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A META-ANALYSIS OF CHROMIUM PICOLINATE SUPPLEMENTATION AND EFFICACY IN TYPE II DIABETES

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ABSTRACT

Chromium is an essential mineral for carbohydrate and lipid metabolism. Results of previous systematic reviews and meta-analyses of chromium supplementation and metabolic profiles in diabetes have been inconsistent. The present study conducted a systematic review and meta-analysis to assess effects on metabolic profiles and safety in diabetes mellitus. Clinical trials were identified through MEDLINE, Google scholar, MeSH, Medscape, www.Clinicaltrial.gov from 1990 to 2015. Historical search of reference lists of related articles was conducted. Studies were included if they were (i) randomized controlled trials (ii) reported HbA1c or fasting plasma glucose and (iii) at least 3-8 weeks. No language restriction was imposed. Treatment effect was estimated with mean difference and odds ratio, respectively. Fourteen randomized controlled trials met inclusion criteria. Chromium picolinate significantly improved glycemic control (mean difference for HbA1c-0.60%, 95% CI-1.06, 0.15, P=0.002, mean difference for FPG-0.25 mmol/L, 95% CI -0.52, 0.02, P=0.004). In particular, chromium mono therapy significantly reduced triglycerides and increased HDL-C levels. Available evidences suggest favorable effect of chromium supplementation on glycemic control in diabetic patient. In addition, it improves triglycerides and HDL-C levels.

KEYWORDS: Chromium; diabetes mellitus; glycemic control; meta-analysis; lipid profiles.

INTRODUCTION

Epidemic of diabetes in Kingdom of Saudi Arabia and rest of World continues to grow rapidly. About 19% of populations in kingdom are suffering from this disease. Most patients begin treatment with diet and exercise.[1] Patients require combinations of anti-diabetic drugs to control glycemic level. However, their use is limited by their tolerability and safety. Chromium is an essential element for carbohydrate and lipid metabolism.[2] Food rich in chromium includes brewer's yeast, egg yolks, whole grain, high-bran cereals, meat, wine and beer.[3] Chromium deficiency has been reported to be associated with insulin resistance and diabetes.[4] Studies shows conflicting results. Patal et al., concluded in their meta-analysis of trials of chromium picolinate (CP) improved fasting plasma glucose level in diabetes mellitus (DM).[5], Since then, a number of clinical trials of chromium have emerged on its use both as mono supplementation and in combination with other micronutrients.[6-9] We performed a systematic review and meta-analysis in an attempt to establish effects on metabolic profiles of CP in diabetes.

METHODS

Search Plan: Reports of CP supplementation in diabetes were searched through MEDLINE, Google scholar, Cochrane, Medscape, www.Clinicaltrial.gov from 1990 to March 2015. Historical search of reference lists of related articles was undertaken with no language restriction. Eligible studies were randomized controlled trials of CP supplement intake of ≥3 months among type 2 diabetes mellitus patients. Primary outcome of interest were HbA1c and FPG. Secondary outcomes were lipid levels (total cholesterol (TC), triglyceride, and LDL-C and HDL-C) and adverse events. Treatment effect was estimated with mean difference in final values of outcome measure between treatment and placebo group. Pooled mean difference and estimated 95% confidence interval were calculated using inverse variance-weighted method.[10] Random effects model was used to combine results of individual studies when chi-square test for heterogeneity was significant at level of 0.1[11] or else fixed effects model was used.[10] Statistical analysis was undertaken with Review Manager (RevMan) program version 5.3 (Cochrane Collaboration, UK). Significant level was $P < 0.05$. Publication bias was assessed for primary outcomes using funnel plot.[12]

RESULTS

We initially identified 273 reports. 240 reports were excluded because they were not randomized-controlled trials. Three trials identified were further excluded as results were not available. Remaining 33 reports were randomized placebo-controlled trials. Of these, four trials[12-13], were excluded due to duplicate reports. One

trial was excluded due to incomplete data. Twenty-five trials fulfilled inclusion criteria (Figure. 1). Of these, 23 studies assessed chromium as a single supplement.[8, 14] Of 28 studies, three included three-arm comparisons of two doses or formulations of chromium and placebo.[15, 16]

Two reports were multiple comparison trials comparing inorganic chromium chloride and brewer's yeast versus placebo.[17, 18] Their doses and duration varied from 150-1000 µg/day and 1.28-42 µg daily, 3-24 weeks respectively. One report assessed CP and chromium dinicocysteinate versus placebo.[6]

Meta-analysis of effects on glycemic control

HbA1c: Among 10 studies, chromium supplementation significantly reduced HbA1c by 0.6% (95% CI 1.06-0.15%; P=0.002) (Figure. 2).

