significant improvement in the symptoms of each patient.

Conclusions. This study reveals that the process of chelating or detoxifying heavy metals is a complex one and that implies the presence of a complementarity between food and nutritional supplement therapy, avoiding one single direction, as results can be obtained for a short or insignificant period of time.

Keywords: mercury, aluminum, arsenic poisoning, personalized diet plan, heavy metal detoxification, omega 3 deficiency associated with heavy metal poisoning

INTRODUCTION

Toxic substances, harmful to the environment, but also to the human body, can have negative effects on our health. These substances may exist in the composition of frequently used products or may be present in air, water, soil [1]. Exposure to toxic substances happens through inhalation of vapors,

gases, dust, by their ingestion or by absorption through the skin, mucous membranes. The impact they can have on health depends on the degree of toxicity, the time and the exposure mode to risk factors, but also the reaction of each person to such substances and how the immune system protects the body [2].

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Article History:

Received: 25 January 2022

Accepted: 2 February 2022

The presence of heavy metals and other toxic substances in the human body is associated with brain degeneration, obesity, diabetes, cardiovascular disease, neurological imbalances and other health problems [3]. In addition to these, other factors such as the presence of excessive amounts of polyunsaturated omega-6 fatty acids and an unbalanced ratio of omega 6 to omega 3, as is the case in contemporary Western diets, stimulate the pathogenesis of several diseases, including cardiovascular diseases, cancer, inflammatory diseases and autoimmune diseases, while a higher level of omega 3 polyunsaturated fatty acids exerts mitigating effects [4].

One of the objectives of this study is to establish a correlation between the presence of heavy metals with potential for intoxication (mercury, aluminum, arsenic), increase the omega 6: omega 3 ratio, decrease the concentration of omega 3 and their impact on health.

The repeated exposure to various sources of intoxication, without a proper detoxification process and without identifying the sources of contamination, so as to avoid them, can be a trigger for the accumulation of toxic metals, affecting the proper functioning of the body.

An unbalanced diet, based mainly on food with a high content of unhealthy fats, sugar and refined carbohydrates can induce omega 6 fatty accumulations. Moreover, a lack of aliments with a significant omega 3 content causes major omega 3 deficiencies in the blood level.

The main sources of mercury contamination are dental amalgam fillings, food such as fish, mollusks, food from agriculture where pesticides contaminating the soil and the water have been used [5], plastics, neon bulbs, low energy bulbs. Inside the human body, the average half-life of inhaled mercury is about 60 days [6].

Clinical manifestations of chronic exposure to organic mercury have a gradual onset, the main area of action being the nervous system, chronic exposure to mercury can cause symptoms such as fatigue [7], weakness, headache and decreased concentration [8]. In severe cases, chronic exposure leads to intellectual damage and neurologic abnormalities.

Possible sources of aluminum contamination are tap water (drinking and household water), kitchen utensils made of aluminum (cutlery, vases and aluminum foil), aluminum packaging, food with synthetic additives, cosmetics (deodorants, antiperspirants, perfumes, toothpaste), vaccines, some drugs (antacid treatments) [9].

Common symptoms of aluminum contamination are burnout, lack of concentration, long or short-term memory problems, calcium and phosphorus

deficiency (risk of osteoporosis), muscle pain, anemia, digestive disorders, abdominal cramps, renal failure, autoimmune diseases [8].

Frequent sources of arsenic contamination (introduced into the body by inhalation, ingestion) can be found in the soil and drinking water levels, food products that resulted from repeated insecticidal treatments (cereals – wheat, rice; vegetables; sea products), electronic devices [10,11]. Arsenic accumulation in rice is one of the most common [12] sources of ingestion, the repeated, long-term consumption representing a major risk factor among both adults and children [13].

Short-term exposure to arsenic affects blood vessels, leads to a change in erythrocytes, leukocytes, abnormal heartbeat, tingling sensations in the hands and feet, which induce a state of discomfort, until the onset of anxiety [14].

Long-term exposure to sources of arsenic contamination can generate skin lesions, peripheral vascular disease, neurological problems, diabetes mellitus, certain types of cancer, chronic fatigue syndrome [15].

Exposure and absorption of heavy metals in the body (mercury, aluminum, arsenic, lead) often affects brain health, the way brain works, inducing various manifestations.

