Glucose and insulin responses to dietary chromium supplements: a meta-analysis

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Authors' objectives
To evaluate the effect of dietary chromium supplements on glucose and insulin response in healthy people and in people with glucose intolerance or type 2 diabetes.

Searching
The Cochrane Controlled Trials Register (April 2000) and MEDLINE (1966 to May 2000) were searched without any language limitations. The keywords were stated. The bibliographies of identified articles were examined and authors who were contacted for further details were asked about additional studies.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) of either a parallel or crossover design were eligible for inclusion. The reports had to explicitly state the studies were randomised before they were included. Five studies presenting insufficient data were excluded. The maximum follow-up ranged from 28 days to 16 months. Most of the included studies were double blind.

Specific interventions included in the review
Comparisons of dietary chromium supplements and a control (either active or placebo) were eligible for inclusion. The included studies used chromium chloride, chromium nicotinate, chromium niacin, chromium 'rich' yeast, Brewer's yeast and chromium picolinate; the chromium dose ranged from 10.8 to 1,000 microg. The control treatments were placebo, torula yeast, Brewer's yeast, nicotinate and carbohydrate supplements. The dose (if any) of chromium in the yeast preparations used as controls was not stated.

Participants included in the review
Studies of healthy adults or people with glucose intolerance or type 2 diabetes were eligible for inclusion. The participants' age, where stated, ranged from 18 to 93 years. The average blood glucose in nondiabetic patients was around 5 mmol/L. The primary studies included elderly, overweight people, athletes, participants in exercise or dietary interventions, people with mild forms of diabetes, people with atherosclerosis, and older African American women.

Outcomes assessed in the review
The inclusion criteria were not explicitly defined in terms of the outcomes. The outcomes assessed in the review were glucose and insulin concentration and glycated haemoglobin (HbA1c). Glucose and insulin concentration were both assessed after fasting and at 120 minutes after an oral glucose tolerance test. One study was excluded because blood glucose was only measured in volunteers.

How were decisions on the relevance of primary studies made?
Two reviewers independently selected the studies for inclusion and resolved any disagreements with the aid of a third reviewer. The reviewers were not blinded to the author.

Assessment of study quality
The text of the review states that the methodological quality was assessed, but the criteria were not explicitly stated although a reference was given. Potential validity criteria mentioned in the review or tables were the proportion of withdrawals and exclusion from analysis, sample size and the extent of blinding. Two reviewers assessed validity and resolved any disagreements with the aid of a third reviewer. The reviewers were not blinded to the author.

Data extraction
Two reviewers independently extracted the data using specially designed forms and resolved any disagreements with the aid of a third reviewer. Data were extracted on study design, number randomised and number analysed, study population, country, chromium dose and formulation, control treatment, maximum follow-up and outcomes. The authors of the primary studies were contacted for missing details. For crossover RCTs, only data from the first period were used. For each study the difference in the means and 95% confidence intervals (CIs) were calculated for glucose, insulin and HbA1c concentrations. For studies with more than one chromium or placebo treatment arm and similar groups, an average response was calculated, weighted by sample size. Groups that were not similar were treated as separate treatments.

Methods of synthesis
How were the studies combined?
The pooled mean differences and 95% CIs between chromium and control (placebo or active) were calculated for diabetic and nondiabetic patients using two different fixed-effect models (weighted mean differences and standardised mean differences). The intention was only to report the weighted mean difference unless results from the models were dissimilar. The nondiabetic population included healthy people and glucose intolerant people. One study was subsequently excluded from the formal meta-analysis because it was the only study conducted in a non-Western country and its inclusion in the meta-analysis led to significant heterogeneity. Studies of diabetics appear to have been combined in a narrative that included the RCT excluded from the meta-analysis.

How were differences between studies investigated?
Statistical heterogeneity was tested using the chi-squared test, taking a P-value of less than 0.05 to indicate significant heterogeneity. Where heterogeneity was explained by one or two studies, these studies were removed from the meta-analysis. Where heterogeneity could not be explained by one or two studies, a random-effects model was used to combine the data. Linear regression was used to assess the influence of chromium formulation, chromium dose and exercise level on the relationship between dietary chromium and glycaemic control.

Results of the review
Information on 20 studies was tabulated, but only 15 RCTs with sufficient data were included in the review (618 people: 193 with type 2 diabetes and 425 who were either in good health or had glucose impairment).

Eleven RCTs analysed data from 90% or more of the patients randomised. Overall, 15% of the randomised patients were lost to follow-up or excluded from analyses. Only 4 RCTs reported baseline chromium levels.

Fasting glucose (14 RCTs; 38 diabetic and 425 nondiabetic patients).
Overall, there was no statistically-significant difference in fasting glucose between chromium supplements and control; the mean difference was 0.027 mmol/L (95% CI: -0.09, 0.15). No significant heterogeneity was found (P=0.97). There was also no statistically-significant difference in fasting glucose between chromium supplements and control among nondiabetics; the mean difference was 0.028 mmol/L (95% CI: -0.086, 0.14). The results for diabetics (4 RCTs) were inconclusive. Three small RCTs found no significant difference between chromium and control. The fourth RCT (180 randomised, 155 analysed) found that 1,000 microg chromium significantly decreased fasting glucose compared with placebo; the mean difference was -1.70 mmol/L (95% CI: -2.41, -0.99). However, it found no significant difference with 200 microg chromium; the mean difference was -1.0 mmol/L (95% CI: -0.93, 0.73). This RCT was the only one conducted in a non-Western country.

