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Effects of short-term chromium supplementation on insulin sensitivity and body composition in overweight children: randomized, double-blind, placebo-controlled study☆

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Abstract

Excessive body weight is inversely associated with insulin sensitivity in children and adults. Chromium supplementation produces modest improvement in insulin sensitivity in adults. The aim of this study was to examine the beneficial effects of chromium supplementation on insulin sensitivity and body composition in overweight children simultaneously modifying lifestyle. Twenty-five overweight children aged 9–12 years were randomized to receive either 400 μg of chromium chloride or placebo in double-blind fashion, during a 6-week lifestyle modification regimen that included nutritional education and 3×90 min of aerobic physical activity weekly. Insulin sensitivity was demonstrated using homeostasis model assessment-insulin resistance and quantitative insulin sensitivity check index (QUICKI). Changes in body mass index (BMI; kg/m^2), BMI *Z*-score, waist circumference, body composition and fasting plasma glucose were measured. Although no significant benefit of chromium supplementation over placebo was evident for BMI, BMI *Z*-score and fasting insulin level, children who received chromium chloride demonstrated more positive changes versus the placebo group in HOMA (−1.84±1.07 vs. 0.05±0.42, *P*=.05), QUICKI (0.02±0.01 vs. −0.002±0.01, *P*=.05), lean body mass (2.43±0.68kg vs. 1.36±1.61kg, *P*=.02) and percentage body fat (−3.32±1.29% vs. 0.65±1.05%, *P*=.04). The desirable effects of chromium supplementation on insulin sensitivity and body composition were more apparent in pre-pubertal children. These results suggest that short-term chromium supplementation can improve insulin sensitivity and body composition in overweight children.

Keywords: Chromium supplementation; Insulin sensitivity; Body composition; Overweight children

1. Introduction

The prevalence of childhood obesity has increased globally more than 2-fold during the last three decades [1,2], which has contributed to an upsurge in insulin resistance (IR) and the attendant clinical complications in children and adolescents [3,4]. Children are becoming overweight at younger ages than in the past, increasing their risk of IR and its metabolic complications, such as hypertension, Type 2 diabetes mellitus (T2DM), dyslipidemia, atherosclerosis, coronary artery disease and sudden death throughout life [5–7]. IR that develops during childhood and adolescent precedes the clustering of cardiovascular risk, which predicts adult cardiovascular disease [8–10]. Interventions designed to address IR and obesity in younger children are prudent strategies to promote better health throughout life.

Chromium is a cofactor necessary for insulin action and dietary supplementation with chromium produced modest improvements in glucose metabolism, insulin sensitivity and body composition in both animal models and human trials. As examples, chromium supplementation has alleviated IR, enhanced insulin signaling in ob/ob obese mice [11] and increased muscle mass and reduced fat mass in pigs and goats [12,13]. An epidemiological study reported an inverse association of chromium intake with fasting insulin level [14] and several clinical trials have reported benefits of chromium supplementation on insulin sensitivity in adults with or without T2DM [15–19]. Chromium supplementation combined with exercise can increase lean body mass in obese and nonobese adults [20,21].

However, the beneficial effect of supplemental chromium on insulin sensitivity in children has not been investigated. If a benefit exists, then chromium supplementation could be used to combat IR and its metabolic consequences that can begin in childhood. Accordingly, the present study is aimed to examine the beneficial effects of supplemental chromium on insulin sensitivity and body composition in overweight children.

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2. Methods and materials

2.1. Subjects

Thirty-one 9–12-year-old overweight children [above the age- and gender-specific 85th percentile of body mass index (BMI), based on the Korean 2007 growth reference charts] were enrolled in a community-based lifestyle modification (LSM) program in June 2009. The exclusion criteria were medical history of Type 1 DM or T2DM, liver diseases, renal diseases and any medical use of medications. Six participants dropped out during the program due to parental objection (n=2), altered after-school schedule (n=3) and participant refusal for postintervention blood sampling (n=1). Twenty-five participants completed the program. Baseline characteristics of the subjects are summarized in Table 1. All participants and their parents provided written informed consent. This study was approved by Institutional Review Board of the Ajou University Hospital, Suwon, South Korea.