FPG: From 14 studies, chromium supplementation significantly decreased FPG level by0.25mM (95% CI-0.522-0.02mM, P=0.07) (Figure. 3).

Meta-analysis of effects on lipid profiles

TC: Among 9 studies, Chromium single supplement lowered TC level by 0.22 mM (95%CI 0.45, 0.01) overall effect was insignificant (P=0.06) (Figure. 4).

Triglycerides: Seven studies of mono supplementation significantly lowered triglyceride level by 0.50 mM (95% CI-0.78--0.23mM, P=0.0004) (Figure. 5).

LDL-C: Of 5 studies, no significant difference in LDL-C was observed between chromium monotherapy and placebo (Mean difference -0.22 mM, 95% CI 0.55-0.11mM P=0.19) (Figure. 6).

HDL-C: Of 5 studies, no significant difference in HDL-C was observed between chromium monotherapy and placebo (Mean difference -0.03mM, 95% CI -0.06-0.11 mM, P=0.55) (Figure. 7).

DISCUSSION

Our pooled results showed that chromium supplementation improved glucose and triglycerides levels. Possible mechanisms include increase in insulin receptor number and binding. Chromium enhances membrane-associated GLUT-4[19-21], and phosphorylation of IRS proteins, Akt and PI3K.[22] It decreased protein tyrosine phosphates level leading to increased insulin sensitivity.[15] Chromium increases AMP-activated protein kinase activity, resulting in suppression of sterol regulatory element-binding protein-1. Chromium inhibits acetyl-CoA carboxylase, decreasing malonyl-CoA levels. CP improved chromium absorption[3, 23] and triglycerides level. HbA1c decreased by 0.6%. On sensitivity analysis, its weighted mean difference went down to 0.42%. Studies by Ghosh, Kleefstra and Vrtovec were homogenous.[16,24,26] Lowering of glycosylated hemoglobin, 1.9 % and 2.8 % were observed.[15] This effect was never duplicated in five other trials with lowering of HbA1c in range of 0 to 1.16%. Lowering of HbA1c by 0.54% and 1.16% respectively[16, 28] were noted and included newly diagnosed DM patients. Study by Albarracin's study design was modified and 21 patients were removed (entrance violations). Fasting blood sugar was significantly decreased with chromium supplementation. Study by Ghosh and Martin showed homogenous data.[24, 25] Study by Anderson showed most lowering of fasting blood sugar, not duplicated in other studies. Vrtovec included patients with controlled sugar by diet alone. Hence, we expect minimal treatment effect. Two hour postprandial blood sugar and fasting insulin were measured in two studies which were lowered. Data were heterogenous.[26]

Findings from this study on lipid profiles are in contrast with previous meta-analyses (no effect of chromium supplementation on lipid profiles in diabetics)[5, 27] while, ours include recent studies, suggesting chromium supplement may improve triglycerides and HDL-C levels. This can be explained as patients involved in individual trials had either borderline or high triglycerides level. Those participating in several trials had near optimal level of LDL-C and <200 mg/dL of TC. Baseline HDL-C level in nearly all trials ranged from 40-60 mg/dL. Concomitant therapy includes statins, fibrates, etc. Effect of chromium supplement on lipid profiles in diabetes needs to be further evaluated. American Diabetes Association has not endorsed chromium supplementation in diabetic patients. Chromium supplementation cannot be recommended.[29}, This was concluded by a meta-analysis published in 2002.[28, 29] However, recent data included in our meta-analysis showed that chromium supplementation may improve glycemic control and lipid profiles in diabetes as current anti-diabetic agents do not reach glycemic targets. These patients benefit from additional effect of chromium in reducing lipid levels.

First limitation of study was inclusion of significant heterogeneity which may be due to differences in extent of glycemic control, duration of diabetes, dose, form and supplementation of chromium. Second, this review included only published trials. Publication bias may be due to small study effect, association between treatment effects and sample size. False-positive results can be produced by small studies.

CONCLUSION

Chromium supplementation improves HbA1c and FPG in diabetes and does not increase risk of adverse events. Chromium may also improve triglycerides levels. Specifically diabetic patients with inadequate glycemic control may benefit from supplementation with chromium (dose above 200 µg -1000 µg). Data on combined supplementation are limited and well-powered high-quality, randomized controlled trials are warranted. Long-term benefit and its safety remain to be determined.

CONFLICT OF INTEREST
The author declares that there is no competing financial interest to disclose.

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