Patients who come for a nutrition consultation had to mention, in the anamnesis stage, aspects related to the general condition, current symptoms, medical history, describe their dietary profile and behavior, personal goals. Frequently, both among children and adults, there is a state of exhaustion, a lack of concentration, attention deficit on various activities and at certain times of day, nervousness, irritability, a state of devitalization even from the moment of awakening, which can be maintained throughout the day and sometimes gets worse after eating certain foods.

Overweight and even obesity are present in most patients, the main objective in our collaboration being in the first stage weight loss, the adoption of a balanced lifestyle with a varied diet. The most common symptoms and conditions encountered in patients who have food imbalances are associated with brain damage, weight problems, cardiovascular diseases, sleep disorders, development of nervous tics (present especially in the face), muscle pain (independently of physical effort), change in visual acuity.

We often talk about performance indicators, various activities that we carry out gradually, we impose ourselves a daily rhythm, a perfect functioning, but all these have an impact on our health, stress being the tacit killing of each of us and the one that directly influences our eating behavior and also the road from potential to performance. We have an

individual potential, but growth and development are conditioned by our lifestyle (nutrition, hydration, observance of day-night circadian rhythm, quality of sleep and air, physical activity, human relationships). Performance comes from the plate, and health is built by positioning ourselves correctly on the path of balance, temperance and variety.

An imbalanced diet leads to a state of devitalization, lack of energy, chronic fatigue syndrome, weight gain, the appearance of various symptoms or health disorders, cravings, especially from food with inflammatory role that induce addictions. Apart from these personally controllable food imbalances, we are witnessing human exposure to high levels of chemicals, heavy metals, genetically modified supplies, industrial food processing, all of this producing various health problems.

If we talk about performance, it is necessary to understand how the brain and the neural structures work. The most important role of the nervous system is to control the various activities of the body, including physical and intellectual performance. The “bricks” that make up both the brain and the other structures of our body are taken from the food we eat. If they are missing due to poor diet, the individual potential of each of us cannot be manifested and the result is low performance. The brain works on essential fatty acids, in an optimal ratio of omega 6: omega 3 and carbohydrates. Their sources are food and therefore it is very important that daily meals provide the necessary intake for proper functioning [16].

Proper hydration, rational nutrition, physical activity are factors that favor our efficiency at work and our physical and emotional availability at home within the family.

According to the latest studies, the incidence of brain disorders is increasing in both children and adults. One in eight seniors develops Alzheimer’s disease and one in eight children is diagnosed with imbalances in brain development, including autism, ADHD, and ADD [17-19]. It is estimated that there are 24 million cases of dementia worldwide and the number will double earlier than 20 years [20].

Anxiety, learning disabilities, lack of focus, depression, memory impairment, sleep disorders are more present in recent years, mostly at people who do not provide daily food for the brain (omega 3) and the result is that the brain suffers a continuous degradation, manifested by different symptoms [21]. In the United States, the most common drugs recommended by specialists are antidepressants [22]. Indeed, there are cases when depression occurs due to emotional problems, but most of the time, the health of the brain is affected.

OBJECTIVES

The objectives of the study relate to the diagnosis, monitoring and treatment of symptoms associated with the presence of heavy metals (mercury, aluminum, arsenic), omega 3 deficiency, and the increase of the omega 6: omega 3 ratio.

The correlation between the presence of heavy metals with potential for intoxication, the increase in the ratio of omega 6: omega 3, the decrease in the concentration of omega 3 and their impact on health were studied.

MATERIALS AND METHODS

In a retrospective study, a group of 77 patients that came to Nutribalance Clinic, between September 2017 and December 2019, showing reduced concentration capacity, attention deficit, sleep disorders, behavioral changes (including food), muscle pain, overweight or obesity, changes in visual acuity, was analyzed. They were later diagnosed with heavy metal poisoning, omega 3 deficiency, and high omega 6 concentrations.

Each patient was explained the methodology of the study and the benefits of a personalized, complex protocol, developed by an interdisciplinary team, starting from the individual results to the investigations we made, avoiding the use of standard treatment schemes. Each patient agreed to be part of this study.

All procedures concerning human subjects were carried out in accordance with the guidelines set out in the Helsinki Declaration (October 2013).

The current study was conducted considering at least two aspects: the presence of symptoms similar to metal poisoning and the lack of omega 3 in a large number of patients, without knowing the trigger, treating only superficial symptoms. Proper diagnosis, based on the symptoms presented by each patient can represent a chance at a quality life for each subject.