Glucose at 120 minutes (5 RCTs; 8 diabetics and 133 nondiabetics).
Overall, there was no statistically-significant difference in glucose at 120 minutes between chromium supplements and control; the mean difference was 0.26 mmol/L (95% CI: -0.24, 0.76). No significant heterogeneity was found (P=0.98). There was also no statistically- significant difference in fasting glucose between chromium supplements and control among nondiabetics; the mean difference was 0.042 mmol/L (95% CI: -0.43, 0.52). Among diabetics (4 RCTs), one RCT found that 1,000 microg chromium significantly decreased glucose compared with placebo, but it found no significant difference with 200 microg chromium. One small RCT found no significant difference between the treatments.
Fasting insulin (10 RCTs).

Overall, there was no statistically-significant difference in fasting insulin between chromium supplements and control; the mean difference was 0.28 mmol/L (95% CI: -7.0, 7.5). No significant heterogeneity was found (P=0.097). There was also no statistically-significant difference in fasting insulin between chromium supplements and control among nondiabetics; the mean difference was 0.25 mmol/L (95% CI: -6.98, 7.48). The results for diabetics (2 RCTs) were mixed with one study (8 patients) finding no significant difference and the other larger study (155 patients) finding that chromium significantly reduced fasting insulin compared with placebo.

Insulin at 120 minutes (5 RCTs; 8 diabetics and 133 nondiabetics).

There was no statistically-significant difference in insulin between chromium supplements and control, both overall and in nondiabetics. The mean difference overall was 11.1 pmol/L (95% CI: -69.0, 91.2); no significant heterogeneity was found (P=0.15). The mean difference for nondiabetics was 5.5 pmol/L (95% CI: -74.0, 85.1). Among diabetics (2 RCTs), one RCT (non Western population) found that chromium (1,000 and 200 microg) significantly reduced insulin at 120 minutes compared with placebo; the mean differences were -63 picomol/L (95% CI: -79.6, -46.4) and -63 picomol/L (95% CI: -78.3, -47.7) for doses of 1,000 and 200 microg chromium, respectively. A second small RCT found no significant difference.

HbA1c (3 RCTs).

One RCT of 33 healthy patients found no significant difference between chromium and control, as did another RCT of 24 patients with glucose intolerance. One RCT (155 diabetics) found that chromium (1,000 and 200 microg) significantly reduced HbA1c in comparison with placebo with a dose-relationship response; the mean differences were -1.90% (95% CI: -2.34, -1.46) and -1.00% (95% CI: -1.55, -0.45) for doses of 1,000 and 200 microg chromium, respectively.

Chromium formulation, chromium dose and exercise level did not influence the effect of chromium on fasting glucose or insulin.

None of the RCTs reported any adverse events with chromium supplements.

Authors’ conclusions

There was no evidence that chromium had any effect on glucose or insulin level in nondiabetic patients. There was insufficient evidence to determine the effect of chromium on diabetic patients.

CRD commentary

The review question was clear in terms of the study design, intervention and participants. Only two databases were searched and this may have resulted in the omission of other relevant studies. No language restrictions were applied and the search terms were stated. Two reviewers selected the studies, assessed validity and extracted the data; this reduced the potential for bias and errors. Validity was reported to have been formally assessed using validated criteria, but only some aspects were mentioned in the text of the review. Some relevant data were extracted and tabulated. The studies appear to have been appropriately combined in a meta-analysis, although the discussion suggested that the populations differed considerably between studies. Statistical heterogeneity was assessed and the influence of three factors on the results was explored. The evidence presented appears to support the authors’ conclusions.

Implications of the review for practice and research

Practice: The authors did not state any implications for practice.

Research: The authors state that there is a need for well-designed placebo-controlled RCTs in well-defined at-risk patients to determine the effect of chromium on glucose, insulin and HbA1c. Such studies should also report the number of patients who change from abnormal to within normal levels for all end points. The authors also state that future studies should assess the safety of chromium, especially at high doses.
Bibliographic details

PubMedID
12081828

Original Paper URL
http://www.ajcn.org/cgi/content/full/76/1/148

Other publications of related interest
This additional published commentary may also be of interest. Pittler MH. Inconclusive data for the effects of chromium on glucose and insulin concentrations. FACT 2003;8:32-3.

Indexing Status
Subject indexing assigned by NLM

MeSH
Blood Glucose /metabolism; Chromium /administration & dosage /therapeutic use; Cross-Over Studies; Diabetes Mellitus, Type 2 /blood /drug therapy; Dietary Supplements; Fasting; Glucose Intolerance /blood; Glucose Tolerance Test; Hemoglobin A, Glycosylated /analysis; Humans; Insulin /blood; MEDLINE; Placebos; Randomized Controlled Trials as Topic

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This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.