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ARTICLE

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# A Double-Blind, Randomized Pilot Trial of Chromium Picolinate for Overweight Individuals with Binge-Eating Disorder: Effects on Glucose Regulation

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**ABSTRACT.** Purpose: Chromium treatment has been shown to improve glucose regulation in some populations. The purpose of this study was to evaluate whether chromium picolinate (CrPic) supplementation improves glucose regulation in overweight individuals with binge-eating disorder (BED). Methods: In this double-blinded randomized pilot trial, participants ( $N = 24$ ) were randomized to high (HIGH, 1000 mcg/day,  $n = 8$ ) or moderate (MOD, 600 mcg/day,  $n = 9$ ) dose of CrPic or placebo (PL,  $n = 7$ ) for 6 months. Participants completed an oral glucose tolerance test (OGTT) at baseline, 3 months, and 6 months. Fixed effects models were used to estimate mean change in glucose area under the curve (AUC), insulin<sub>AUC</sub>, and insulin sensitivity index (ISI). Results: Results revealed a significant group and time interaction ( $p < 0.04$ ) for glucose<sub>AUC</sub>, with glucose<sub>AUC</sub> increasing significantly in the PL group ( $p < 0.02$ ) but decreasing significantly in the MOD group ( $p < 0.03$ ) at 6 months. Insulin<sub>AUC</sub> increased significantly over time (main effect,  $p < 0.02$ ), whereas ISI decreased significantly over time (main effect,  $p < 0.03$ ). Conclusion: As anticipated, a moderate dose of CrPic was associated with improved glycemic control, whereas PL was associated with decreased glycemic control. It was unexpected that the improved glycemic control seen in the MOD dose group was not seen in the HIGH dose group. However, although participants randomized to the HIGH dose group did not have improved glycemic control, they had better glycemic control than participants randomized to the PL group. These findings support the need for larger trials.

**KEYWORDS.** alternative medicine, binge-eating disorder, chromium, glucose

Binge-eating disorder (BED) is a psychiatric disorder that has recently been included in the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5)* as an independent eating disorder diagnosis for the first time (American Psychiatric Association 2013). BED is characterized by recurrent episodes of binge eating, defined as the consumption of an unusually large amount of food in a short period of time accompanied with a feeling of loss of control over eating, in the absence of inappropriate compensatory behaviors. BED is the most prevalent eating disorder, affecting 3.5% of adult women and 2% of adult men in the U.S. (Hudson et al., 2007). BED is highly comorbid with several psychiatric and medical conditions, including depression, metabolic syndrome (i.e., meeting at least three risk factors for atherosclerotic cardiovascular disease), and diabetes (Reichborn-Kjennerud et al., 2004, Yanovski et al., 1993, Bulik, Sullivan, & Kendler, 2002, Grilo, White, & Masheb, 2009). Notably, individuals with BED have significantly greater risk of developing components of the metabolic syndrome (e.g., abdominal obesity, dyslipidemia, hypertension, and abnormal glucose metabolism) independent of the risk of obesity alone and type 2 diabetes (T2DM) than individuals without BED (Hudson et al., 2010). Individuals with T2DM who also struggle with binge eating and/or depression have worse diabetes-related complications and poorer diabetes outcomes (Rotella et al., 2012, de Groot et al., 2001, Katon et al., 2009, Lin et al., 2010). For example, in one study of individuals with T2DM, eating pathology was associated with unsatisfactory glycemic control (Rotella et al., 2012).

Currently available options for BED treatment include several psychological and pharmacological interventions (Berkman et al., 2015; Brownley et al., 2016). Although some of these interventions are effective in helping patients reduce binge eating and its related psychological distress and physical consequences, not all patients respond adequately in terms of achieving binge abstinence and mood and metabolic stabilization. BED has historically been treated with medications such as citalopram, fluoxetine, fluvoxamine, imipramine, orlistat, sertraline, sibutramine, and more recently lisdexamfetamine (McElroy et al. 2015; McElroy et al., 2016). However, many patients drop out of pharmacological BED treatment due to medication side effects. Side effects associated with these medications in the treatment of BED include blurred vision, constipation, decreased libido, depression, dizziness, dry mouth, fatigue, headache, increased urinary frequency, insomnia, nausea, nervousness, sexual dysfunction, sedation, and somnolence (Brownley et al., 2007). Of concern, little information exists regarding the treatment and prevention of T2DM in individuals with BED. Although lifestyle interventions are effective, they are difficult to sustain (Korkiakangas, Alahuhta, & Laitinen, 2009). Drug treatments for T2DM have numerous side effects and limited durability. Addressing these unmet treatment needs in BED requires further investigation of novel interventions that ultimately help patients achieve binge eating abstinence and healthy weight and metabolic stabilization.