In this study, the diagnosis of patients was carried out on the basis of inclusion and exclusion criteria that have been designed to achieve a homogeneous batch of patients. The inclusion criteria are represented by the presence of at least one toxic metal with values exceeding the upper limit of the reference range, omega 3 deficiency, high values of the omega 6: omega 3 ratio, lack of dietary supplements/allopathic treatments, signing of consent. The exclusion criteria from the study were: depression treated with allopathic treatments, values within normal limits for the tested parameters (heavy metals, omega 3, omega 6:omega 3 ratio), conditions affecting life expectancy, previous stroke, patients with limited cooperation or limited legal capacity.

The initial assessment included anamnesis about medical history, demographics, risk factors, lifestyle. In the next stage of the assessment, a complete set of blood tests was collected for all subjects, the full toxic metal profile, the omega 3 concentration, the omega 6: omega 3 ratio being of high interest. Thus, the demographic parameters of patients, clinical and biological characteristics were taken into account. On demography were analyzed: gender, age, rural or urban provenience (very important in the elaboration of the daily food plan), field of activity, average monthly incomes, the number of working hours during a week.

The applied research method is statistical, with independent variables, quantitatively measured (laboratory analyzes) and dependent (observable, physically characterized). The obtained data were noted into specific databases using Microsoft Office Excel 2019, and the statistical analysis was elaborated with Python. Thus, with the help of descriptive data, the obtained values could be interpreted, according to the form of the distribution. The instruments used were Pandas, Numpy, Scipy (for data import, data processing, statistical tests running), but also Matplotlib, Seaborn (for generating graphics). The study's research obtained the opinion of the Ethics Committee of the Nutribalance Nutrition Cabinet, Bucharest, Romania no. 1/31 October 2019, being allowed to carry out this retrospective observational study.

OUTCOMES

The study included a sample of 77 patients - 40 men and 37 women - aged 13 to 69 years, with a period of 120 days of monitoring, during which each subject in the study group followed a personalized diet and a dietary supplements program, adapted to the medical analyzes (mercury, aluminum, arsenic, omega 3, omega 6:omega 3 ratio). At the end of the period we refer to, namely 120 days, we assume that there will be a difference in terms of symptoms in subjects diagnosed with potentially intoxicated metals, as well as increases in omega 3, the decrease of omega-6:omega-3 ratio and the decrease of the amount of heavy metals in the blood, detected during the first stage of diagnosis.

Depending on the symptoms and the conditions described by each subject there were made the appropriate medical tests, with a particular focus on the results for omega 3, omega 6:omega 3 ratio, mercury, aluminum, arsenic.

There have been selected 77 subjects whose analyzes results exceeded the upper limit of the reference range for mercury, aluminum, arsenic, omega 6: omega 3 ratio and had omega 3 deficiencies. The symptoms, the specific conditions of the presence of these metals in each patient, the concentration of

omega 3, the ratio of omega 6: omega 3, possible sources of contamination with the identified metals, dietary behavior (risk factors and therapeutic foods) lifestyle were examined.

Specific symptoms are often the first indicators of contamination and they help identify the contaminated person. Symptoms that occur because of accumulation of toxic metals include reduced concentration capacity, deficit of attention, central nervous system disorders, kidney disease, liver disease, sleep disorders, emotional instability, depression, significant weight gain, cardiovascular disease, diabetes. It can be seen some common symptoms with omega 3 deficiency, an increase in the omega 6: omega 3 ratio, in which context we decided to study the correlation between the presence of metals with potential for intoxication (mercury, aluminum, arsenic), omega 3 deficiency and an increase in the omega 6: omega 3 ratio.

In this regard, we took into consideration: the sources of contamination, clinical manifestations generated by the presence of mercury, aluminum, arsenic.

Examination of patients with 1-3 metals identified at the blood level involves analyzing the dietary profile, the frequency of the main food groups, particularly tracking the excessive consumption of farmed fish or possibly contaminated food, but also the exposure to repeated vaccinations [23, 24], drinking water sources and cosmetics.

The initial analysis of the 77 subjects in the study group showed the presence of the following: attention deficit in 77 out of 77 subjects, reduced concentration capacity 77 out of 77 subjects, sleep disturbance in 77 of 77 subjects, cardiovascular disease in 21 out of 77 subjects, development of nervous tics in 62 out of 77 subjects, mood swings in 77 out of 77 subjects, muscle weakness in 77 out of 77 subjects, change in visual acuity in 77 out of 77 subjects.

It was identified that all 77 subjects were eating farmed fish (raw or cooked), which implies exposure to methyl-mercury, even if they had a different frequency in the weekly menu. The presence of amalgam fillings was found among 69 subjects in the selected group and symptoms specific to chronic fatigue syndrome were detected.

