Wiśniewska Patrycja, Czyżewska Izabela, Jarosz Piotr. The range of possible chromium III applications in medicine - the short review. Journal of Education, Health and Sport. 2020;10(8):286-290. eISSN 2391-8306. DOI http://dx.doi.org/10.12775/JEHS.2020.10.08.033
https://apcz.umk.pl/czasopisma/index.php/JEHS/article/view/JEHS.2020.10.08.033
https://zenodo.org/record/3992586

The journal has had 5 points in Ministry of Science and Higher Education parametric evaluation. § 8. 2) and § 12. 1. 2) 22.02.2019.

Received: 01.08.2020. Revised: 05.08.2020. Accepted: 20.08.2020.

The range of possible chromium III applications in medicine - the short review

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Abstract

Introduction: The key importance of chromium III in many physiological processes of human body, its influence on insulin regulation and glucose metabolism became an indicator to make an attempt to apply chromium III supplementation in disorders treatment. Mostly because diseases such as Alzheimer's diseases, type 2 diabetes or polycystic ovary syndrome are caused by disorders of this process.

Objective: The aim of this review was to present currently available knowledge on online database PubMed about an application, effectivity and the range of possible chromium III supplementation in medicine.

Abbreviated description of the state of knowledge: Knowledge on the subject of the function of chromium III is constantly widening. Up to the year 2014 chromium was thought to be the very necessary root responsible for appropriate functioning of human body. Nowadays, the essential role of chromium III is questionated. It is the result of the lack of sufficient manifestation of chromium deficiency in humans and animals. The recent clinical trials have been distinctly indicated that the impact of chromium III should be considered rather as a pharmacological activity than an essential trace element for humans.

Conclusions: The possible ways of chromium III supplementation in treatment of many marjory society diseases are still being searched. The recent clinical trials provided evidence both in favor and against the effectiveness and validity of chromium III supplementation.

Studies finished with success are very promising but there is still a need for more updated researches.

Key words: chromium supplementation; trace element; Alzheimer's diseases; type 2 diabetes; polycystic ovary syndrome

1. Introduction

Chromium (Cr) belongs to the transition metals group. It is found primarily in two of the most stable forms which have biological and environmental value: trivalent chromium (Cr III) and hexavalent chromium (Cr VI) [1].

Chromium III is involved in the energy metabolism, both in humans and animals. Its deficiency affects the evidence of normal glucose metabolism and lipids profile. It is an integral part of the GTF - proteine named as glucose tolerance factor. Cr influences some enzymes that regulate the synthesis of cholesterol [2].

Dietary Reference Intakes (DRI) developed by the Institute of Medicine of the National Academy of Sciences determines AI (adequate intake) of chromium for about 25 μg and 35 μg per day for women and men, respectively [3]. It was established in 2001 but in 2014 the European Food Safety Authority (EFSA) published a new updated disposition. EFSA reported that information connected with the thought that Cr III has an essential role in human physiology was nearly completely based on clinical results of patients on total parenteral nutrition. It was reported that Cr III supplementation constrained neurological and metabolic defects. Nevertheless, the symptoms of deficiency were not regarded in every patient. EFSA reported that attempts to create animal models of chromium deficiency have not provided any clear results. Due to the above EFSA considered that Cr III possibility could be an essential micronutrient for optimal human functioning, but on the other hand science has not convinced so far any clear proof of this [4]. It was emphasised in the newest researches and the scientists have been suggested that Cr should be categorised as a pharmacologically beneficial [5].

Objective

Conflicting available knowledge with a number of dietary supplements and sports nutrients including chromium salts and chelates which are accessible on the market, as well as, increasing society's attention about these products - what forced the authors of this review to investigate published on database PubMed a piece of information about chromium III application, an effectivity and the range of its possible supplementation in medicine.

2. The state of knowledge

2.1 Type 2 diabetes (T2D)

Type 2 diabetes (T2D) is the most common form of this disease. Patients with T2D accounts for above 90% of patients suffering from diabetes. T2D is characterised by a combination of increased hyperinsulinemia and relative insulin lack caused by pancreatic β-cell failure and insulin resistance in target area of body [6].

The activity form of chromium III in human body is an oligopeptide named low molecular weight chromium binding substance (LMWCr) also known as chromodulin. LMWCr is important in amplifying the insulin signaling effect, binding insulin to its receptor and stimulates the kinase activity of its receptor [7]. Chromium mobilizes the glucose transporter type 4 (GLUT4), to the plasma membrane in 3T3-L1 adipocytes. The increase of GLUT4 at the plasma membrane enhances the insulin-stimulated glucose transport [8]. Trivalent chromium is an essential trace metal necessary for the formation of glucose tolerance factor [9].

Yanni AE et al. in a randomized clinical trial, in which whole wheat bread (WWCrB) with chromium enriched yeast was supplemented, observed lower levels of glucose, insulin and glycated hemoglobin **(**HbA1c) and improved insulin resistance. The results of these studies also show that systolic blood pressure (SBP) and considerable reduction in body weight was noted. The scientists reported that WWCrB intake was not influenced on lipid profiles and markers of inflammation [10]. Silimary, a study carried out by Paiva AN. et al. showed that chromium picolinate supplementation on patients with poorly controlled type 2 diabetes had a positive effect on glycemic control and led to significantly lowered total cholesterol HDL-c and LDL-c without impact on the lipid profile [11].

