

Effects of Chromium Picolinate Supplementation on Insulin Sensitivity, Serum Lipids, and Body Composition in Healthy, Nonobese, Older Men and Women

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Background. Chromium is an essential nutrient required for carbohydrate and lipid metabolism. Chromium supplementation in humans has been reported to improve glucose metabolism and improve serum lipid parameters and to reduce body fat; parameters that worsen with aging. As a result, chromium picolinate has been widely promoted as a health aid for the general population. The purpose of the study was to examine the effects of chromium supplementation on insulin sensitivity, serum lipids, and body composition in nonobese, healthy men and women of advanced age.

Methods. A randomized, double-blind, placebo-controlled study with 19 subjects (9 men and 10 women), aged 63–77, were given either chromium picolinate, 1000 $\mu\text{g}/\text{d}$, or a placebo for 8 weeks. Serum lipids were measured at baseline and 8 weeks. Insulin sensitivity and body composition were measured with the minimal-model intravenous glucose tolerance test and dual-energy x-ray absorptiometry scan, respectively, at baseline and after 8 weeks of chromium or placebo supplementation.

Results. No significant change in serum lipids, insulin sensitivity, or body composition was observed in the chromium group compared with the placebo group.

Conclusions. Chromium picolinate supplementation alone does not appear to improve insulin sensitivity, serum lipids, or change body composition in nonobese, healthy men and women of advanced age.

CHROMIUM is an essential nutrient required for carbohydrate and lipid metabolism (1). The estimated safe and adequate daily dietary intake (ESADDI) for chromium is 50–200 $\mu\text{g}/\text{d}$ (1). Dietary intake of chromium in the United States is below the recommended daily allowance and particularly low in elderly individuals (2). A variety of chromium supplements are available, with chromium picolinate being the most common. The most stable form available of supplementation appears to be chromium picolinate, which is least affected by nutritional and environmental factors.

A role for chromium in glucose metabolism has been inferred from the observation that patients on long-term total parenteral nutrition develop impaired glucose tolerance, which is reversed by chromium supplementation (3). Several studies have examined the effect of chromium supplementation on insulin sensitivity and serum lipids with inconsistent results. Some of these studies have demonstrated beneficial effects on insulin sensitivity, glucose tolerance, and/or serum lipid profiles (4–10) whereas others have shown no effect (12–14). In addition, some studies have demonstrated a tendency toward increased lean mass and a reduction in body fat in subjects taking supplemental chromium picolinate (15,16) whereas others have failed to support this claim (17–19). Most of these studies were nonrandomized, used varying doses and formulations of chromium, and involved small numbers of heterogeneous subjects.

It is well documented that insulin sensitivity and glucose tolerance decline as a function of age (20). Insulin resistance, in turn, has been associated with a variety of pathological processes including diabetes, hypertension, and hyperlipidemia (21). Aging is also associated with reduced protein synthesis, decreased lean body mass and bone mass, and increased body fat (22). The purpose of this study was to examine the effect of chromium picolinate on insulin sensitivity, serum lipids, and body composition in healthy, nonobese, older men and women.

METHODS

Subjects

Subjects were recruited from among a group of volunteers who had answered a questionnaire expressing an interest in participating in aging-related studies. Nineteen subjects (9 men and 10 women) were entered into the study. All subjects were healthy, and on no medications other than hormone replacement therapy (4 of 10 women). All subjects were nonsmokers, nonobese, with a body-mass index (BMI) of between 22 and 28 kg/m^2 . Medical illness was excluded by history and physical examination, urinalysis, complete blood count, and serum renal, hepatic, and thyroid profiles. The study was approved by the Human Subjects Committee of the University of California, San Diego. All subjects gave oral and written informed consent.