After individual assessments, we developed a personalized nutrition and dietary supplements program, for each patient, for a period of 120 days, a program that took into consideration the lifestyle of each subject.

The common element in this group of subjects was the dietary supplement protocol, which included: an omega -3 supplement with an increased concentration of DHA – 0, 15 ml/ kg body weight/ day.

Râciu clay was integrated into the daily plan, being used both internally (2 tablespoons of clay were

TABLE 1. Symptomatology before and after the personalized nutrition protocol

Symptoms	Before		After		Before (%)		After (%)	
	Yes	No	Yes	No	Yes	No	Yes	No
Predisposition to attention deficit	77	0	6	71	100%	0%	7,79%	92,21%
Reduce capacity to concentrate	77	0	6	71	100%	0%	7,79%	92,21%
Sleeping disorders	77	0	0	77	100%	0%	0%	100%
Cardiovascular problems	21	56	0	77	27,27%	72,73%	0%	100%
Development of nervous tics	62	15	1	76	80,27%	19,48%	1,3%	98,7%
Mood changes	77	0	0	77	100%	0%	0%	100%
Muscle weakness	77	0	0	77	100%	0%	0%	100%
Change in visual acuity	61	16	0	77	79,22%	20,78%	0%	100%

infused in 500 ml alkaline water during the night and the infusion was drunk before breakfast, including the remaining undissolved powder) and externally (daily foot baths in the evening, 2 hour after dinner, for 30 minutes, using 200 g Râciu clay and 5 l of warm water).

Daily protocol also included coriander essential oil (1 drop *3/day, sublingual), selenium (200 mcg/day), probiotic (1 capsule *3/day), as well as 3 weekly infusion treatments, with glutathione 600 mg/4 ml dissolved in 100 ml NaCl. They also had to do infrared sauna 3 times each week.

During the period of the study, the symptoms of each patient were monitored and a personalized plan of dietary supplements and nutrition was followed, avoiding the administration of additional treatment schemes.

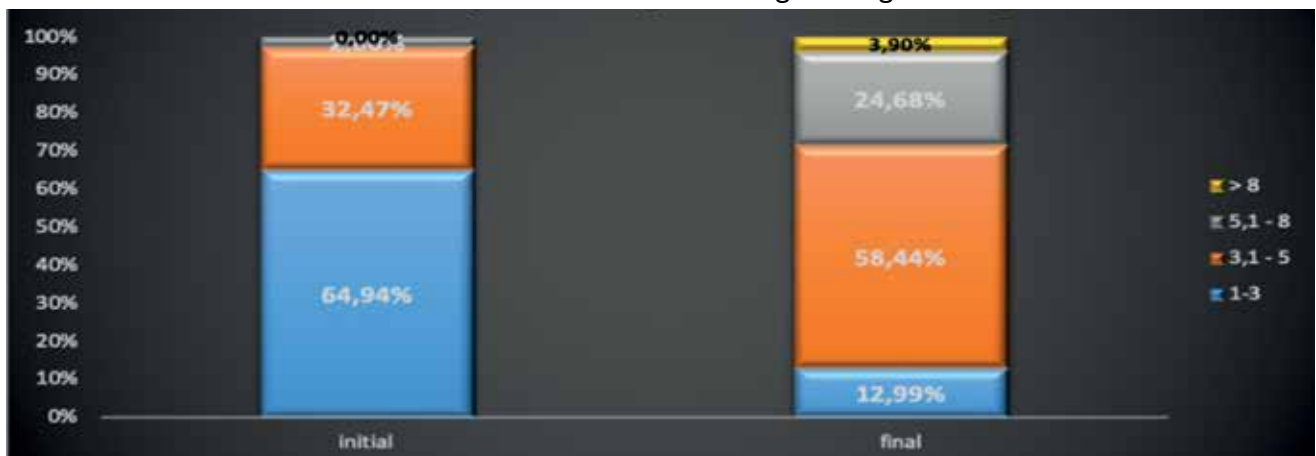
We made the reassessment of each patient at an interval of 14 days, during which we analyzed the evolution on the food profile defined as a favorable one in the management of the mentioned symptoms. At each reassessment, the food program was adapted according to the compatibility with each food or food group and according to the symptoms that have occur after the introduction of new aliments (for example: improving the ability to con-

centrate, reducing attention deficit, improving sleep quality, weight loss, reducing the frequency and intensity of nervous tics, reducing muscle pain).