Chromium is an essential mineral that affects insulin and serotonin functioning and has the potential to also influence dopamine functioning (Davis & Vincent, 1997, McCarty, 1994), making it a plausible candidate for treatment of the complex patient with comorbid BED, depression, and T2DM. Prior studies have shown that chromium supplementation attenuates weight gain and visceral fat ac-

cumulation in patients with T2DM and improves insulin sensitivity and glycemic control in patients with T2DM, metabolic disorder, and polycystic ovary syndrome (Martin et al., 2006, Albarracin et al., 2008). In addition, chromium supplementation reduced carbohydrate cravings and appetite in patients with atypical depression (Docherty et al., 2005). The dose of chromium studied affects treatment efficacy, although the optimal dosage level is unknown (Broadhurst & Domenico, 2006). Building on these findings and our understanding of the physiological and psychological components of BED, the purpose of the present study was to evaluate whether a high or moderate dose of chromium supplementation improves glucose regulation in overweight individuals with BED. We hypothesized that high and moderate doses of chromium supplementation would be associated with improved glycemic control, as measured by their response to an oral glucose tolerance test (OGTT).

## ***METHODS***

### ***Participants***

A total of 220 potential participants self-referred to the study, of whom 43 passed screening and 41 met initial eligibility criteria (i.e., age between 18 and 60, DSM-IV criteria for BED, not pregnant or lactating, not currently engaged in other BED treatments or using chromium). Out of the 41 patients assessed, three declined to participate, and 10 met exclusion criteria. The remaining 28 eligible participants met DSM-IV criteria for BED and all other inclusion criteria. Inclusion and exclusion criteria are outlined in Table 1. This study was approved by the Institutional Review Board at the University of North Carolina at Chapel Hill.

### ***Procedure***

The 28 eligible participants underwent a 1-month placebo run-in, after which four participants were excluded due to placebo response. The remaining participants

**TABLE 1. Inclusion and exclusion criteria**

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#### Inclusion Criteria

- DSM-IV criteria for BED
- BMI between 25 and 45
- Age between 18 and 60

#### Exclusion Criteria

- Current suicidal or homicidal intent
  - Current psychiatric condition that requires acute care
  - Currently using any medication known to control glucose metabolism or insulin or to influence appetite or weight
  - Fasting glucose level was >126 mg
  - Current use of psychotropic medication was prohibited with the exception of stable monotherapy involving citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, or sertraline
  - Creatinine level >1.0 for women or >1.2 for men
  - Pregnant, planning on becoming pregnant during the study, or lactating
  - Currently engaged in other BED treatments
  - Current chromium use
- 

Notes: DSM-IV = Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition; BED = Binge-Eating Disorder.

were randomized to HIGH (1000 mcg/day,  $n = 8$ ) or MOD (600 mcg/day,  $n = 9$ ) dose of CrPic or PL ( $n = 7$ ) for 6 months. The CrPic doses were chosen in light of previous studies with non-BED populations. Specifically, a moderate dose of 600 mcg/day was chosen, as literature suggests that this level of dosage would be sufficient for improving fasting glucose, insulin binding, and reducing depressive symptoms and cravings (Anderson et al., 1987, Davidson et al., 2003, Docherty et al., 2005). A high dose of 1,000 mcg/day was chosen, as the literature suggests that this level of dosage is needed to prevent weight gain in subjects with T2DM (Martin et al., 2006). Adherence was assessed by asking participants to return all unused pills at each study visit.

Participants who were randomized into the study completed an OGTT at baseline, 3 months, and 6 months. Prior to each OGTT, participants fasted overnight. For the OGTT, a glucose solution standardized for body weight at 1.75 g/kg was consumed. Blood samples were obtained via an intravenous catheter at minute 0 (fasted) and then minutes 30, 60, 90, and 120 after ingestion of the glucose solution. Nineteen participants completed all study visits, with four participants withdrawing from the study due to personal reasons and one due to pregnancy.

