

# Effect of chromium supplementation on glucose tolerance and lipid profile

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## ABSTRACT

**Objectives:** To investigate chromium status of the adult population in the western region of Saudi Arabia and the possibility of using serum chromium status measurement as indicator of this status.

**Methods:** The effect of chromium supplement on glucose tolerance and lipid profile was studied in 44 normal, free living adults. 200µg chromium/day as CrCl<sub>3</sub> or a placebo was given in a double blind cross-over study, with 8 weeks experimental periods. Fasting, 1 hour and 2 hour post glucose challenge (75g of glucose) glucose, serum fructosamine, total cholesterol, high-density lipoprotein-cholesterol, triglycerides, chromium and dietary intakes were estimated at the beginning and the end of each stage.

**Results:** Mean serum chromium increased significantly after supplement ( $P<.001$ ) indicating proper absorption of the element. Supplement did not effect the total cholesterol, however, the mean high-density lipoprotein-cholesterol level was significantly increased ( $P<.001$ ), the mean triglycerides levels significantly decreased ( $P<.001$ ), and the mean fructosamine level significantly decreased

( $P<.05$ ). In addition, chromium supplement effected 1 hour and 2 hour post glucose challenge glucose levels in subgroups of subjects with 2 hour glucose level > 10% above or below fasting level and significantly differing to it ( $P<.05$  in both cases), by decreasing or increasing them significantly ( $P<.05$  in all cases) so that the 2 hour mean became not significantly different to the fasting mean. Since no significant changes in weight, dietary intake or habits were found, and placebo had no effect, all noted biochemical changes were attributed to chromium.

**Conclusion:** Improved glucose control, and lipid profile following chromium supplement suggests the presence of low chromium status in the studied population. However, serum chromium could not be recommended for use as an indicator of chromium status as subjects with widely varying levels responded favorably to the chromium supplement.

**Keywords:** Chromium supplement, glucose control, lipid profile, serum chromium.

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Evidence of a human nutritional requirement for chromium was reported in the mid-sixties.<sup>1-3</sup> Later supplementation studies confirmed its role in improving impaired glucose tolerance,<sup>4-8</sup> in reducing serum triglycerides levels,<sup>9</sup> and increasing high-density lipoprotein (HDL)-cholesterol.<sup>10,11</sup> The recommended safe and adequate intake for trivalent chromium (Cr) was estimated at 50-200µg/day for adults.<sup>12,13</sup> Only individuals consuming unbalanced inadequate diets, and showing some irregularities in their glucose metabolism might be expected to benefit from Cr supplement. The response to Cr

supplementation was noted to be stronger in developing countries with nutritional problems than it is in well-developed countries.<sup>14</sup> The newly adopted life style in Saudi Arabia has seriously affected the traditional way of life and diet, leading to increased consumption of refined and processed foods which lose much of their Cr content during such treatment.<sup>15</sup> Hence it is likely that some of the inhabitants of this area of the world are at risk of Cr deficiency. A study of the prevalence of such deficiency in our population will be of value, and might aid in better management of glucose

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intolerance, diabetes and hyperlipidemias.

Attempts to find adequate measures of the Cr status in the body have been made since the early seventies. Plasma levels of Cr in diabetic patients were reported to be significantly lower than in matched controls.<sup>16</sup> An increase in 24-hour urinary Cr excretion in diabetic subjects over values from a normal control group was also reported.<sup>17</sup> Therefore, serum and urinary Cr levels were estimated in normal and diabetic subjects chosen from the residents of the western part of Saudi Arabia in an attempt to estimate Cr status in the region.<sup>18</sup> The mean serum Cr level was found to be significantly lower in the NIDDM patients group and the mean fasting urinary Cr significantly higher, but an overlap between values in the 2 groups was found in both cases. Thus, it seemed difficult to judge the status of Cr in the population depending on fasting serum or urinary Cr alone, and a supplementation study was suggested in order to help clarify further the prevalence of Cr deficiency in this area of the world. Better glucose controls, or an improved lipid profile following supplementation or both will suggest the presence of Cr deficiency in the studied population. Estimating serum Cr before and after supplementation might also help to explore further the use of this parameter as means of indicating Cr deficiency in various individuals.

