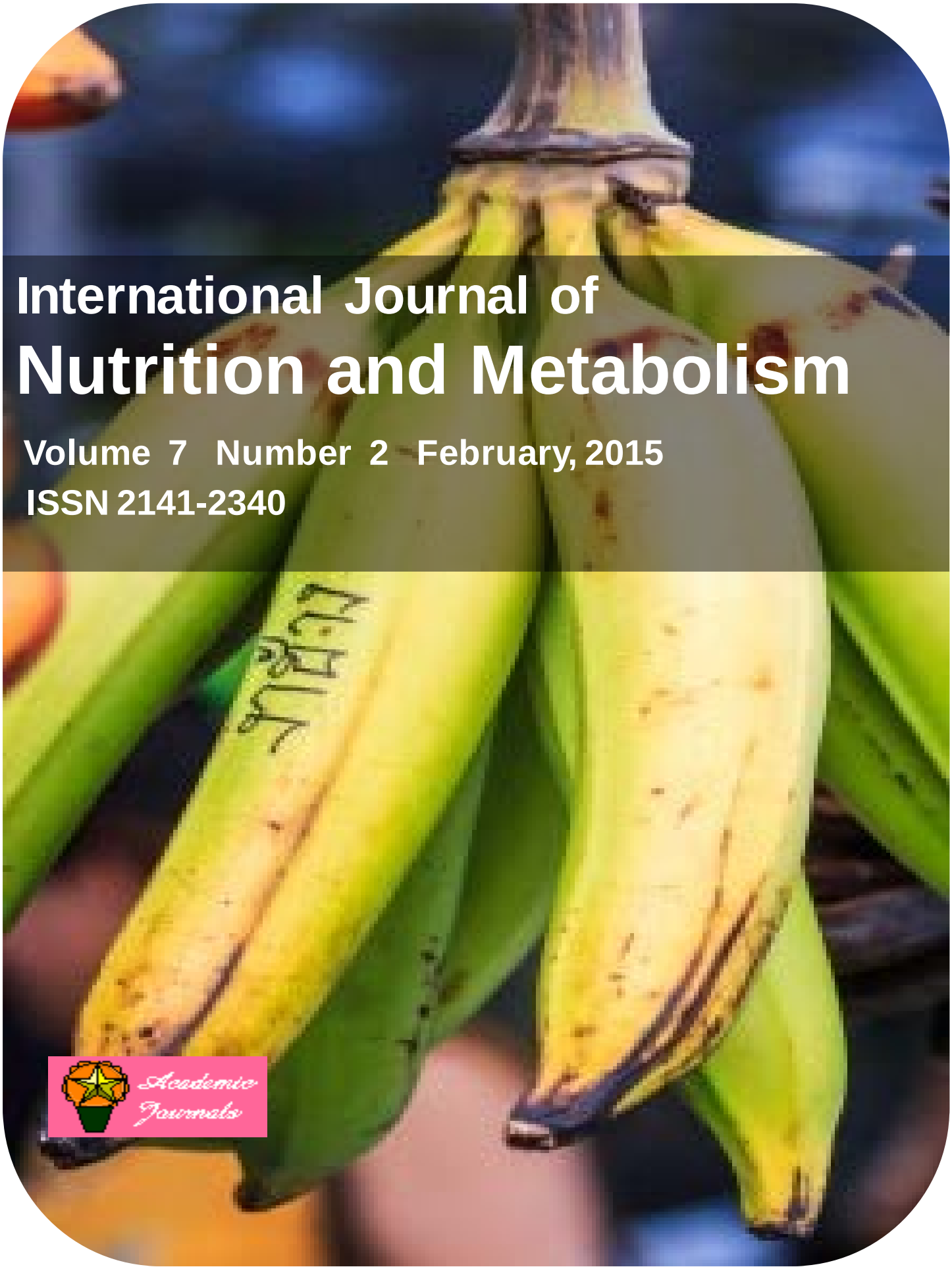

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Moran GJ, Amii RN, Abrahamian FM, Talan DA (2005). Methicillinresistant Staphylococcus aureus in community-acquired skin infections. Emerg. Infect. Dis. 11: 928-930.

Pitout JDD, Church DL, Gregson DB, Chow BL, McCracken M, Mulvey M, Laupland KB (2007). Molecular epidemiology of CTXM-producing Escherichia coli in the Calgary Health Region: emergence of CTX-M-15-producing isolates. Antimicrob. Agents Chemother. 51: 1281-1286.