Glucose was assayed with an Ortho Clinical Diagnostics Vitros 950 analyzer (UNC Hospitals). Insulin was measured using a competitive radioimmunoassay (Diagnostic Systems Labs, Webster, TX) at the UNC Endocrine Lab. Assay sensitivity was 1.3  $\mu$ IU/mL with a standard range of 5-300  $\mu$ U/mL. Glucose and insulin area under the curve (AUC) were calculated using the trapezoidal rule. ISI was evaluated by the formula:  $10,000 / \sqrt{(\text{fasting glucose} \times \text{fasting insulin} \times \text{mean glucose} \times \text{mean insulin})}$  (Matsuda & DeFronzo, 1999). Fixed effect models with a random intercept were used to estimate the mean change in  $\text{glucose}_{\text{AUC}}$ ,  $\text{insulin}_{\text{AUC}}$ , and ISI over the 3-month and 6-month active treatment period.

## RESULTS

### *Characteristics of the Sample*

Our sample included 24 randomized participants. The mean age of the sample was 36.6 (SD 10.6) years and their mean BMI was 34.2  $\text{kg/m}^2$  (SD 5.4). Most of the sample was white (87.5%) and female (83.8%). Participants exhibited a mild level of depression, as measured by the Quick Inventory of Depressive Symptomatology Self-Report [mean (SD) = 6.8 (3.8)] and were nondiabetic [mean (SD) fasting plasma glucose = 90.3 (9.4) mg/dL]. The mean HbA1c of the sample was 5.5. There were no statistically significant differences between the HIGH, MOD, and PL groups on any of these measures.

### *Outcomes*

Figures 1–3 depict the results of our study. The analyses revealed a statistically significant group and time interaction ( $p < 0.04$ ) for  $\text{glucose}_{\text{AUC}}$ , with a statistically significant increase in the PL group at 6 months ( $p < 0.02$ ), but a statistically significant decrease at 6 months in the MOD group ( $p < 0.03$ ). From baseline to 6 months,  $\text{glucose}_{\text{AUC}}$  increased 12.6% in the PL group, decreased 10.1% in the MOD dose group, and increased 6.5% in the HIGH dose group.  $\text{Insulin}_{\text{AUC}}$  increased

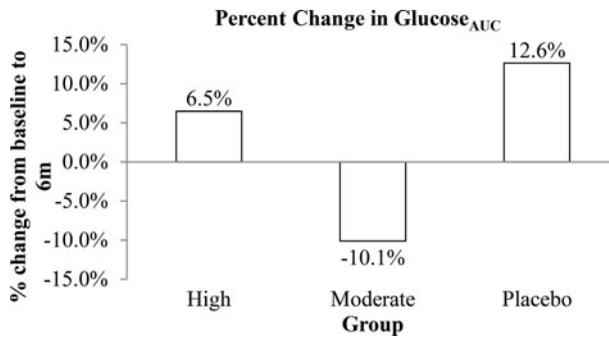


FIGURE 1. Percent change in glucose<sub>AUC</sub> from baseline to 6 months. AUC = area under the curve.

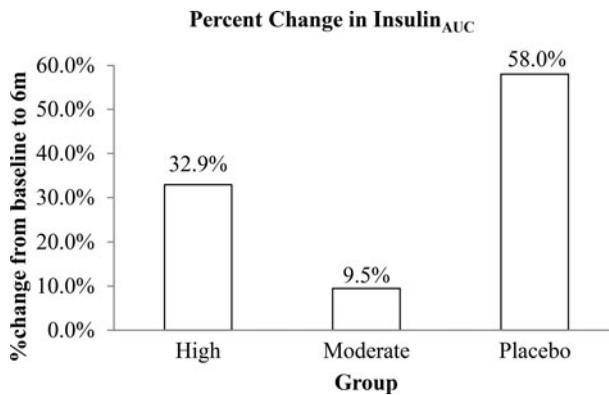


FIGURE 2. Percent change in insulin<sub>AUC</sub> from baseline to 6 months. AUC = area under the curve.

significantly over time (main effect,  $p < 0.02$ ). From baseline to 6 months, insulin<sub>AUC</sub> increased 58.0% in the PL group, increased 9.5% in the MOD dose group, and increased 32.9% in the HIGH dose group. ISI decreased significantly over time (main effect,  $p < 0.03$ ). From baseline to 6 months, ISI decreased 42.6% in the PL group, increased 13.6% in the MOD dose group, and decreased 24.1% in the HIGH dose group.