After the 120-day monitoring period of each subject in the study group, we assessed the symptoms mentioned at the anamnesis stage, analyzes for mercury, aluminum, arsenic, omega 3, the omega 6: omega 3 ratio and we did a comparative analysis between the initial and final evaluation.

By analyzing the 77 participants in the study group, after the 120-day monitoring period we noticed the presence of the following: predisposition to attention deficit in 6 out of 77 subjects (an improvement is observed, but there are specific elements of attention deficit on different types of activities), reduced ability to focus in 6 out of 77 subjects (improvement from baseline is observed), sleeping disorders in 0 out of 77 subjects, cardiovascular disease in 0 out of 77, development of nervous tics in 1 out of 77 subjects, mood changes in 0 out of 77 subjects, muscle weakness in 0 out of 77 subjects, change in visual acuity in 0 out of 77 subjects (Table 1).

The symptoms of chronic fatigue in the 77 subjects also improved after excluding farmed fish from the diet.

Patient's distribution on omega 3 ranges**FIGURE 1.** Distribution of patients according to the results of the analyzes specific to the omega 3 concentration

Patient’s distribution on omega 6/omega 3 ranges

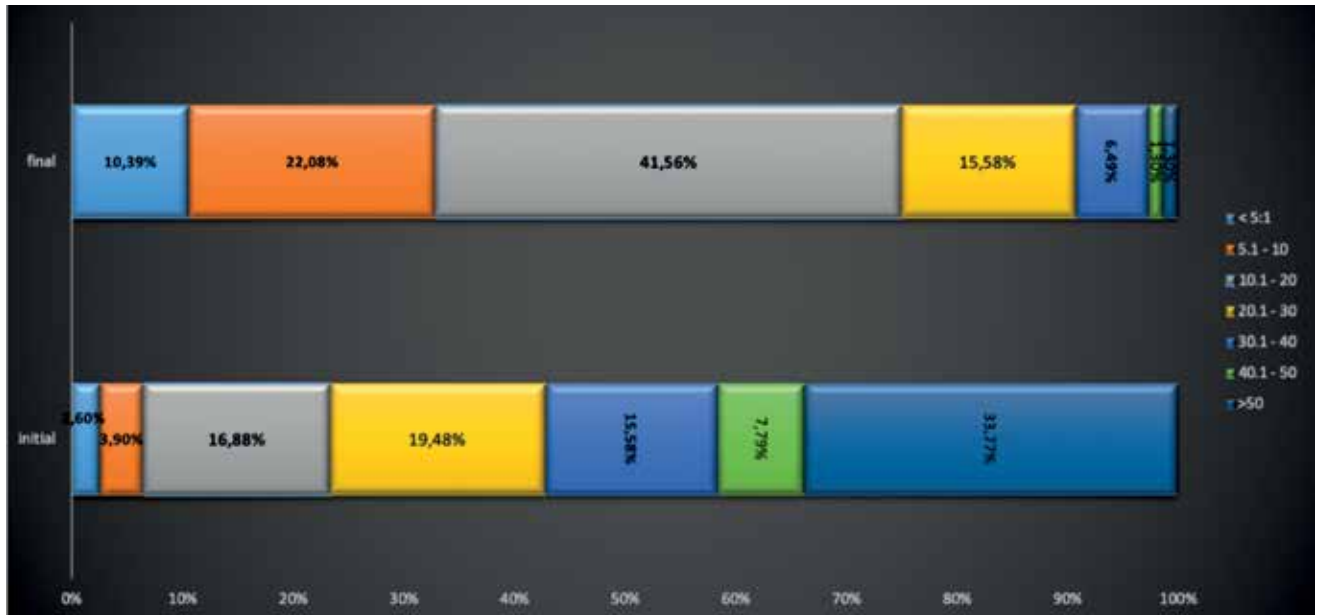


FIGURE 2. Distribution of patients according to the results of analyzes specific to the ratio of omega 6: omega 3

