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Beneficial effects of oral chromium picolinate supplementation on glycemic control in patients with type 2 diabetes: A randomized clinical study

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ABSTRACT

Background: Chromium is an essential mineral that contributes to normal glucose function and lipid metabolism. This study evaluated the effect of chromium picolinate (CrPic) supplementation in patients with type 2 diabetes mellitus (T2DM).
Methods: A four month controlled, single blind, randomized trial was performed with 71 patients with poorly controlled (hemoglobin A1c [HbA1c] > 7%) T2DM divided into 2 groups: Control ($n = 39$, using placebo), and supplemented ($n = 32$, using 600 μg/day CrPic). All patients received nutritional guidance according to the American Diabetes Association (ADA), and kept using prescribed medications. Fasting and postprandial glucose, HbA1c, total cholesterol, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, triglycerides and serum ferritin were evaluated.
Results: CrPic supplementation significantly reduced the fasting glucose concentration (−31.0 mg/dL supplemented group; −14.0 mg/dL control group; $p < 0.05$, post- vs. pre-treatment, in each group) and postprandial glucose concentration (−37.0 mg/dL in the supplemented group; −11.5 mg/dL in the control group; $p < 0.05$). HbA1c values were also significantly reduced in both groups ($p < 0.001$, comparing post- vs. pre-treatment groups). Post-treatment HbA1c values in supplemented patients were significantly lower than those of control patients. HbA1c lowering in the supplemented group (−1.90), and in the control group (−1.00), was also significant, comparing pre- and post-treatment values, for each group ($p < 0.001$ and $p < 0.05$, respectively). CrPic increased serum chromium concentrations ($p < 0.001$), when comparing the supplemented group before and after supplementation. No significant difference in lipid profile was observed in the supplemented group; however, total cholesterol, HDL-c and LDL-c were significantly lowered, comparing pre- and post-treatment period, in the control group ($p < 0.05$).

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Conclusions: CrPic supplementation had a beneficial effect on glycemic control in patients with poorly controlled T2DM, without affecting the lipid profile. Additional studies are necessary to investigate the effect of long-term CrPic supplementation.

1. Introduction

Diabetes mellitus (DM) is a chronic metabolic disease, resulting from progressive defects in insulin secretion and/or peripheral insulin resistance. The prevalence of poorly controlled diabetes remains a growing challenge, and is associated with micro- and macro-vascular alterations that may lead to severe complications and the development of co-morbidities. Thus, DM is considered a public health problem [1]. Even with advances in therapeutic interventions and lifestyle changes, the number of patients that cannot maintain glycemic control remains large [2].

In spite of controversies [3], chromium (Cr) supplementation has been studied as a co-adjuvant diabetes therapy, due to its role in glucose/insulin metabolism [4]. Chromium may enhance insulin sensitivity by activating intracellular signaling pathways involved in glucose transporter 4 (GLUT4) translocation, consequently increasing glucose and amino acids transport [5,6]. Furthermore, Cr interferes with cholesterol metabolism, most likely by inhibiting the hepatic enzyme 3-hydroxy-3-methyl-glutaryl-CoA reductase [7]. Additionally, data suggests that patients with type 2 diabetes mellitus (T2DM) exhibited alterations in Cr metabolism, most likely due to increased Cr excretion as a result of glucose/insulin homeostasis imbalance [6,8,9].

Based on these data, administration of Cr as a supplement could improve glycemic parameters in patients with T2DM. Although the World Health Organization (WHO) [10] reported that doses from 125 to 200 μg/d might improve glucose and lipid control, Anderson [8] found that patients with T2DM showed a better response when receiving 400–600 μg Cr/d.

Thus, the present study investigated the effect of oral Cr picolinate (CrPic) supplementation (600 μg/d) in patients with poorly controlled T2DM (hemoglobin A1c [HbA1c] ≥ 7%).