Study Design

A randomized, double-blind, placebo-controlled trial of 8-week duration was conducted. Sample size was calculated by estimation of the α error at 0.05, the β error at 0.20 (power of 80%), and Δ (size of treatment effect sought) of 1 standard deviation (*SD*) of the measurement of the outcome variable, insulin sensitivity. Individuals were randomized to a treatment or placebo group by computer-generated random numbers. The treatment group received 1000 $\mu\text{g}/\text{d}$ of chromium picolinate in two divided doses of 500 μg each morning and evening. All subjects were instructed by a nutritionist to continue their current diet and exercise regimens. All subjects completed a 3-day food record and exercise questionnaire at the beginning and end of the study that was coded and analyzed by the Nutrition III Version 7.0 software program. Compliance was checked by pill counts and retrospectively by serum chromium concentrations.

Study Protocol and Procedures

Potential adverse effects were monitored by means of interview, physical examination, urinalysis, and standard lab tests. Subjects were seen at baseline, 4, and 8 weeks. Blood was drawn at each visit after an overnight fast of 10 hours for determination of serum total cholesterol, triglycerides, low-density lipoproteins (LDLs), high-density lipoproteins (HDLs), apolipoproteins A1 and B, serum chromium, complete blood count, and liver and renal function tests. Heights and weights of all subjects were recorded at each visit.

Body composition was assessed by DEXA (dual-energy x-ray absorptiometry, Hologic 2000) scan performed at baseline and at 8 weeks.

Insulin sensitivity was assessed at baseline and at 8 weeks by the minimal model intravenous glucose tolerance test (23): administration of 300 mg/kg of dextrose as an intravenous (iv) bolus over 2 minutes followed 20 minutes later by an iv bolus of regular insulin (0.03 U/kg). Frequent blood samples were obtained at -5, 0, 2, 3, 4, 5, 6, 8, 10, 12, 14, 16, 19, 20, 22, 24, 25, 27, 30, 40, 50, 60, 90, 120, and 180 minutes for determination of insulin and glucose. Insulin sensitivity and glucose effectiveness were analyzed with the MINMOD computer program.

Assays

Serum insulin concentrations were measured by a double-antibody radioimmunoassay with an assay sensitivity of 2.1 $\mu\text{U}/\text{ml}$ and intra-assay and interassay coefficients of variation of 5% and 8%, respectively. Serum total cholesterol, triglycerides, LDLs, HDLs, and apolipoproteins A1 and B tests were performed by a commercial laboratory (Unilab Corporation, Tarzana, CA). LDL was calculated with the formula $\text{LDL} = \text{total cholesterol} - (\text{HDL} + \text{TG}/5)$, where TG is the triglyceride level. Coefficients of variation vary between 2% and 10%. Serum chromium assays were performed with an absorption spectrometric method by Mayo Clinical Laboratory, Rochester, MN. Complete blood counts, liver and hepatic function studies, thyroid-stimulating-hormone (TSH) studies, and urinalysis were performed by the University of California, San Diego, Medical Center Clinical Laboratories, San Diego, CA.

Table 1. Basal Comparison of Chromium ($n = 9$) and Placebo ($n = 10$) Groups

Parameter	Placebo	Chromium	
Age (y)	65.7 \pm 1.2	69.3 \pm 1.4	NS
Gender	5W, 5M	5W, 4M	
BMI (kg/m^2)	26.3 \pm 0.8	25.4 \pm 0.7	NS
SI ($\times 10^{-4}$ min/ μU ml)	2.72 \pm 0.5	3.02 \pm 0.3	NS
Serum chromium ($\mu\text{g}/\text{L}$)	0.47 \pm 0.04	0.32 \pm 0.05	NS
Total cholesterol (mg/dl)	192.4 \pm 9.8	213.0 \pm 14.3	NS
Triglyceride (mg/dl)	101.4 \pm 11.3	132.4 \pm 41.6	NS
HDL (mg/dl)	42.5 \pm 3.0	42.0 \pm 3.48	NS
LDL (mg/dl)	120.1 \pm 14.8	144.6 \pm 13.4	NS
Apo-A1 (mg/dl)	141.7 \pm 6.1	150.9 \pm 8.3	NS
Apo-B (mg/dl)	113.0 \pm 6.4	130.9 \pm 11.1	NS

Notes: M = men; W = women; BMI = body-mass index; SI = insulin sensitivity; HDL = high-density lipoprotein; LDL = low-density lipoprotein; Apo-A1 = apolipoprotein-A1; Apo-B = apolipoprotein-B; NS = nonsignificant. Values are the mean \pm SEM.