Patient’s distribution by BMI initial/final

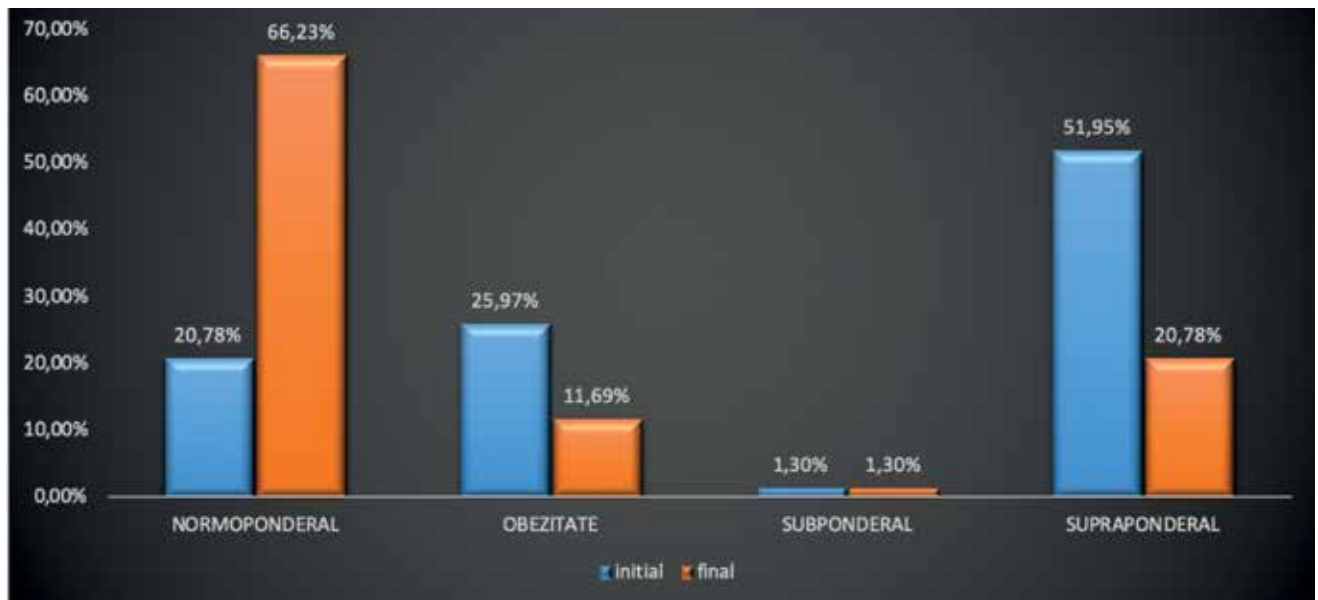


FIGURE 3. Distribution of patients by BMI before and after the implementation period of a personalized diet plan and dietary supplements

Although fish is well known for their significant intake of omega 3 our recommendation is to avoid it because the presence of mercury compensates for the benefits. Individual tolerability is the one that plays a decisive role in the frequency of certain food groups in the weekly menu, depending on the detoxification capacity, which may be limited, including at the DNA level.

Figure 1 shows the distribution of patients according to the results of the analyses specific to the omega 3 concentration. The results show a signifi-

cant decrease in the percentage of patients whose omega-3 concentrations were in the range [1-3] from 64.94% to 13% and a significant increase in the percentage of patients who had concentration values in the range [3,1-5].

Figure 2 shows the distribution of patients according to the results of analyzes specific to the ratio of omega 6: omega 3. From this figure we can see that the highest percentage of patients was the one with values higher than 50 of the initial omega 6: omega 3 ratio and after the period of the diet, this percentage decreased by 26 times.

From the results shown in Figure 1 and Figure 2 we can see that after the 120 days, the average omega 3 concentration increased from 2,71 to 4,59 and the result of the omega 6: omega 3 ratio decreased from 37,97 to 15,56. In terms of body mass index, the results that we obtained show that the average BMI was reduced from 28,46 to 24,16.

DISCUSSIONS

We have not identified neither in Romania nor worldwide such research regarding the correlation between the presence of metals with potential for intoxication, the deficiency of omega 3, the increase in the values of the omega 6: omega 3 ratio and the associated symptoms.

The specialized international research studies have been carried out on collateral topics with the theme of our study and they also demonstrates, as we assumed at the beginning of the study, that there is a correlation between the presence of potentially toxic metals, omega 3 deficiency and the associated symptoms.

A study addressing the correlation between low levels of omega 3 fatty acids and neuropsychiatric disorders is the review of Thomas Larrieu and Sophie Layé (2018) [21].

In this bibliographic study, the subject analyzed was related to the effects of food on mood and the relevance of omega-3 fatty acids in depression and anxiety.

The reference books indicated that low intake of omega-3 fatty acids may predispose certain individuals to depression and anxiety, and that the introduction of dietary supplements based on long-chain omega-3 fatty acids is an interesting strategy for preventing or treating depression and anxiety in some individuals.