Pelczar JR, Harley JP, Klein DA (1993). Microbiology: Concepts and Applications. McGraw-Hill Inc., New York, pp. 591-603.

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Short Communication

Triglyceride lowering by chromium picolinate in type 2 diabetic people

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In some studies in diabetic people, chromium picolinate supplementation has lowered readings for both plasma triglycerides and blood sugar. In the present study, relatively low dose supplementation (200 µg chromium) did not lower blood sugar readings, but did lower triglyceride values in people with the following characteristics: type 2 diabetes, moderately elevated blood sugar, and not using insulin therapy. These results support the supposition that chromium picolinate can affect triglyceride concentrations independently of effects on carbohydrate metabolism.

Key words: Chromium, diabetes, triglycerides.

INTRODUCTION

Chromium (Cr) is a trace element that can affect carbohydrate, lipid, and protein metabolism (Anderson, 1998a; Evans, 1989). Cr supplementation can affect blood glucose, total cholesterol, HDL and triglycerides in some circumstances (Abdollahi et al., 2013; Anderson et al., 1997; Cefalu and Hu, 2004; Heimbach and Anderson, 2005; Morris et al., 1999). This has led to classifying Cr as an essential nutrient (Anderson, 1998b), though others have suggested that Cr acts only as a drug in some unhealthy situations (Vincent, 2013). One argument against the essential nutrient role has been a lack of consistent positive effects of Cr supplementation in healthy people (Masharani et al., 2012). A counter argument states that Cr supplementation will not have such effects in all healthy people, but only in people with at least a moderate Cr deficiency. However, no accurate method for evaluating Cr status has been verified (DiSilvestro, 2005).

In people with diabetes, Cr supplementation has produced a decrease in fasting blood glucose values (Abdollahi et al., 2013; Bahijiri et al., 2000; Geohas et al., 2007; Pei et al., 2006; Rabinovitz et al., 2004). However, in other studies, Cr fails to affect blood glucose values (Abdollahi et al., 2013; Lee and Reasner, 1994; Preuss et al., 2000; Uusitupa et al., 1983). If Cr does indeed function as an essential nutrient, these variations could arise due to variations in the subjects' Cr status. If Cr acts solely as a drug, then the variations would depend on other factors. There have also been studies examining the effect of Cr on triglyceride levels in humans. A number of studies show a decrease in triglyceride values while also showing improved glucose control (Bahijiri et

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Table 1. Subject characteristics.

Parameter	Placebo	Chromium picolinate
Gender	6 M and 6 F	5 M and 5 F
Age	56 ± 3	56 ± 4
BMI	35 ± 1	31 ± 1
Pre glu	123 ± 8	133 ± 10
Post glu	147 ± 13	132 ± 7
Pre Tg	117 ± 7.6	121 ± 7.6
Post Tg	129 ± 9.6	106 ± 5.7

al., 2000; Geohas et al., 2007; Rabinovitz et al., 2004). These results reinforce an earlier proposed concept that Cr effects on lipid metabolism are mediated by effects on carbohydrate metabolism (Mertz, 1993). In contrast to this concept, in one human study, blood glucose readings are unchanged, but triglyceride values decrease (Lee and Reasner, 1994). Such a result suggests that Cr could affect lipid metabolism through either drug or nutritional mechanisms that go beyond modulation of carbohydrate metabolism. In this study lowering triglyceride but not glucose values, the study subjects had the following characteristics:

a) Mainly a US Hispanic population,
b) Diabetic people with fairly high fasting glucose values,
c) People using insulin injections and/or oral glucose-lowering drugs.

It needs to be determined if in other types of subjects, Cr supplementation can lower triglyceride concentrations without lowering glucose levels. Moreover, such additional studies should modify one protocol detail of the previous study. That study only compared post supplement values to post placebo values. New studies should also look at changes pre-to post-treatment with Cr or placebo. The present study did this for type 2 diabetic subjects who had the following characteristics:

a) Live in the central Ohio area,
b) Have just moderately elevated glucose levels,
c) Do not take insulin injections.

This new study examined the same dose, intervention time, and Cr complex as the previous work where Cr affected readings for triglycerides, but not blood sugar (Lee and Reasner, 1994).