**Methods.** Forty four healthy free-living subjects (31 females and 13 males), ranging in age from 19 to 56 years old were recruited into the study from the student population and staff of the Faculty of Medicine and Allied Sciences at King Abdulaziz University, as well as willing relatives and friends. They differed in life-style (very active to sedentary), social class (upper to lower class) and type of work (university teachers to manual workers). Subjects were mainly of Saudi nationality, but varied in ethnic origin, and some (16 subjects) were Arabs with at least 10 years residence in the country. Potential subjects were excluded if they were taking mineral or vitamin supplements, or chronically ingested yeast. All subjects agreed to maintain their usual eating habits and health related behaviors throughout the study. They all consulted their family doctor before taking the supplement. The general research committee at King Abdulaziz University granted ethical approval, and informed consent was obtained from all subjects prior to the study.

**Experimental design.** Selected subjects were given code numbers, their weights and heights were measured to calculate their body mass index (BMI), and blood samples were obtained while fasting, 1 hour and 2 hours after a 75g glucose load. While waiting, a 24 hour dietary recall and a dietary history was obtained from each subject, and reviewed by personal interview. The subjects were then randomly divided into 2 groups (A and B) in preparation for the

supplementation study. The study designs was double blind and cross over with each test period (or stage) lasting 8 weeks. Two types of supplements (200µg/d of Cr as Cr chloride and placebo) were given consecutively in the form of capsules similar in size and numbers, so that neither the subjects nor the researchers involved in chemical analysis knew which type was taken at any time. Group A subjects received Cr chloride in the first stage, followed by placebo in the second stage, while group B started with placebo, followed by Cr chloride. Compliance was monitored by counting capsules at the end of each stage, and subjects were re-weighed, their dietary intakes and histories recorded and blood samples taken while fasting, 1 hour and 2 hours after the glucose load. Blood samples were collected in all plastic syringes, with minicath siliconized needles to avoid contamination with Cr and transferred into appropriate tubes for analysis of the various parameters (fluoride/oxalate for glucose analysis, and plain tubes for others). The sample for Cr analysis was centrifuged immediately, the resulting plasma was allowed to clot and the serum was transferred to a plastic tube and frozen at -20°C to the end of the study for analysis; after adding magnesium nitrate as a matrix modifier/ashing aid.<sup>19</sup>

Plasma glucose and serum triglycerides were estimated on the same day of sample collection. Fully automated methods were used for the analysis on Hitachi system 705, employing gluco-quant glucose reagent pack for glucose estimations, and triglycerides fully enzymatic "TG" reagent pack for triglycerides estimations. Both are from Boehringer Mannheim. Quality control checks were carried out at the beginning and end of each run. Total cholesterol was estimated using "cholesterol enzymatiques PAP" kit from "Bio Merieux". HDL-cholesterol was determined using kits from "Bio Merieux" also.

Serum fructosamine was determined by nitroblue tetrazolium (NTB) method.<sup>20</sup> Chemicals were purchased from Sigma Chemical Company, and measurement was carried out on Beckman spectrophotometer model 42. Serum Cr was measured using Perkin-Elmer 5000 atomic absorption spectrophotometer which was equipped with a tungsten-halogen lamp for enhanced background correction capabilities at 357.9nm Cr line, a graphite furnace (model HGA 500, Perkin-Elmer), and a strip-chart recorder (model 65, Perkin-Elmer). The method was based on work by Kayne et al,<sup>19</sup> and Veillon et al<sup>21</sup> with some modification involving furnace programmed reported earlier.<sup>18</sup> Using the collected 24-hour food intake data, total calories consumed per day, carbohydrates, fats, proteins, calcium, iron, vitamins A and C intakes were calculated for each subject using the nutrient values given in various food composition tables<sup>22-24</sup> as well as dietary information available with some of the packed foods consumed.