2.2. Study design

This study was a double-blind placebo-controlled design. The LSM program included aerobic exercise (2 days a week, 1.5 h per session) and diet education (1 day per week, balanced low-calorie diet) 2 weeks in advance of randomization. The first blood sample was obtained prior to beginning the LSM regimen. Each participant was asked not to perform additional physical activity and subjects who were taking vitamin or mineral supplements including chromium at baseline were educated not to take them during the program. Participants and investigators were blinded to the randomization, which was assigned in a stratified randomized way based on age, gender and BMI percentile for age and sex, to receive either 400 μg of chromium chloride (n=12; TEI Korea, Seoul, Korea) or a placebo (n=13) daily for 6 weeks. In each session, the participants were instructed to follow the scheduled LSM program and take the assigned supplementation.

2.3. Anthropometry, body composition and assay

All participants underwent anthropometric evaluation and blood sampling at baseline and at the end of intervention. Fasting plasma glucose (FPG), lipids, insulin and adiponectin level were assessed at pre- and post intervention visits. Insulin sensitivity index was calculated using homeostasis model assessment-IR (HOMA-IR) and Quantitative Insulin Sensitivity Check Index (QUICKI) [22]. Pubertal status was determined as previously described [23,24]. In subgroup analyses, participants were classified into two groups [prepubertal children (Tanner stage I) and early pubertal children (Tanner stage II or III)]. Height, waist circumference and weight were measured to the nearest 0.1 cm and 0.1 kg, respectively, using a wall mounted stadiometer. BMI and BMI Z-score were calculated. Blood pressure was measured after sitting for a minimum of 5 min. Bio-impedance was recorded using TANITA TB410 apparatus (TANITA, Tokyo, Japan) to estimate percentage body fat, body fat mass and lean body mass. Blood sampling was undertaken after 10 h of fasting. FPG and lipids were measured enzymatically using an ADVIA 1650 apparatus (Bayer, Tokyo, Japan). Fasting plasma insulin concentration was determined by the E170 electro-chemiluminescence immunoassay method (Roche, Basel, Switzerland). Adiponectin level was measured by radioimmunoassay (Linco, St. Charles, MO, USA). Insulin sensitivity was estimated by HOMA-IR [fasting insulin (μU/ml)×FPG (mmol/L)/22.5] and QUICKI [1/(log fasting insulin+log FPG)].

Table 1
Subject characteristics at baseline

	Placebo	Chromium	P
N	13	12	
Boys/girls	8/5	4/8	
Age (years)	10.38±0.31	10.75±0.25	.58
Tanner stage	1.85±0.25	1.83±0.27	.95
BMI	23.76±0.58	23.42±0.54	.78
BMI Z-score	1.70±0.09	1.54±0.09	.25
Waist circumference (cm)	80.84±1.86	79.45±2.36	.49
Fasting insulin (pmol/L)	79.17±7.85	102.44±8.26	.21
HOMA-IR	2.53±1.12	3.56±1.22	.09
QUICKI	0.33±0.01	0.32±0.01	.09
Percentage body fat (%)	30.22±1.74	34.32±1.38	.12
Body fat mass (kg)	15.75±1.21	18.25±1.01	.11
Lean body mass (kg)	33.85±1.48	34.6±1.56	.70
SBP (mmHg)	122.62±2.88	124.08±3.26	.58
DBP (mmHg)	69.85±1.57	68.14±1.43	.44
Total cholesterol (mmol/L)	174.00±7.41	192.33±11.79	.24
Triglyceride (mmol/L)	103.68±1.16	97.18±1.19	.64
HDL cholesterol (mmol/L)	48.45±1.03	55.90±1.07	.09
Fasting plasma glucose (mmol/L)	5.02±0.12	5.45±0.16	.07
Adiponectin (μU/mg)	6.6±1.3	6.7±1.8	.58

Abbreviations: SBP, systolic blood pressure; DBP, diastolic blood pressure; P value was obtained by the Mann-Whitney U test to compare baseline values between chromium group and placebo group. Data are presented means±S.E.