Analysis of Data

The baseline characteristics of the two groups were compared by a group *t* test (two tailed). Serum lipids, body composition, and insulin sensitivity were analyzed by a one-way analysis of variance. Data are presented as the mean [\pm standard error of the mean (SEM)], and $p < .05$ was considered significant for all analyses.

RESULTS

The chromium and placebo groups were similar with respect to age, BMI, insulin sensitivity, serum chromium levels, and serum cholesterol, TG, HDL, and LDL levels (Table 1). No statistically significant changes in the diet (total energy, percentage of protein, percentage of carbohydrates, percentage of fat) or exercise regimen of individuals occurred over the duration of the trial. Serum chromium concentrations were elevated from baseline in the treatment group after 8 weeks of chromium supplementation (Figure 1). No change in chromium levels occurred in the placebo group.

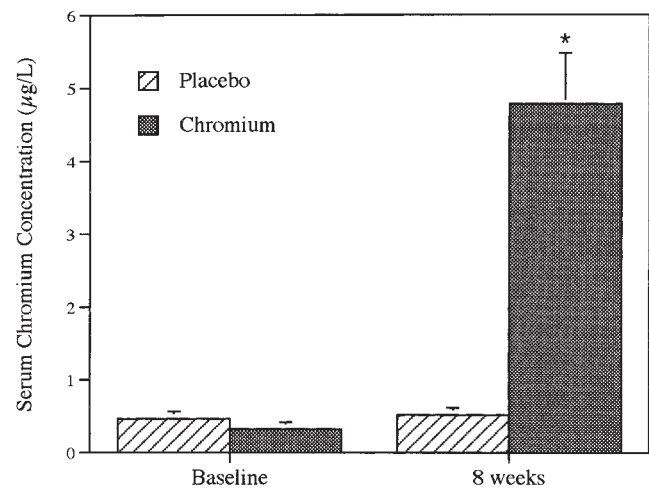


Figure 1. Mean (\pm SEM) serum chromium concentrations at baseline and after 8 weeks of chromium picolinate (1000 $\mu\text{g}/\text{d}$) or placebo. * $p < .0001$.

Table 2. Effects of Chromium Picolinate (1000 µg/d) Supplementation and Placebo on Serum Lipids

Parameter	Chromium (n = 9)		Placebo (n = 10)		
	Baseline	8 weeks	Baseline	8 weeks	
Chol (mg/dl)	213.0 ± 14.3	217.9 ± 13.5	192.4 ± 9.8	179.1 ± 6.9	NS
TG (mg/dl)	132.4 ± 41.2	154.2 ± 31.0	101.4 ± 11.3	104.9 ± 14.5	NS
HDL (mg/dl)	42.0 ± 3.5	41.7 ± 3.2	42.5 ± 3.0	41.1 ± 2.4	NS
LDL (mg/dl)	144.6 ± 13.4	154.0 ± 14.4	120.1 ± 14.8	120.7 ± 5.9	NS
Apo-A1 (mg/dl)	150.9 ± 8.3	146.0 ± 7.5	141.7 ± 6.1	147.0 ± 7.6	NS
Apo-B (mg/dl)	130.9 ± 11.1	129.6 ± 9.1	113.0 ± 6.4	104.6 ± 4.2	NS

Notes: Chol = total cholesterol; TG = triglycerides; HDL = high-density lipoprotein; LDL = low-density lipoprotein; Apo-A1 = apolipoprotein-A1; Apo-B = apolipoprotein-B; NS = nonsignificant compared with baseline values. Values are the mean ± SEM.

Serum HDL, LDL, and apolipoproteins B and A1 did not change significantly in either the chromium or the placebo groups (Table 2).

There was no significant change in anthropometric indices (percentage of body fat or BMI) in either the chromium or placebo groups (Table 3).

Insulin sensitivity, as determined by Bergman's minimal-model technique, and glucose effectiveness did not change significantly with chromium picolinate administration (Table 3).