**Statistical analysis.** Results are expressed as mean  $\pm$  SD, and statistical analysis was by paired student's T-test. Significance was assigned at  $P < 0.05$ .

**Results.** All of the recruited subjects completed the supplementation study and compliance to therapy was excellent, with no reports of adverse effects. The mean  $\pm$  SD for the BMI at the start of the study was  $23.01 \pm 3.29$ , and showed no significant change at any time. Dietary intakes of total calories and all calculated nutrients before and after supplementation are presented in Table 1. All intakes except iron (which was  $< 77\%$  of recommended dietary allowance (RDA) in some female subjects) were within acceptable limits at the beginning of the study. However, wide variations in composition and types of food consumed by studied subjects were noted. Some subjects (mostly sedentary, older, and overweight individuals) were consuming very high

amounts of protein in their diet ( $> 2 \times$  RDA, mainly from animal sources) while others, (students and single males eating irregular canteen prepared meals and snacks, and leading active life) were depending mostly on carbohydrates, simple sugars, and fats to provide them with the needed calories. There was no significant change in the mean total intake of calories or calculated nutrients at any stage of the study when compared with the zero time values.

The glucose levels pre and post glucose loads, before and after supplementation are presented in Table 2. At zero time, fasting and 2 hour post glucose load levels ranged between 64-118 mg/dl. Cr had no significant effect on mean glucose levels pre and post glucose load when the data from all subjects were combined. Therefore, subjects were divided into subgroups according to their response to glucose load at zero time in a similar approach to that carried out by Anderson et al.<sup>25</sup>

Subgroup 1 with 2 hour post glucose load value  $\sim$

**Table 1** - Daily dietary intake (mean + SD) before and after supplements.

	No of subjects	Food energy (kcal)	Carbohydrate (g)	Fat (g)	Protein (g)	Calcium (mg)	Iron (mg)	Vitamin A (IU)	Vitamin C (mg)
All subjects at zero time	44	2449 $\pm$ 385	305 $\pm$ 48	100 $\pm$ 20	68 $\pm$ 9.3	622 $\pm$ 73	16.4 $\pm$ 3.7	761 $\pm$ 85	52 $\pm$ 12
+Placebo before chromium supplement	22	2502 $\pm$ 391	312 $\pm$ 52	106 $\pm$ 23	72 $\pm$ 12.3	640 $\pm$ 82	17.1 $\pm$ 4.2	789 $\pm$ 91	53 $\pm$ 14
+Chromium supplement	44	2603 $\pm$ 389	314 $\pm$ 53	107 $\pm$ 21	71 $\pm$ 11.9	644 $\pm$ 79	17.4 $\pm$ 4.2	784 $\pm$ 90	55 $\pm$ 13
+Placebo after chromium supplement	22	2534 $\pm$ 390	310 $\pm$ 50	104 $\pm$ 23	71 $\pm$ 12.2	632 $\pm$ 76	17.5 $\pm$ 4.3	773 $\pm$ 87	56 $\pm$ 14