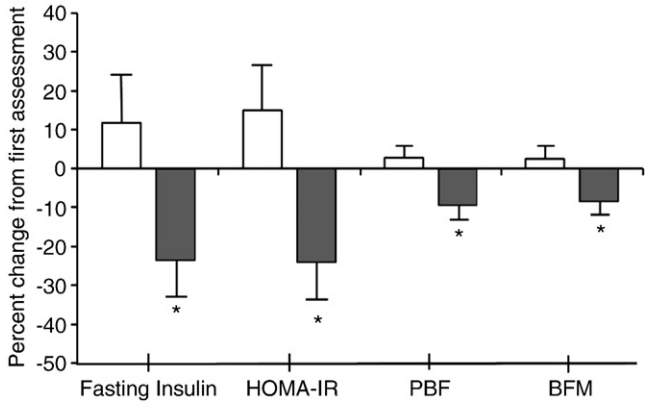

Fig. 1. Mean percent change in fasting insulin level, HOMA-IR, percentage body fat (PBF) and body fat mass (BFM) in overweight children taking either chromium chloride (black bars) or placebo (white bars) for 6 weeks, compared with baseline. Chromium supplementation reduced insulin resistance and body fatness while placebo did not make any significant change. *P<.05.

2.4. Statistical analyses

The overall changes from baseline in each group were analyzed using the Wilcoxon rank sum test. The Mann-Whitney U test was used to examine the effects of chromium supplementation on changes in the target parameters (FPG, fasting insulin, insulin sensitivity indexes, anthropometry and body composition) compared to baseline values. Each parameter at baseline was compared between the chromium supplementation group and control group to identify potential randomization imbalance. Statistical analyses were conducted by SPSS version 12.0 (SPSS, Chicago, IL, USA). The level of significance was .05. Data are presented as mean±S.E. unless otherwise indicated.

3. Results

At baseline, there were no significant differences in fasting insulin level, insulin sensitivity indices, anthropometry, body composition, blood pressure, lipid profile, FPG and adiponectin between chromium group and placebo group (Table 1).

When comparing to baseline, participants who received with 6-weeks chromium supplementation showed a significant decrease in fasting insulin level and HOMA-IR, as compared to those taking placebo (Fig. 1). Though significant reductions were noted in BMI Z-

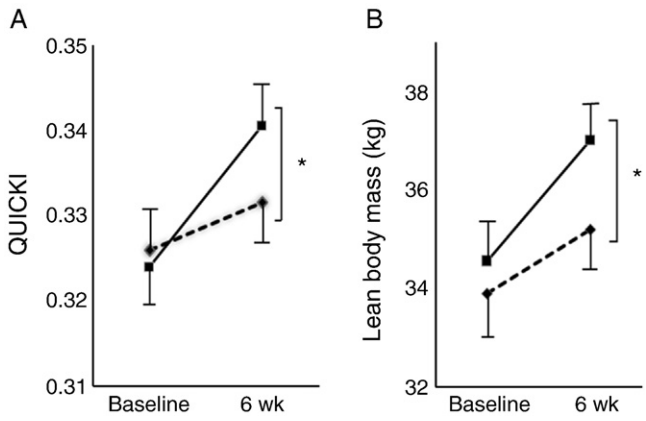

Fig. 2. Mean±S.E. change in quantitative insulin sensitivity check index (QUICKI) and lean body mass. The increases in QUICKI and lean body mass were significantly greater in the chromium group than in the control group after 6 weeks of chromium chloride supplementation. Asterisk indicates P=.05 and P=.02 for changes in QUICKI and lean body mass, respectively.

Table 2
The comparison between changes in chromium and placebo groups in anthropometry, body composition, metabolic profiles, insulin sensitivity and adiponectin

	Placebo	Chromium	P
BMI (kg/m^2)	−0.09±0.03	−0.22±0.02	.56
BMI *Z*-score	−0.05±0.08	−0.07±0.07	.32
Waist circumference (cm)	−1.81±2.97	−1.03±2.26	.36
Fasting insulin (pmol/L)	−1.39±12.57	−43.75±23.27*	.07
HOMA-IR	0.05±0.42	−1.84±1.07	.05
QUICKI	−0.01±0.01	0.01±0.01	.05
Percentage body fat (%)	.39±3.78	−2.84±4.53*	.04
Body fat mass (kg)	0.19±2.33	−1.32±2.25*	.06
Lean body mass (kg)	1.47±5.6*	3.02±3.10*	.02
SBP (mmHg)	−12.25±1.56	−11.25±2.94	.97
DBP (mmHg)	−5.08±1.98	−6.5±2.52	.87
Total cholesterol (mmol/L)	0.46±0.18	0.38±0.16	.95
HDL cholesterol (mmol/L)	0.07±0.04	−0.01±0.1	.84
Triglyceride (mmol/L)	−0.3±0.13	−0.32±0.15	.78
Fasting glucose (mmol/L)	0.15±0.37	−0.38±0.64*	.20
Adiponectin (μU/mg)	−1.07±1.19	1.03±1.22	.35