This review reiterates the idea of the utility of omega-3 fatty acids in the daily diet as a beneficial tool for designing and testing new non-pharmacological strategies in the treatment of neuropsychiatric disorders such as mood-related diseases.

In terms of fighting heavy metal poisoning with omega 3 fatty acids, a rat study [25] supports the claim that omega 3 fatty acids could mitigate the adverse effects caused by heavy metal poisoning by improving the survival rates of the intestinal gland cell line (IEC 6).

The results also suggest that omega-3 fatty acids protected IEC 6 cells from damage caused by heavy metals, leading to the conclusion that supplementation of omega-3 fatty acids in the diet is a promising therapeutic practice to alleviate the damage caused by heavy metals.

Moreover, another study on cadmium neurotoxicity [26] showed that omega-3 fatty acids act as an

antioxidant with neuroprotective impact and treatment against cadmium toxicity and polyunsaturated fatty acids supplementation is more useful in co-treatment than in pre-treatment.

Other collateral studies on the effect of omega-3 fatty acids on health are reviewed in the bibliographic study conducted by Peter Van Dael [27]. It details aspects of the experts' recommendations regarding the diet enriched with omega 3 fatty acid supplements that can have a beneficial impact on certain health problems.

For example, expert recommendations generally support the beneficial effect of omega-3 fatty acids on cardiovascular health and recommend a daily intake of 500 mg in the form of DHA and EPA or 1-2 servings of fish per week. Other expert recommendations for treating depression include taking 200–300 mg/day; up to 1–2 g/day for major depressive disorder of omega-3 fatty acids. Other studies in this review support a beneficial role of omega-3 fatty acids in reducing the risk of premature birth, with a daily intake of 600-800 mg of DHA in pregnancy.

In conclusion, available scientific studies support the fact that dietary recommendations for omega 3 fatty acids should be established for the general population and for subjects with specific physiological conditions.

CONCLUSIONS

The presence of toxic metals (aluminum, mercury, arsenic) can induce a poor ability to concentrate, attention deficit on various types of activities, sleep disorders, cardiovascular diseases, muscle pain, development of nervous tics, mood changes, changes in visual acuity, changes in food behavior, with a tendency to consume foods with a high sugar content, refined carbohydrates, unhealthy fats, thus weight increases occur.

The analyzed subjects did not feel the need to introduce beneficial foods consistently, and healthy aliments were accepted only if they were imposed. The increase in the omega 6: omega 3 ratio and the high omega 3 deficiencies identified at the initial stage of testing reflect food imbalances.

The results of this study, namely the decrease in the omega 6:omega 3 ratio, the significant increases in omega 3 (identified at the final stage of testing) reflect the beneficial impact of diet and supplements used on health, as well as the reduction of the risks associated with baseline values. Increasing the concentration of omega 3, reducing the omega 6: omega 3 ratio can support the process of detoxification of heavy metals.

There is a directly proportional relationship between the decrease in concentrations of toxic metals (mercury, aluminum, arsenic) and the decrease in

values corresponding to the ratio of omega 6: omega 3. There is an inversely proportional relationship between decreased concentrations of toxic metals (mercury, aluminum, arsenic) and increased concentrations of omega 3.

This study claims that the process of chelating or detoxifying heavy metals is a complex one, requir-

ing the presence of a complementarity between dietary supplement therapy and nutritional one, avoiding the use of a single direction, as the results obtained are for a short or insignificant period of time.