## DISCUSSION

The purpose of this study was to evaluate the effect of CrPic supplementation on glucose regulation in patients with BED. In this small sample, a moderate dose of CrPic supplementation was associated with improved glycemic control, whereas a PL dose was associated with decreased glycemic control. Specifically, glucose<sub>AUC</sub> decreased in the moderate dose group but increased in the placebo group. All participants and particularly those in the placebo group experienced an increase in insulin<sub>AUC</sub>. ISI decreased significantly over time, with the largest magnitude decrease occurring in the PL group.

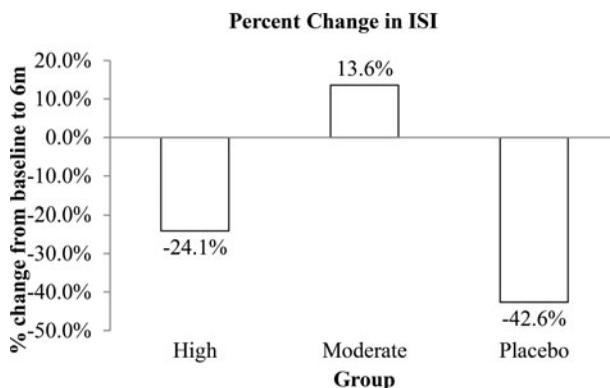


FIGURE 3. Percent change in ISI from baseline to six months. ISI = insulin sensitivity index.

Glucose<sub>AUC</sub> increased in the PL group but decreased in the MOD group over time. The significant decrease in the MOD group is consistent with other chromium supplementation studies (Martin et al., 2006). However, it was unexpected that the improved glycemic control seen in the MOD dose group was not seen in the HIGH dose group. One explanation for this is that the individuals in the moderate group could have experienced optimal improvement in glycemic control because they had the highest HbA1c levels to begin with, as previous research has shown that chromium provides the greatest benefits to individuals with higher HbA1c levels (Albarracin et al., 2008). Alternatively, the results could have occurred due to differences in binge frequency. The HIGH group had the highest number of binge episodes at baseline. Although the HIGH group experienced a reduction in binge frequency over the course of the trial, their number of binge episodes at the end of treatment were still not as low as that of the MOD group. Finally, it is possible that this unexpected finding occurred due to the limited statistical power of this study. Additional adequately powered studies are warranted to evaluate chromium supplementation for glycemic control in individuals with BED who are at increased risk of metabolic disease. However, it is important to note that the magnitude of increase was larger in the PL group than in the HIGH dose group.

Insulin<sub>AUC</sub> increased in all groups, with the largest magnitude increase occurring in the placebo group. The overall increase in insulin<sub>AUC</sub> was also found in another study evaluating chromium supplementation in individuals with T2DM (Martin et al., 2006). The particularly high increase in insulin<sub>AUC</sub> in the placebo group is evidence for worsening metabolic disease states in untreated patients with BED, which is consistent with a longitudinal study on patients with BED conducted by Hudson and collaborators (2010).

ISI decreased significantly over time, with the largest magnitude decrease occurring in the placebo group. These results differ from the results of another study, which found that CrPic supplementation has no effect on insulin sensitivity in obese nondiabetic adults (Iqbal et al., 2009). It is possible that CrPic supplementation has an effect on insulin sensitivity in some populations but not others.

Limitations of this study include its small and homogeneous self-referred sample, the lack of an indicator of compliance (e.g., urinary chromium levels), and the fact

that the entire study was conducted in a single center. Despite limitations, this was the first trial to evaluate different doses of CrPic on the improvement of glucose regulation in individuals with BED.

In summary, this double-blind placebo-controlled six month pilot trial evaluated whether CrPic supplementation improves glucose regulation in individuals with BED. A 600 mcg/day dose of CrPic was correlated with improved glycemic control. On average, participants experienced an increase in insulin<sub>AUC</sub> and a decrease in ISI. The largest insulin<sub>AUC</sub> increase and the largest ISI decrease occurred the PL group. However, our sample was small and future adequately powered studies are warranted.

**Declaration of Interest:** Dr. Bulik is a grant recipient from and a consultant for Shire and has consulted for Ironshore.

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