**Table 2** - Effect of chromium supplementation on glucose level before and after glucose load (mg/dl).

Subjects	No of subjects	Zero time			+Placebo			+Chromium		
		0	1 hr	2 hr	0	1 hr	2 hr	0	1 hr	2 hr
All subjects	44	88.9 $\pm$ 10.9*	148.8a $\pm$ 15.3	90.2c $\pm$ 14.8	89.3 $\pm$ 10.8	151.2a $\pm$ 15.3	91.4c $\pm$ 14.5	89.3 $\pm$ 10.8	146.6a $\pm$ 9.5	91.8c $\pm$ 9.4
Subjects with 2 h glucose $\sim$ fasting level ( $\pm 3$ mg/dl)	20	86.7 $\pm$ 8.2	150.6a $\pm$ 8.8	87.1c $\pm$ 8.5	85.9 $\pm$ 7.9	148.6a $\pm$ 8.6	86.8c $\pm$ 8.7	87.1 $\pm$ 7.9	148.4 $\pm$ 8.3	90.2c $\pm$ 8.1
Subjects with 2 h glucose $>$ fasting level	11	94.8 $\pm$ 7.5	165.7a $\pm$ 7.2	104.5c $\pm$ 7.6	95.2 $\pm$ 7.4	166.3a $\pm$ 7.1	105.1c $\pm$ 7.3	90.3 $\pm$ 7.2	153.7b $\pm$ 6.9	95.3d $\pm$ 6.8
Subjects with 2 h glucose $<$ fasting level	13	87.8 $\pm$ 7.6	130.2a $\pm$ 7.1	75.2c $\pm$ 7.3	88.3 $\pm$ 7.3	133.4a $\pm$ 7.5	76.3c $\pm$ 6.9	87.2 $\pm$ 7.1	143.6b $\pm$ 7.3	84.3d $\pm$ 7.0

\*Mean + SD  
Values for glucose before and after supplement in the same row with different symbols (a,b,c,d) are significantly different at  $P < 0.05$ .  
No significant difference was detected for fasting glucose level.

fasting value ( $\pm 3$  mg/dl) (20 subjects of various ages and near ideal weight). Subgroup 2 with 2 hour post glucose load level 10% or more above fasting level (11 subjects, mainly sedentary, overweight, >36 years of age, with protein intake >>RDA). Subgroup 3 with 2 hour post glucose load level 10% or more below fasting levels (13 subjects, mainly lean active individuals, < 30 years of age, with high intake of sugars, and carbohydrate).

The fasting mean differed significantly from 2 hour post glucose load mean in subgroups 2 and 3 ( $P < .05$  in both cases), but not in subgroup 1. Placebo had no significant effect on mean glucose levels at any time, nor on the response of individuals to glucose load. Following Cr no values < 70 or > 108 mg/dl were found in the fasting state, or 2 hour after glucose load. In addition, Cr decreased the mean levels 1 hour and 2 hour post glucose load in subgroup 2 significantly ( $P < .05$  in both cases), and increased the means significantly in subgroup 3 ( $P < .05$  in both cases). The 2 hour post glucose load means in subgroups 2 and 3 became not significantly different to the corresponding fasting mean. No significant effect was found in subgroup 1.

Serum fructosamine values before and after

supplementation are presented in Table 3. None of the subjects had levels >3.7 mmol/l, considered to be the upper limit of the normal range<sup>26</sup> at any stage of the study. Cr but not placebo, decreased the mean fructosamine value of the whole studied group significantly ( $P < .05$ ). Furthermore the standard deviation was also decreased leading to much narrower observed range with no values <0.87 or >2.51 mmol/l found. Serum Cr values, before and after treatment, are presented in Table 3. Most values at zero time fell between 0.15 and 0.39  $\mu$ g/l. The mean serum Cr of the whole group was increased significantly ( $P < .001$ ) following supplementation. Individual increase in the level ranged from 2.5-3.5 folds when compared to pre-supplementation level. Placebo taken before Cr did not affect the level of serum Cr significantly. When placebo followed Cr supplements, serum Cr decreased significantly ( $P < .01$ ) but it remained significantly higher ( $P < .01$ ) than the zero time mean. Subjects with serum Cr at the lower end of our range at zero time (<15  $\mu$ g/l) as well as subjects with values at the upper end (>.39  $\mu$ g/l) showed slight irregularities in their glucose control (subgroups 2

