Chromium Supplementation Does Not Improve Glucose Tolerance, Insulin Sensitivity, or Lipid Profile

A randomized, placebo-controlled, double-blind trial of supplementation in subjects with impaired glucose tolerance

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Chromium supplements are thought to be the second most commonly taken nutritional supplement, used by an estimated 10 million Americans (1). Chromium is an essential element in humans, and deficiency is associated with the development of diabetes, which was first noted in patients receiving long-term parenteral nutrition before the advent of routine chromium supplementation (2,3). In these patients, diabetes resolved following chromium replacement (2–4).

The dietary requirement for chromium is controversial, with the recommended daily intake in the U.S. being 0.05–0.20 μg (5). Chromium is abundant in the environment; however, aside from the extreme situation of unsupplemented parenteral nutrition, it has proven difficult to ascertain any clinical effects, due solely to chromium deficiency. Despite these difficulties, chromium supplements are widely promoted in the complementary health industries.

There are many studies examining the effects of various forms of chromium supplementation (rev. in 6,7). These studies utilized a variety of chromium formulations, varying doses, and patients with normal glucose tolerance, diabetes, or gestational diabetes. The outcomes have been inconsistent. Some studies showed no benefit, and other studies have shown inconsistent improvements in glucose, insulin resistance, and/or lipids. The paucity of data has prompted the National Institutes of Health to release a program announcement to address the issue: "Chromium as an adjuvant therapy for type 2 diabetes and impaired glucose tolerance."

This randomized, placebo-controlled, double-blind study was performed to examine the effect of chromium picolinate supplementation on glucose tolerance, insulin resistance, and lipids in patients with impaired glucose tolerance (IGT).

RESEARCH DESIGN AND METHODS

The study was investigator initiated, designed, analyzed, and funded. Bullivants Natural Health Products (Baulkham Hills, NSW, Australia) supplied the active tablets and the placebo free of charge. They had no other role in the study.

The subjects were recruited from outpatient clinics at two tertiary referral centers within metropolitan Sydney. Potential participants were identified based on history of abnormal glucose tolerance, including past gestational diabetes. All patients underwent a 75-g oral glucose tolerance test (OGTT), and those confirmed to have IGT were invited to participate. All subjects gave written informed consent, and the two respective institutional ethics committees approved the study.

All subjects completed a medical history and physical examination. Blood was collected in the fasting state for insulin, chromium, total cholesterol, and triacylglycerides.

Chromium supplementation was administered in the form of chromium picolinate at a dose of 400 μg twice daily (800 μg/day). Patients were randomized by sequential randomly preloaded coded envelopes to the placebo or active arms of the study in a 1:1 ratio. Placebo tablets were prepared by Bullivants Natural Health Products and were identical in appearance. Compliance was assessed by tablet counting at follow-up visits.

Chromium samples were carefully collected to avoid contamination, as previously described (6), and measured by graphite furnace atomic absorption spectrometry with a Varian SpectrAA800 Zeeman effect instrument (Varian Australia, Melbourne, Australia). Plasma glucose was measured by the hexokinase method, insulin by radioimmunoassay (Phadaseph, Uppsala, Sweden), and total cholesterol and triacylglycerides by enzyme colorimetric testing (Boehringer Mannheim Systems, Mannheim, Germany).

Insulin resistance was calculated using the homeostasis model assessment (HOMA), using the formula HOMA of insulin resistance (HOMA-IR) = (fasting insulin × fasting glucose)/22.5.

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Abbreviations: HOMA, homeostasis model assessment; HOMA-IR, HOMA of insulin resistance; IGT, impaired glucose tolerance; OGTT, glucose tolerance test.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

Table 1—*Characteristics of subjects before and after 3 months of chromium supplementation*