2. Subjects and methods

2.1. Study population

Seventy-one patients participated in this study (Brazilian Clinical Trials Registry – ReBEC, Universal Trial Number 79nxr8). All participants (male and female) were adults diagnosed with T2DM, at the Clinical Endocrinology and Metabolic Diseases at University Hospital Onofre Lopes (HUOL), Federal University of Rio Grande do Norte (UFRN), Natal-RN, Brazil.

Inclusion criteria were: T2DM diagnosis (according to American Diabetes Association, 2011) [11], hemoglobin A1c (HbA1c) ≥ 7% (characterization of poorly controlled diabetes, according to the goals for good glycemic control suggested by the ADA) [11], age from 30 to 70 years, and no use of Cr supplements within the 4 months prior to the study. Exclusion criteria included: patients with T2DM undergoing insulin treatment; type 1 DM (T1DM) diagnosis; pregnant or lactating women; diagnosis of anemia, nephropathy, cancer, steatohepatitis, infection, or other endocrinopathies (Cushing's syndrome, acromegaly, active hyperthyroidism and hypothyroidism); and patients undergoing corticosteroid therapy.

Approval from the Research Ethics Committee at University Hospital Onofre Lopes (HUOL) (Protocol number: 507/10) was obtained prior to the study. After being informed about the aims and procedures of the study, all the participants provided written informed consent.

2.2. Study design

The study was a single blind, controlled, and randomized clinical trial. Sample size was calculated considering the difference to be detected in triglycerides (2 mg/dL), the parameter that presented the lower difference between the groups, with a standard deviation difference of 3 mg/dL. The power of the test was 80% and the significance level was 5%. Thus, at least a total of 70 patients should have been enrolled (distributed in 2 groups: supplemented and control) [12].

Oral anti-diabetic drugs (OADs) were administered during the supplemention period. The enrollment and procedures occurred from November 2011 to May 2013.

Selections using the medical records for patients scheduled that day were performed to evaluate the inclusion and exclusion criteria. If they met the criteria, clinical and nutritional evaluations, as well as blood analyses, were performed. The patients returned to the clinic for the analysis of the results and, if they met all the research protocol requirements, they were included in the study.

Next, randomization was performed. Each patient chose an unidentified envelope containing the type of treatment, placebo or CrPic. The patient received a bottle with the number of capsules required for the first 30 days of treatment (60 capsules/bottle), and a dietary plan (individually calculated, according to ADA (2011) [11] recommendations). The patients returned to the clinic after 30, 60, and 90 days for evaluation of possible treatment adverse effects and to receive another bottle of supplement or placebo in each time point (each patient received 4 bottles of capsules and took a total of 240 capsules at the end of the 120 days). In the case of any complications, a new clinical evaluation by an endocrinologist was performed. After 120 days of treatment, another nutritional evaluation and a blood collection was performed to determine laboratory parameters.

2.3. Nutritional supplementation

The CrPic supplement and placebo capsules were manufactured at the pharmacy *Companhia da Fórmula* (Natal-RN, Brazil). Each capsule consumed by the supplemented group contained 300 μg CrPic (HarikaDrugs, Telangana, India, lot CHP/004/08/2015) and 120 mg excipient (90 mg lactose [Galena Química Farmacêutica Ltda., Campinas-SP, Brazil]; 23.5 mg microcrystalline cellulose [Pharma Nostra Comercial Ltda., Rio de Janeiro-RJ, Brazil]; 1.2 mg aerosil [Gemini Indústria de Insumos Farmacêuticos Ltda., Anápolis-GO, Brazil]; and 0.5 magnesium stearate [SM Empreendimentos Farmacêuticos, São Paulo-SP, Brazil]). The capsules consumed by the control group contained 120 mg of the excipient. Both treatment capsules were identical in color, size, and shape.

The patients received a bottle with 60 capsules, a quantity sufficient for 30 days of treatment, and were directed to take one capsule twice a day, one after breakfast and another after dinner, for a total 600 μg CrPic/day. This dosage was established according to the literature that revealed doses up 1000 μg CrPic/day have no negative effects on patients [13]. Moreover, a pilot study with a dif-