P value was obtained from the Mann-Whitney *U* test to compare the effect of chromium chloride to placebo on change in variable over 6 weeks.
*$P<.05$ compared to baseline value (obtained from the Wilcoxon rank sum test).

score from baseline values both in chromium group ($P=.01$) and in placebo group ($P=.05$) at the end of the study, significant increase in lean body mass and decrease in body fat mass were observed only in the chromium supplemented group (Fig. 1). Chromium supplementation also resulted in a significant decrease in triglyceride levels from baseline ($P=.02$).

Concerning intergroup difference, a modest decrease in fasting insulin level was observed in the chromium supplemented group, compared with the placebo group ($P=.07$). Supplementation with chromium chloride significantly decreased HOMA-IR, while placebo increased it (−1.86±3.42 vs. 0.08±1.47, $P=.05$). Chromium supplementation resulted in a greater increase in QUICKI than placebo (0.01±0.01 vs. −0.01±0.01) (Fig. 2A) and a significantly greater increase in lean body mass, compared with placebo (Fig. 2B), so that the reduction in percentage body fat was greater in the chromium group than the placebo group (−2.84±4.53% vs. 0.39±3.78%, $P=.04$). No treatment effect for BMI, BMI *Z*-score, waist circumference, blood pressure and metabolic variables such as FPG, total cholesterol, triglyceride, high-density lipoprotein cholesterol and adiponectin were noted at the end of intervention (Table 2).

The effect of chromium chloride differed by pubertal development (Table 3). In both prepubertal and pubertal children, there were no significant differences between the chromium group and the placebo group in baseline values (data not shown). Prepubertal children who received chromium chloride displayed significantly greater decrease in fasting plasma insulin concentration ($P=.02$), HOMA-IR ($P=.02$) and percentage body fat ($P=.02$), and significantly greater increases in QUICKI and lean body mass ($P=.02$ and $P=.01$, respectively) compared with the placebo controls. However, these beneficial effects of chromium supplementation on insulin sensitivity and body composition were not statistically significant in early pubertal children.

4. Discussion

Presently, 6 weeks of supplementation with 400 μg chromium chloride in conjunction with lifestyle modification improved insulin sensitivity indices and ameliorated body composition in overweight children. Prepubertal participants displayed more remarkable positive changes than pubertal children.

Chromium supplementation is effective in individuals with low insulin sensitivity even before development of T2DM. Obese adults with high fasting insulin level and a family history of T2DM displayed the improved insulin sensitivity [18]. In one study, chromium supplementation significantly reduced serum insulin levels only in healthy adults with high insulin concentration (>35 pmol/L) [25], suggesting IR. All but one of the children in the present study had a fasting insulin level >35 pmol/L. In Zucker (fa/fa) rats, chromium supplementation improves insulin sensitivity via reduction of skeletal muscle membrane cholesterol, which causes peripheral IR [26]. Chromium incorporated adipocyte cell membrane displays reduced cholesterol content and redistribution of glucose transporter 4 in cells cultured under high glucose conditions, so that glucose uptake by adipocyte is facilitated [27].

In a meta-analysis of randomized controlled trials that reviewed the weight reducing effects of chromium supplementation, the weight reduction was significant but not large enough to be clinically interesting [28]. Another study indicated that the studies analyzed in the meta-analysis had a short duration (10–13 weeks) and that

Table 3
The comparison of changes between intervention and placebo groups at different pubertal stages