MATERIALS AND METHODS

Subjects

The protocol was approved by The Ohio State University Human Subjects Biomedical Institutional Review Board. All subjects signed an Institutional Review Board (IRB) approved consent form. Adult males and non pregnant females were recruited from in and around Columbus, Ohio and Wooster/Canton, Ohio. Subjects fit the following inclusion criteria:

1. Age 40-60 years old,
2. Physician confirmed type 2 diabetes.
3. Glycosylated hemoglobin (HbA1c) greater than 7.0%,
4. Fasting plasma glucose between 7.6 and 10 mmol/L,
5. No use of insulin,
6. Body mass index (BMI) between 25 and 35,
7. Non-smoking,
8. No intake history of Cr supplementation within the last 3 months,
9. No major health problems other than type 2 diabetes.

Conformance to these criteria was based on answers to an eligibility questionnaire.

Research design

Subjects were randomly assigned to one of two groups:

1. Placebo (starch capsules).
2. Cr picolinate (200 µg Cr/day/1 capsule) supplied by Kelatron Corporation of Ogden, UT, USA.

Neither the subjects nor the person giving the supplements knew the group assignment. Subjects were instructed to maintain their previous dietary and exercise practices during participation. Subjects consumed the assigned product for 8 weeks and had blood samples taken before and after the supplementation period. Each sampling followed an overnight fast.

Blood analysis

Blood was collected by venipuncture into heparinized tubes. The tubes were centrifuged for approximately 10 min at 3000 rpm. Plasma was removed and stored at -70°C. Plasma glucose and triglycerides was assessed using the Roche Cobas C111 Clinical Chemistry Analyzer (Indianapolis, Indiana, USA).

RESULTS

Subject characteristics are noted in Table 1. Neither Cr supplementation nor placebo affected plasma glucose readings (Table 1). Cr supplementation, but not placebo, lowered plasma triglyceride values (Figure 1). The mean change in triglyceride values for the Cr group was significantly different than the change in the placebo group (Figure 2). In fact, in the placebo group, the mean value increased. Power values for the Cr matched samples, as well as the change comparison between groups, were over 0.99 for $p < 0.05$, two sided test. Plasma cholesterol values [total, high density lipoprotein (HDL) and low density lipoprotein (LDL)] were unchanged by either placebo or Cr (data not shown).

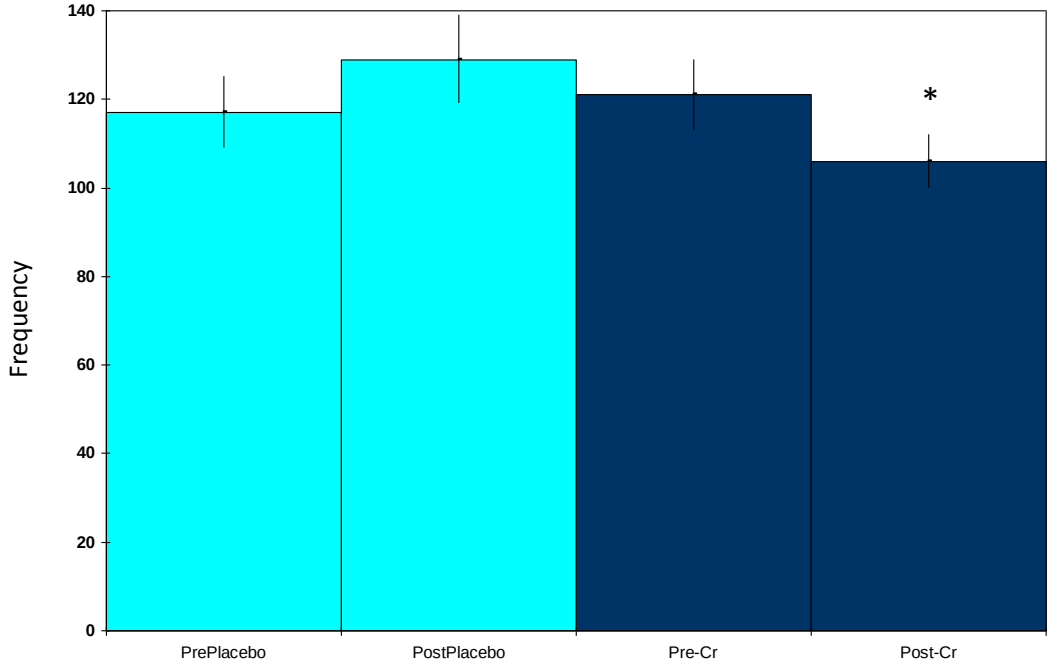

Figure 1. Plasma triglyceride values pre- and post-treatment (8 wk) with placebo or chromium picolinate (Cr). Data are mg/dl plasma ± SEM.
*Significantly different from pre-treatment values ($P < 0.05$, paired t test).