**Table 3** - Effect of chromium supplementation on fructosamine values and chromium level.

Serum fructosamine (mmol/L)	Mean $\pm$ SD	Observed range
Zero time (n=44)	2.05 $\pm$ 0.80	0.50 - 3.60
+placebo before chromium supplement (n=22)	2.11 $\pm$ 0.82	0.48 - 3.61
+chromium (n=44)	1.70 $\pm$ 0.42	0.87 - 2.51
+placebo after chromium supplement (n=22)	1.90 $\pm$ 0.79	0.51 - 3.21
<b>Serum chromium (ug/L)</b>		
Zero time (n=44)	0.170 $\pm$ 0.086	0.097 - 0.48
+placebo before chromium supplement (n=22)	0.166 $\pm$ 0.081	0.09 - 0.455
+chromium (n=44)	0.538 $\pm$ 0.130	0.285 - 0.835
+placebo after chromium supplement (n=22)	0.234 $\pm$ 0.088	0.138 - 0.593

**Table 4** - Effect of chromium supplementation on the levels of total cholesterol, HDL-cholesterol and triglycerides (mmol/l).

	No. of subjects	Total cholesterol	HDL - Cholesterol	Triglycerides
Zero time (all subjects)	44	4.24 $\pm$ 0.86*	1.03 $\pm$ 0.31	1.36 $\pm$ 0.49
+Placebo before chromium supplement	22	4.31 $\pm$ 0.89	0.98 $\pm$ 0.35	1.38 $\pm$ 0.47
After chromium chloride	44	4.18 $\pm$ 0.95	1.28 $\pm$ 0.27	0.93 $\pm$ 0.40
+Placebo after chromium supplement	22	4.36 $\pm$ 0.83	1.11 $\pm$ 0.25	1.23 $\pm$ 0.38
*Mean $\pm$ SD				

and 3), improved after supplementation with Cr.

Table 4 shows the estimated level of total cholesterol, HDL-cholesterol and triglycerides before and after supplementation with Cr. At zero time, 10 subjects had triglycerides level above the desirable value of 1.7 mmol/l, including 4 subjects with levels exceeding the upper limit of 2.0 mmol/l. Five subjects had cholesterol level above the desirable value of 5.2 mmol/l, but non-exceeded the unacceptable limit of 6.5 mmol/l. Two of these subjects had HDL-cholesterol level <0.9 mmol/l, and triglycerides level >1.7 mmol/l (indicating moderate risk of ischemic heart disease). Both subjects were in subgroup 1, and had serum Cr level in the middle of our calculated range. The other 3 subjects were in subgroup 2 with HDL-cholesterol level >0.9 mmol/l, triglycerides levels >1.7 mmol/l (>2.0 mmol/l in 2 of them), and serum Cr level at the lower end of our range (<0.15 µg/l). The remaining 5 subjects with triglycerides level >1.7 mmol/l, had cholesterol level <5.2 mmol/l, with 3 of them in subgroup 2 having serum Cr <0.15 µg/l, and the other 2 in subgroup 1 with serum CR level at the top of our range. The mean serum cholesterol did not change significantly at any stage of the study. However, the mean of HDL-cholesterol, although not effected by placebo given before or after the Cr supplements, showed a significant increase following Cr administration ( $P < .001$ ). The mean triglyceride level was not effected by placebo before or after Cr supplement, but Cr ingestion decreased the mean significantly ( $P < .001$ ). No values > 1.7 mmol/l could be found at this stage.

**Discussion.** The aim of the study was to investigate the possibility of the existence of Cr deficiency in free living individuals residing in the western region of Saudi Arabia, and to explore the use of serum Cr as an indicator of the Cr status of the body. It was necessary; therefore, to include subjects, representing the varies sectors of society in the study. From our collected data, it can be seen that the selected subjects vary in age, life style, ethnic background, social class, type of work, as well as food composition and quantity of intake: and hence, BMI. Therefore, it was felt that the selected subjects were good representatives of the adult population in this region of Saudi Arabia.

The marked increase in serum Cr of all subjects following supplementation indicates proper absorption of the element. The lack of change in dietary intakes, and BMI throughout the study indicates that the noted biochemical changes must be due to Cr since placebo had no effect.