	Chromium		Placebo	
	Baseline	3 months	Baseline	3 months
Waist circumference (cm)	108.1 ± 21.5	105.7 ± 19.4	114.5 ± 16.0	111.7 ± 14.1 ($P = 0.052$ vs. baseline)
BMI (kg/m^2)	34.1 ± 8.9	34.7 ± 5.6	34.5 ± 8.7	34.5 ± 5.2
Serum chromium (nmol/l)	1.4 ± 1.3	5.2 ± 8.9*	3.3 ± 4.5	4.4 ± 4.0
Fasting plasma glucose (mmol/l)	5.5 ± 0.9	5.6 ± 0.8	5.8 ± 0.8	5.8 ± 0.8
1-h glucose (mmol/l)	9.8 ± 2.6	10.0 ± 2.2	10.6 ± 2.2	10.6 ± 2.0
2-h glucose (mmol/l)	8.2 ± 2.4	7.9 ± 2.5	8.5 ± 2.3	8.1 ± 2.0
AUC	23.4 ± 5.3	23.5 ± 4.9	24.9 ± 4.1	24.2 ± 4.4
Fasting insulin (mIU/l)	11.7 ± 7.1	19.3 ± 22.2	15.3 ± 9.8	14.5 ± 10.3
HOMA-IR	2.95 ± 2.10	4.76 ± 5.02	3.89 ± 2.54	3.73 ± 2.92
Triacylglycerides (mmol/l)	1.89 ± 0.63	1.94 ± 0.83	2.47 ± 0.98	2.31 ± 0.94
Total cholesterol (mmol/l)	4.78 ± 0.77	5.22 ± 0.98	4.83 ± 0.67	5.37 ± 0.78*

Data are means ± 1 SD. *$P < 0.05$. AUC, area under the curve during the OGTT.

The number of patients in the study gave 80% power to detect a difference of ~±0.2 mmol/l in glucose during the OGTT, ±1.1 in HOMA-IR, and/or ±2 mmol/l in area under the curve for glucose during the OGTT.

RESULTS — Forty subjects were included. Twenty were randomized to placebo and to active therapy. Sixty percent were female. Demographic characteristics and results before and after 3 months of treatment are shown in Table 1.

There were no significant differences between the two groups at baseline. After 3 months of treatment, the only changes to achieve statistical significance were a small rise in serum chromium in the active treatment group (from 1.4 ± 1.3 to 5.2 ± 8.9 nmol/l, $P = 0.048$) and a small deterioration in total cholesterol in the placebo group (4.83 ± 0.67 vs. 5.37 ± 0.78 mmol/l, $P = 0.002$ by paired *t* test). Both groups trended toward lower waist circumference, which did not achieve significance. There was no difference in rate to progression or regression of IGT.

CONCLUSIONS — This randomized, double-blind, placebo-controlled study found no significant beneficial effects of chromium supplementation in 40 subjects with IGT. Results of negative studies are often difficult to interpret. Potential explanations include inadequate study power, noncompliance, inadequate dosage, problems with bioavailability, absence of relevant chromium deficiency in Australia, and lack of efficacy of chromium supplementation.

Despite the relatively small study size, the paired cohort design gave good statistical power to detect differences down to clinically relevant levels, such as blood glucose differences of 0.2 mmol/l (3.6 mg/dl) during the OGTT. Compliance was assessed by tablet count, and no differences were found. All patients were reminded not to take chromium supplementation outside of the study medications, and none were known to do so over the study period. A significant rise in serum chromium occurred only in the active treatment group, suggesting that compliance with the assigned treatment was reasonable in both groups.

In this study, the chromium dose (at 800 μg/day) was at the higher end of the ranges used in previous studies. A previous study using a chromium isotope suggested that chromium picolinate was the most bioavailable formulation available. Bioavailability remains a subject of interest because of the relatively small increase in serum chromium in the active treatment arm. However, the most appropriate biological marker of adequate chromium status is unknown, with issues of contamination, difficulty with accurate measurements, and lack of a known measurable biological end point to set a normal range in any collectible sample.

Extensive studies of chromium status in normal subjects in Australia have not been undertaken. However, using careful collection methods to avoid contamination, the subjects in the study had similarly low levels at baseline and levels consistent with those found during pregnancy (6). Examination of postorthopedic surgical patients in Sydney found much higher levels of chromium (data not shown), suggesting that the baseline levels in our group were low and thereby theoretically amenable to supplementation.

In conclusion, we found no beneficial effect of chromium supplementation in the treatment of people with IGT despite increases in serum chromium levels, which suggested an adequate dosage regimen. Further studies in people with type 2 diabetes should be undertaken.

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