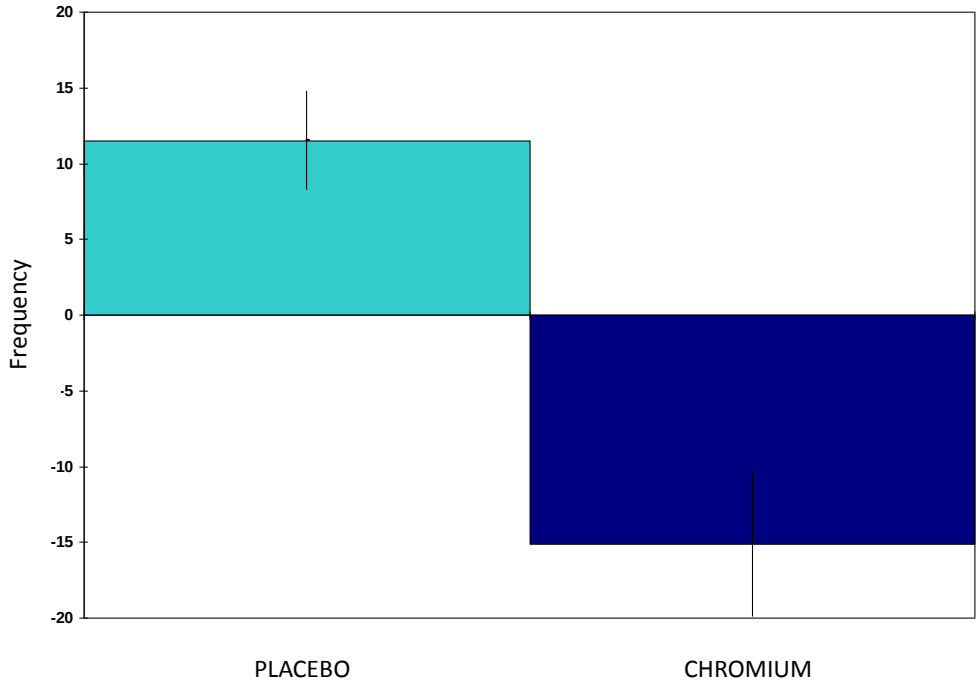

Figure 2. Change in plasma triglyceride values after placebo or chromium (Cr) supplementation. Data are the difference post- minus pre-treatment in mg/dl plasma ± SEM.
*Significantly different from placebo by unpaired t-test ($p = 0.01$).

DISCUSSION

A number of studies in diabetic subjects have reported that Cr supplementation improves glucose status and decreases plasma triglycerides (Bahijiri et al., 2000; Geohas et al., 2007; Rabinovitz et al., 2004). However, not all studies on Cr supplementation in diabetic subjects show an effect on glucose status. Most of these studies do not look at triglyceride readings. On the other hand, one study has shown a decrease in triglyceride values without a change in blood glucose values (Lee and Reasner, 1994). This study was done in a US Hispanic type 2 diabetic population with fairly high fasting glucose values. Some of the subjects in the study had enough problem with controlling blood sugar that they were using insulin injections to try to treat the problem. The present study demonstrated that in subjects with moderately elevated blood glucose, and who were not using insulin injections, Cr supplementation can lower triglyceride concentrations without lowering glucose levels. The subjects studied here were recruited from a typical USA mid-western diabetic population. Thus, the results of this study expand on the previous study. Taken together, the two studies indicate that Cr supplementation can impact lipid metabolism via mechanisms not directly related to carbohydrate metabolism.