All subjects completed the study. Chromium picolinate was well tolerated with no adverse effects reported. Physical examination, liver and renal function tests, complete blood count, and urinalysis revealed no abnormalities throughout the study.

DISCUSSION

Several studies have addressed the issue of chromium supplementation in healthy subjects without glucose intolerance or clinically overt diabetes mellitus yielding contradictory results. In a group of young, healthy nonobese subjects, there was no difference in fasting glucose, insulin, or lipid concentrations between chromium and placebo groups after 90 days of chromium nicotinate (200 µg/d) supplementation except for a small decrease in fasting insulin levels in a subgroup of subjects with elevated baseline fasting insulin concentrations (4). Twenty-three, healthy, elderly subjects, aged 63–86 years, were treated with 200 µg/d of chromium chloride and there were no significant changes in glucose tolerance, insulin concentrations, or serum lipids (13). A study in which 30 healthy adult men were treated with 50 µg of chromium chloride or placebo for 12 weeks found no

significant change in glucose tolerance in either group (7). Twenty-three healthy adult men were treated with 200 µg of chromium chloride or placebo for 12 weeks, resulting in improved insulin sensitivity as measured by the oral glucose tolerance test in the chromium group (5).

Our results cast doubt on the role of chromium picolinate supplementation for the maintenance of glucose homeostasis in healthy men and women of advanced age. These data do not support the assertion that chromium picolinate supplementation is beneficial in these subjects.

Similarly, the effect of chromium supplementation on body composition is also highly controversial. Although some studies support an effect of chromium on body composition (15,16), other studies have failed to demonstrate an effect (17–19). In our study, chromium picolinate supplementation did not result in any significant change in lean body mass.

Our investigation is limited by the relatively small number of subjects in each group. In addition, we cannot exclude the possibility that the duration of treatment, 8 weeks, may have been too short to demonstrate a statistically significant difference in our main outcome parameters, namely, insulin sensitivity, serum lipids, and body composition. Obese subjects and subjects with clinically overt diabetes mellitus were not included in the study. Therefore our conclusions must be limited to healthy, nonobese, elderly subjects. Further trials are needed to clarify whether chromium picolinate offers any beneficial effects to patients with clinically overt diabetes mellitus. A further limitation is that it is extremely difficult to control for changes in diet and exercise without strict daily monitoring of caloric intake and physical activity.

The safety of long-term chromium picolinate supplementation has been called into question with a published report that chromium picolinate causes damage to chromosomes of Chinese hamster ovary cells in vitro (24). Doses of chromium picolinate used were several thousandfold higher than serum chromium concentrations measured during supplementation with the usual recommended dose. Anderson and colleagues (25) demonstrated a lack of toxicity of chromium chloride and chromium picolinate in rats at levels several thousand times the upper limit of the ESADDI for humans. There have not been any documented toxic effects in any of the human studies involving chromium picolinate supplementation.

In humans, chromium deficiency has been demonstrated unequivocally in only one clinical situation, patients on total parenteral nutrition without added chromium. It is still unclear whether chromium deficiency, latent or overt, is common in

Table 3. Effects of Chromium Picolinate Supplementation and Placebo on Body Composition and Glucose Metabolism

Parameter	Chromium (n = 9)		Placebo (n = 10)		
	Baseline	8 weeks	Baseline	8 weeks	
Percentage of body fat	28.6 ± 2.7	28.0 ± 2.6	28.7 ± 2.6	29.0 ± 2.6	NS
BMI (kg/m ²)	25.4 ± 0.7	25.4 ± 0.7	26.3 ± 0.8	26.2 ± 0.7	NS
SI (× 10 ⁻⁴ min/µU ml)	3.02 ± 0.3	2.98 ± 0.11	2.72 ± 0.53	3.11 ± 0.57	NS
Sg (min ⁻¹)	0.019 ± 0.002	0.020 ± 0.002	0.018 ± 0.002	0.016 ± 0.001	NS

Notes: BMI = body-mass index; SI = insulin sensitivity; Sg = glucose effectiveness; NS = nonsignificant. Values are the mean ± SEM.

any other human condition. Whether chromium picolinate has any long-term health benefits in humans remains unclear.

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