Conflict of interest: none declared

Financial support: none declared

REFERENCES

- Mohammed AS, Kapri A, Goel R. Heavy Metal Pollution: Source, Impact, and Remedies. In: Khan M, Zaidi A, Goel R, Musarrat J. (eds) *Biomangement of Metal-Contaminated Soils*. Environmental Pollution. Dordrecht: Springer, 2011:1-28.
- Jan AT, Azam M, Siddiqui K et al. Heavy Metals and Human Health: Mechanistic Insight into Toxicity and Counter Defense System of Antioxidants. *Int. J. Mol. Sci.* 2015;16(12): 29592–29630.
- Kharrazian D. Why Isn't My Brain Working?: A Revolutionary Understanding of Brain Decline and Effective Strategies to Recover Your Brain's Health. Elephant Press, 2013.
- Simopoulos AP. Omega-3 fatty acids in inflammation and autoimmune diseases. *J Am Coll Nutr.* 2002;21(6):495-505.
- Gutiérrez-Mosquera H, Marrugo-Negrete J, Díez S et al. Mercury distribution in different environmental matrices in aquatic systems of abandoned gold mines, Western Colombia: Focus on human health. *J. Hazard. Mater.* 2021;15:124080.
- Chang LW. Neurotoxic effects of mercury – a review. *Environ. Res.* 1977;14(3):329-373.
- Bates N. Metallic and inorganic mercury poisoning. *Emerg Nurse.* 2003;11(1):25-31.
- Asano S, Eto K, Kurisaki E et al. Review article: acute inorganic mercury vapor inhalation poisoning. *Pathol. Int.* 2000;50(3):169-74.
- Krewski D, Yokel RA, Nieboer E et al. Human health risk assessment for aluminium, aluminium oxide, and aluminium hydroxide. *J Toxicol Environ Health B Crit Rev.* 2007;10(Suppl 1):1-269.
- Naujokas MF, Anderson B, Ahsan H et al. The broad scope of health effects from chronic arsenic exposure: update on a worldwide public health problem. *Environ. Health Perspect.* 2013;121(3):295-302.
- Ramos-Chávez LA, Rendón-López CR, Zepeda A et al. Neurological effects of inorganic arsenic exposure: altered cysteine/glutamate transport, NMDA expression and spatial memory impairment. *Front. Cell. Neurosci.* 2015;9:21.
- Sohn E. Contamination: The toxic side of rice. *Nature.* 2014; 514:S62-S63.
- Meharg AA. Arsenic in rice – understanding a new disaster for South-East Asia. *Trends Plant Sci.* 2004; 9(9):415-417.
- Yoshida T, Yamauchi H, Fan Sun G. Chronic health effects in people exposed to arsenic via the drinking water: dose-response relationships in review. *Toxicol. Appl. Pharmacol.* 2004; 198(3):243-252.
- Hopenhayn C. Arsenic in Drinking Water: Impact on Human Health. *Elements.* 2006; 2:103-107.
- Spencer SJ, Korosi A, Layé S et al. Food for thought: how nutrition impacts cognition and emotion. *NPJ Sci Food.* 2017;1:7.
- Rice C, Schendel D, Cunniff C, Doernberg N. Public health monitoring of developmental disabilities with a focus on the autism spectrum disorders. *Am J Med Genet C Semin Med Genet.* 2004;125C(1):22-27.
- Autism and Developmental Disabilities Monitoring Network Surveillance Year 2008 Principal Investigators; Centers for Disease Control and Prevention. Prevalence of autism spectrum disorders – Autism and Developmental Disabilities Monitoring Network, 14 sites, United States, 2008. *MMWR Surveill Summ.* 2012;61(3):1.
- Costello EJ, Mustillo S, Erkanli A et al. Prevalence and development of psychiatric disorders in childhood and adolescence. *Arch. Gen. Psychiatry.* 2003;60(8):837-844.
- Mayeux R, Stern Y. Epidemiology of Alzheimer disease. *Cold Spring Harb. Perspect. Med.* 2012;2(8):a006239.
- Larrieu T, Layé S. Food for Mood: Relevance of Nutritional Omega-3 Fatty Acids for Depression and Anxiety. *Front. Physiol.* 2018;9:1047.
- Kessler RC, Petukhova M, Sampson NA et al. Twelve-month and lifetime prevalence and lifetime morbid risk of anxiety and mood disorders in the United States. *Int J Methods Psychiatr Res.* 2012;21(3):169-184.
- Farina M, Aschner M, Rocha JB. Oxidative stress in MeHg-induced neurotoxicity. *Toxicol. Appl. Pharmacol.* 2011;256(3):405-17.
- Geier DA, King PG, Hooker BS et al. Thimerosal: clinical, epidemiologic and biochemical studies. *Clin. Chim. Acta.* 2015;444:212-220.
- Zhang F, Yu H, Ni X et al: ω -3 PUFAs improve cell viability and decrease oxidative damage of IEC-6 cells. *Biomed Rep.* 2016;4:635-641.
- Alnahdi H.S., Sharaf I.A. Possible prophylactic effect of omega-3 fatty acids on cadmium-induced neurotoxicity in rats' brains. *Environ. Sci. Pollut. Res.* 2019;26: 31254–31262.
- Van Dael P. Role of n-3 long-chain polyunsaturated fatty acids in human nutrition and health: review of recent studies and recommendations. *Nutr Res Pract.* 2021;15(2):137-159.