Since plasma cholesterol concentrations were not changed by Cr, Cr would seem to affect this aspect of lipid metabolism via different mechanisms than the effects of triglyceride metabolism. Any Cr effects on cholesterol may be tied more directly to the effects on carbohydrate metabolism, which appeared to not occur in the present study. It is not yet certain why Cr supplementation impacts blood glucose related parameters in some studies but not others (DiSilvestro, 2005). Cr dose does not appear to be the only factor, though the dose used in the present study falls in the lower end of what has been used in diabetes studies (DiSilvestro, 2005). In the present study, the mean percent decrease in triglyceride values in the Cr picolinate group was not especially large (15%). However, in this study group, the mean initial triglyceride value was not extremely high. A larger decrease might occur when diabetics have a high starting blood triglyceride level. It is also possible that a higher Cr dose than used here might produce a bigger response.

It is not yet possible to determine whether the Cr dose used here worked by correcting some degree of deficiency or via a pharmacological effect. Unfortunately, a good means of assessing Cr status has not yet emerged (DiSilvestro, 2005). The present study's dose, 200 µg/day, is the upper end of what was established in 1989 as the estimated safe and adequate daily dietary intake range for Cr (National Research Council, Food and Nutrition Board, 1989). On the other hand, as noted earlier, this dose falls at the lowest end of what typically has been employed in diabetes studies (Di Silvestro, 2005). It is difficult to relate the current study's dose to a dietary Cr requirement for four reasons. One, no recommended dietary allowance has been established yet for healthy people (Institute of Medicine, Food and Nutrition Board, 2001). Two, the possibility that diabetes raises Cr needs has not been ruled in or out yet. Third, if some degree of Cr deficiency does commonly exist in people with type 2 diabetes, a corrective action may temporarily require giving a dose above the normal requirement. Four, Cr has been suggested to not even be an essential nutrient for humans (Vincent, 2013).

Lipidemia in diabetic populations presents a major risk for heart disease (Vijayaraghavan, 2010). Controlling triglyceride level with an inexpensive Cr supplement could decrease this risk. The current study showed that a Cr effect on triglycerides can occur without affecting blood glucose values, and without extreme conditions such as very high triglyceride readings or extremely poor glucose control.

ACKNOWLEDGEMENTS

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Conflict of interest

The authors declare that there are no conflicts of interest.

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Short Communication

Malnutrition in Albania, related problems and flour fortification as a solution

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Micronutrient deficiencies are caused mainly by an inadequate intake of vitamins and minerals, as a consequence of an unbalanced diet composed mostly of carbohydrates in the conditions of poverty, the inability to take a variety of nutrients, the lack of knowledge on the most appropriate feeding practices and the relatively high incidence of infectious diseases. From a public health perspective, the importance of these deficiencies depends on the magnitude of their impact on health, especially among pregnant women, infants and children, given the consequences in the development of the fetus, in the growth of the child, the resistance to infections and the work performance later during the adult life. According the Albanian Demographic Health Survey (ADHS) 2008 to 2009, conducted jointly by the Albanian Institute of Public Health (IPH) and the National Institute of Statistics (INSTAT), the nutrition status of the Albanian population indicates amongst many other characteristic, that anemia prevalence is highest among children living in mountainous areas, coastal areas and rural areas, respectively. In addition, 19% of women have anemia with the highest prevalence in breastfeeding women and those living in rural areas. Therefore this study aims at evaluating the cost-effective analysis of interventions targeting malnutrition in Albania and how to improve them especially through flour fortification.

Key words: Malnutrition, micronutrients, vitamins, minerals, deficiency, fortification, Albania.

INTRODUCTION

Malnutrition, including undernutrion and overnutrition, and the interconnected physical and mental development, is a worldwide concern, still more pronounced in the developing countries. As such, nutrition is indispensably the cornerstone of the development agenda both at local policy level and international aid and cooperation level.

The elaboration of the thesis for further actions is based on analysis of the public health situation in the country, available scientific evidence, expert opinions and recommendations supported and endorsed by World

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Health Organization (WHO), United Nations International Children Education Fund (UNICEF), Food and Agricultural Organization (FAO), Food Fortification Initiative (FFI), and a cost-effective analysis of the interventions targeting malnutrition in Albania. It reflects the position of the public health experts and is addressed to the food industry, the flour industry and all policymakers and decision-makers involved in designing and implementing a Programme of Flour Fortification in Albania (Jack, 2010; Oakley and Tulchinsky, 2010). The core recommendations stand on the type and the quantities of vitamins and minerals that should be added intentionally to the flour derived from wheat, in order to raise the intake of micronutrients and reduce the prevalence of micronutrient-related deficiencies in the population, considering it as a public health intervention (Jack, 2010; Stevens et al., 2011).