However, results of examinations are not clear, double-blind, randomized clinical trial, conducted by Guimarães MM. et al. in which 56 patients with T2D divided into three groups (50µg, 200µg chromium nicotinate and placebo) were supplemented for 90 days with chromium nicotinate, shows that no beneficial effect in glucose homeostasis and anthropometry was observed [12].

Some studies showed a positive role of Cr supplementation on T2D [10,11] while other [12] evidence revealed that chromium had no beneficial effects. Reported results in this field still have not been clearly known.

2.2 Alzheimer's disease

Alzheimer's disease (AD) is a complex progressive neurodegenerative disease. AD is the main cause of dementia worldwide and is estimated up to 80% of all dementia diagnoses [13]. AD is characterized by amyloid plaques and neurofibrillary tangles. Dysfunction in amyloid precursor protein (APP) cleavage, production of the APP fragment beta-amyloid and hyperphosphorylated tau protein aggregation, plays a key role in the pathophysiology of Alzheimer’s diseases. This process leads to reduction in sympathetic strength, loss of synapses, what results in neurodegeneration [14].

About 80% of patients suffering from Alzheimer's disease are affected by type 2 diabetes mellitus (T2DM) or insulin resistance. Hyperinsulinemia and insulin resistance, which are two pathophysiological hallmarks of T2DM are also observed in patients with AD, and have an impact on development of cognitive dysfunction. It is relevant with an altered insulin pathway which may have an impact on deposition of beta-amyloid protein and phosphorylation of tau protein [15].

Intake medications that reduce insulin resistance has a beneficial effect on memory function of patients with cognitive impairment and Alzheimer's diseases in early stages. Krikorian R. et al. observed that chromium picolinate supplementation has a positive and preventive potential, it can improve cognitive inhibitory control and enhance cerebral function of a

person at risk of neurodegeneration [16]. A recent study conducted by Akhtar A et al. on rats showed that chromium picolinate (CrPic) application attenuated cognitive deficit. Scientists observed that neuroinflammation induced by streptozotocin (STZ) was significantly reduced and the levels of CRP, TNF and IL-6 were decreased. Insulin signaling was also improved. It was conducted that CrPic treatment improves memory, reduces neuroinflammation, oxidative stress, mitochondrial dysfunction, and normalises insulin signaling, and thereby reverses Alzheimer's diseases pathology [17].

2.3 Polycystic ovary syndrome

Polycystic ovary syndrome (PCOS) is the common endocrine disease in the group of premenopausal women. It has recently been estimated that depending on the criteria used and the population studied up to 10–15% of women in reproductive age are suffering from PCOS [18]. An array endocrine, metabolic and reproductive dysfunctions are ascribed with PCOS, which include anovulation, infertility, obesity, hyperandrogenism, hyperinsulinism and an increased risk of cardiovascular disease and type 2 diabetes [19]. The etiology of PCOS remains unknown, but insulin resistance (IR) and metabolic compilation are regarded as an important factor of development and persistence of PCOS [20].

Jamilian M. et al. showed that a 200 μg/day dose chromium picolinate supplementation for eight weeks resulted in a significant reduction in hirsutism, acne, and plasma malondialdehyde (MDA), serum high-sensitivity C-reactive protein (hs-CRP) and a significant increase in plasma total antioxidant capacity (TAC) [21]. Another study by Jamilian M. et al. examined an effect of chromium picolinate and carnitine co-supplementation (200 μg/day and 1000 mg/day, respectively) for 12 weeks to overweight patients with PCOS. Significantly beneficial effects on glycemic control, body weight, BMI, lipid profiles except HDL cholesterol levels, and gene expression associated with insulin (PPAR-γ) and lipid (LDLR) were observed [22] Ashoush S. et al. found an improvement in reduce IR and stimulate ovulation following chromium picolinate in PCOS patients [23].

However, findings are not consistent regarding PCOS improvement. Meta-analysis inducted six randomized clinical trials with 351 PCOS women conducted by Tang et al. indicates that chromium picolinate supplying has a positive effect in lowering insulin resistance but deleterious effect with regard to increasing total and free testosterone in these women. No significant improvement on hormone status, insulin metabolism and lipid profiles was observed [24].
The results are not sufficient for implementation of Cr III supplementation to the standard therapy in preventing and treating insulin resistance of women suffering from PCOS [25].

Summary:
The indications regarding to the influence on the insulin resistance occurred in type 2 diabetes, Alzheimer's diseases and polycystic ovary syndrome allowed to presume the efficacy of chromium supplementation in these diseases. However, the available evidence concerning use of chromium III remains ambiguous. The stage of current knowledge does not confirm completely the previous postulates. Due to detailed recognition of chromium supplementation effect on human physiology could apply it appropriately in medicine, and selection of diseases in which this treatment can be beneficial will be possible. Chromium III therapy is a promising method for more effective treatment some of the most common diseases occur in society. Beneficial effects of chromium supply have been demonstrated in some studies. Nonetheless, it is necessary to conduct future studies in this direction of

appropriate large sample size, for sufficient duration, and on a well-defined population of patients, who are most likely to benefit from chromium supplementation.

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