	Prepuberty			Early puberty		
	Placebo	Chromium	P	Placebo	Chromium	P
N	5	6		8	6	
BMI	−0.09±0.25	−0.39±0.13	.36	−0.27±0.13	−0.36±0.24	.30
BMI *Z*-score	−0.03±0.04	−0.07±0.02	.36	−0.06±0.03	−0.08±0.04	.44
WC (cm)	−1.66±1.31	−0.48±0.92	.41	−2.14±1.17	−1.33±1.11	.65
Insulin (pmol/L)	7.59±7.29	−8.58±8.05	.02	−7.29±7.61	−8.58±8.05	.37
HOMA-IR	0.69±0.3	−1.11±0.47	.02	−0.36±0.63	−2.57±2.15	.37
QUICKI	−0.01±0.01	0.02±0.01	.02	0.01±0.01	0.03±0.02	.30
PBF (%)	3.22±2.17	−5.50±2.01	.02	−0.96±0.67	−1.13±1.20	.85
BFM (kg)	1.92±1.28	−2.57±1.00	.03	−0.74±0.52	−0.58±0.67	.85
LBM (kg)	−1.36±0.88	3.47±0.99	.01	3.06±2.42	1.38±0.79	.61
SBP (mmHg)	−12.6±1.81	−13.17±4.68	.92	−12.0±2.47	−9.33±3.82	.83
DBP (mmHg)	−7.4±2.6	−8.17±3.84	.85	−3.63±2.77	−4.83±3.48	.89
TC (mmol/L)	0.68±0.34	0.29±0.13	.36	0.31±0.22	0.47±0.31	.60
TG (mmol/L)	−0.21±0.19	−0.27±0.1	.36	−0.35±0.19	−0.37±0.30	1.0
HDL-C (mmol/L)	0.10±0.05	0.06±0.05	.58	0.04±0.05	−0.09±0.20	.84
FPG (mmol/L)	0.08±0.09	−0.13±0.14	.46	0.12±0.15	−0.28±0.25	.44
Adiponectin (μU/mg)	0.28±0.89	0.67±0.71	.39	−0.49±0.25	−0.72±0.71	.28

Abbreviations: PBF, percentage body fat; BFM, body fat mass; LBM, lean body mass; SBP, systolic blood pressure; DBP, diastolic blood pressure; TC, total cholesterol; TG, triglyceride; HDL-C, high density lipoprotein-cholesterol.
P value was obtained from Mann-Whitney *U* test to compare the change in variable of chromium to that of placebo over 6 weeks. (There was no significant difference between variables of chromium and those of placebo at baseline.)

further supplementation could lead to meaningful reduction of body weight [29]. The present 6-week duration of chromium supplementation may not have been long enough to induce the significant body weight change between the two groups. However, 400 μg of chromium chloride supplementation for 6 weeks in overweight children was enough to increase lean body mass and decrease body fat more so than in controls, consistent with two previous studies conducted in adults [20,21]. Some studies have not indicated improvement in body composition after chromium supplementation [30,31]. However, the subjects in these studies were athletes or healthy adults who might not have IR. Alternatively, the dosage of supplemental chromium may not have been sufficient to improve body composition.

Since baseline insulin sensitivity can affect the results of chromium supplementation [32] and insulin sensitivity can be altered by pubertal development [33], the present study adopted subgroup analysis stratified by pubertal stage. The approach revealed that fasting plasma insulin concentration, IR and body composition improved more apparently in pre-pubertal children. A previous study reported that although insulin sensitivity was 30% lower in pubertal girls and boys than in pre-pubertal children, insulin secretion did not differ between the two groups [34], suggesting suboptimal insulin secretion in the pubertal group. Since the action of supplemental chromium depends on insulin level, the weak impact of chromium on insulin sensitivity in pubertal children may be attributed to suboptimal insulin secretion in pubertal stage.

The present study had several limitations. First, the number of subjects was small, which might have been the reason for the failure to demonstrate significant changes in parameters other than insulin sensitivity and body composition. Second, methodological limitations included estimating insulin sensitivity using HOMA-IR and QUICKI, instead of hyperinsulinemic-euglycemic clamps. However, both HOMA-IR and QUICKI are validated techniques that strongly correlate with hyperinsulinemic-euglycemic clamps in children [22,35]. Although we did not use dual energy X-ray absorptiometry to measure body composition, bioelectrical impedance analyzer for children is a validated alternative tool to measure body composition, providing results that correlate well with dual energy X-ray absorptiometry [36].

Presently, even short-term supplementation with chromium appeared beneficial for insulin sensitivity and body composition in overweight children, in cooperation with modifications in life style. Further studies are encouraged to determine the long term efficacy and safety of chromium supplementation as an approach to alleviate IR and preventing its consequences in early life and in later years.

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