METHODOLOGY

Data from baseline assessments, follow-up assessments and evaluations within the framework of the National Project "Reducing malnutrition among children in Albania", supported jointly by United Nation Agencies (UNICEF, FAO, WHO), were used in the elaboration of the thesis. Following the findings of the Albanian Demographic Health Survey (ADHS) 2008 to 2009 and the public health profile of the country, indicating that residents in mountainous and rural areas suffer more than residents in other areas of the country from anemia, wasting, stunting, mental disorders, immunodeficiency, infectious diseases, late stages of various diseases, further exploring studies were conducted during 2010, to better understand the reasons and the situation of anemia in the rural and mountainous regions of Kukes and Shkodra and two suburban areas of Tirana (the capital city).

RESULTS

Iron deficiency anemia

1. This includes 30% of children less than five years of age had anemia. The anemia prevalence was higher among children under five years of age living in the suburban areas of Tirana.
2. 29% of school age children had anemia. The highest level of anemia among school children was found among children in the northwestern region of Shkodra (42.9 %).
3. 42.6% of women of reproductive age had anemia. The highest level of anemia among women of reproductive age was found in the northern region of Kukes (57.1%).

Neural tube defects, as a consequence of the lack or insufficiency of the intake of folic acid before and during the first weeks of pregnancy, are manifested as spina bifida, anencephaly, or encephalocele:

1. The incidence at country level: 1.07 cases per 1000 live births.
2. The incidence in Tirana: 2.1 cases per 1000 live births.
3. The proportional mortality from neural tube defects: 17% of the total deaths among population 0 to 1 years of age (Jack, 2010).

DISCUSSION

Taking into consideration the findings of the aforesaid studies and based on the WHO classification of the magnitude of anemia, considering anemia levels 5 to 19.9% as an intermediate public health problem, and anemia level 20 to 39.9% as a serious public health problem, a group of Albanian public health professionals and clinicians concluded that malnutrition related to micronutrient deficiencies should be considered a public health problem in Albania and that an action plan is paramount. According to the Document of Consensus of Copenhagen (2008), some of the most cost-effective measures for reducing malnutrition are:

1. Fortification of food with microelements such as iron, iodine, etc.
2. Supplements of micronutrient to children such as Vitamin A, zinc, etc.
3. Bio fortification.
4. Nutrition programs at community level.
5. Parasite control programs as school level.

A cost-effectiveness study conducted under the National Project "Reducing malnutrition among children in Albania" showed that the economic impact of malnutrition in the country accounts for 107 million USD or 1% of gross domestic product (GDP). Around 2/3 of the population could be protected from the effects of iron and folic acid deficiencies through the implementation of a programme of flour fortification. The cost of the fortifying premix is calculated at 2 USD for1 ton of flour (0.2 Albanian Lek*/kg) and the cost per person at 0.07 Albanian Lek/person/day.

Flour fortification is considered as of the most successful long term strategies for the elimination of iron, folic acid, and vitamin B12 deficiencies and their related health consequences, because of the following strategic advantages:

1. It is consumed by all social economic strata of the population, including low-income groups which are more likely of being at risk of malnutrition;
2. It is not costly and provides one of the most cost-effective means for covering large populations at risk;
3. It can be distributed throughout the country, accessible by target groups;
4. It is consumed daily and in constant quantities contributing to one's physiologic needs for micronutrients;
5. It can be processed in large quantities, allowing for the controlled fortification;

Table 1. Average level of the recommended micronutrients for the flour fortification based on the flour extraction rate, the composition of the fortification substance and the daily consumption per person**.**

Nutrient	Flour extraction Rate	Composition	The quantity of the nutrient to be added (ppm) based on the daily flour consumption per person (g/day)
			>300 g/day
Iron	High	NaFeEDTA	15
Folic acid	Low or high	Folic acid	1.0
Vitamin B12	Low or high	Cyancobalamin	0.008

6. It does not change the organoleptic qualities of flour, such as appearance, taste, color;
7. It is stable despite the minimal interaction with the fortification micronutrients, preserving the right concentration of nutrients following further processes and cooking;
8. It is safe because the low dose of micronutrients cannot lead to any accidental overdose of the fortification micronutrients;
9. It is socially acceptable because it doesn't require any change in the dietary habits;
10. It is sustainable because it is a market-based strategy.