The use of double-blind cross over design, allowing all subjects to take Cr and placebo has helped to minimize most nonspecific variations as a result of placebo (assay variations, physiological differences, variation with time). It was not possible

to divide the subjects at the start into subgroups, since one of the aims of the study was to determine if there were any subgroups within the selected normal group of subjects who would respond to Cr supplementation. The later division into subgroups according to glucose level 2 hour after glucose load was based on finding some subjects having consistently higher or lower values than fasting values at zero time and after placebo which decreased or increased following Cr (subgroups 2 and 3). Such division has helped to show that normal individuals who differ in their ability to utilize glucose also differ in their response to Cr supplement. Cr seemed to eliminate near borderline values at both ends of the range, thus effectively improving glucose control. Similar results were reported earlier.<sup>25</sup> The decreased fructosamine mean, and narrower range found after Cr supplement verifies the results arrived at, and reflects better long-term glucose control in the studied subjects.

Earlier studies also reported a reduction in triglyceride,<sup>9</sup> and an increase in HDL-cholesterol,<sup>10-11</sup> as seen in our results following Cr supplement. All noted biochemical changes are considered to be beneficial to the health of the studied individuals, and indicate the presence of low Cr status (deficiency) amongst them, corrected by the Cr supplement. Such a deficiency could be one of the reasons for the increased incidence of glucose intolerance and various types of hyperlipidemias noted in our population in recent years. Predicting the most likely causes of low Cr status, and the likely group of people to suffer from such a deficiency, would help physicians recommend supplementation to "at risk" individuals.

Deficiency of any nutrient could either be due to inadequate intake or increased excretion or both. The diet of some subjects (subgroup 3) seemed to be generally high in fat, carbohydrates, and simple sugars, which have low Cr content according to previous studies on Cr contents of food,<sup>27</sup> and causes increased losses of Cr.<sup>28</sup> This could have lead to low Cr status in this group of individuals. On the other hand, the dietary data of the subgroup 2 seemed to indicate adequate intake of Cr rich foods throughout the study. However, subjects in both subgroups showed better glucose tolerance after supplementation, pointing to the existence of low Cr status, to start with. It was interesting to note that subgroup 2 was composed mainly of sedentary individuals, who were overweight to various degrees and, > 36 years of age (increased insulin/Cr requirement). Thus, it can be suggested that the risk factors leading to low Cr status in our population are: a) high simple sugars intake leading to increased excretion of Cr; b) high intake of foods rich in fats and carbohydrate and low in Cr; c) overweight; even in the presence of Cr rich diets; due to increased

resistance to insulin leading to increased Cr requirement. Disappearance of improvement in glucose tolerance and lipid profile 8 weeks after stopping the supplement; reflected on a re-increase in the means of fructosamine and triglycerides, and a re-decrease in the mean of HDL-cholesterol; points to increased excretion of Cr in our studied population. However, a study of the Cr urinary excretion patterns of those groups of subjects is needed to verify the suggestions made and clarify the picture further.

Even though serum Cr was reported as a promising indicator of Cr status,<sup>16</sup> our study failed to verify this, as individuals with serum Cr at the top or middle of our calculated range, as well as ones with levels at the lower end of the range were found to respond favorably to Cr supplement. Therefore, search must continue for practical and accurate measures of Cr status. Meanwhile, since our study points to the existence of Cr deficiency in the studied population, and no adverse effects were noted in any of the supplemented subjects. It might be advisable to recommend Cr supplements to patients with glucose intolerance, diabetes mellitus, or hyperlipidemias, especially if their history indicated the presence of any of the above mentioned risk factors for low Cr status. A study of the effect of Cr supplementation on glucose control, lipid, profile and drug dosage in diabetic patients is underway. Favorable results might help to reduce the cost of long term management of this disorder since Cr is less expensive than insulin or other available drugs used currently in the management of diabetes.

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