Flour fortification is based on fundamental public health principles aiming at the effective and safe prevention of mineral and vitamin deficiencies within a population. The world experience tells us that 65 countries in the world have in place obligatory flour fortification legislation with at least two micronutrients: iron and folic acid. The selection of flour fortification micronutrients is based on the compromise between reasonable cost, fortificant bioavailability and the acceptance of any organoleptic changes, assuring the safety of the product.

The following recommendations focus on selected micronutrients whose intake is deficient by the Albanian population and that offer the possibility for inclusion in a national flour fortification programme (MOH-MDGIF-UN, 2011; John, 1998).

Iron

Iron is essential for the physical and mental health of the pregnant women and children as well as for the physical activity and the work productivity at all ages. The timely treatment of iron deficiency is associated with health improvements and a 20% increase of the work productivity at national level (WHO, 2009). There is solid scientific evidence on the daily-recommended supplementary quantity of iron that is associated with an improvement of the iron sufficiency at the population level. Based on the individual daily flour consumption, there are 4 regimens of flour fortification. Iron as NaFeEDTA is recommended for the fortification of the flour that is rich in phytates because it is 2 to 3 times more bioavailable compared to other iron compounds. It does not accelerate the process of the flour turning rancid if stored for a long time. Based on the consensus statement of the joint group of experts of WHO, FAO, UNICEF, Global Alliance for Improved Nutrition (GAIN), The Micronutrient Initiative (MI) and FFI and based on:

1. The average flour consumption rate in the Albanian population: 360 gram per person per day;
2. The flour extraction rate: high (about 70%);
3. The fortification formulation: NaFeEDTA.

The average dose of the supplemented iron is recommended at 15 ppm.

Folic acid

Folic acid is one of the most important micronutrients needed for the development of the human being. The intake of sufficient quantities of folic acid by pregnant women prior to conception reduces by 50% the number of neural tube defects at infants. Actually, around 22,000 neural tube defects are prevented through the flour fortification with folic acid. Based on the consensus statement of the joint group of experts of WHO, FAO, UNICEF, GAIN-MI and FFI, folic acid as foliate form is recommended for flour fortification and the average dose of the supplemented folic acid is 1.0 ppm.

Vitamin B12 (cobalamin)

Cereal does not contain vitamin B12, which is present only in animal products. Vitamin B12 deficiency is encountered at all ages in developing countries and mostly among the elderly population. The deficiency of vitamin B12 can lead to anemia, neurological disorders, cognitive disorders, negative pregnancy outcomes and damages of the bone mineralization among other consequences. Evidence shows that vitamin B12 deficiency exists in Europe and the supplementation in small quantities of it can prevent the deficiency. An obligatory flour fortification system in Europe can eliminate the vitamin B12 deficiency existence in the continent. Cyanocobalamin is the formulation recommended for vitamin B12 flour fortification and average dose of the supplemented vitamin B12 is 0.008 ppm. The following table (Table 1) represents a summary of the average level of the recommended micronutrients for flour

for flour fortification based on the flour extraction rate, the composition of the fortification substance and the daily consumption per person.

The type of flour proposed for fortification

Based on the Albania assessment of milling industry for the purpose of wheat, the average annual flour consumption in Albania is 460,000 tons (432,000 tons processed in the country and 27,000 tons imported). The principal types of wheat flour processed in the country are 00, 40, 45, 50, 60 and 70, which are the ones that are recommended for fortification (Oakley and Tulchinsky, 2010; WHO, 2009; Winkels et al., 2008).

Conclusion

The malnutrition of children and women at reproductive age in Albania, and the related effects on health, as a result of the insufficiency of micronutrients in the daily diet such as iron, folic acid and vitamin B12, is considered a serious public health problem in Albania. Flour fortification is one of the principal long-term strategies for reducing micronutrient deficiency at the population level, leading to subsequent health improvement. At the same time, this intervention provides a unique opportunity to the milling industry for expanding its market and increasing its profits, playing a key role to the improvement of the nutrition and health of the population.

Conflict of interest

The authors declare that there are no conflicts of interest.

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