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The Influences of Chromium Supplementation on Metabolic Status in Patients with Type 2 Diabetes Mellitus and Coronary Heart Disease

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Abstract

This investigation was conducted to determine the effects of chromium supplementation on metabolic status in diabetic patients with coronary heart disease (CHD). This randomized, double-blind, placebo-controlled trial was performed in 64 diabetic patients with CHD between October 2017 and January 2018. Patients were randomly divided into two groups to obtain either 200 μg chromium ($n = 32$) or placebo ($n = 32$) for 12 weeks. Chromium supplementation significantly reduced body weight (− 0.9 ± 1.6 vs. + 0.1 ± 0.8 kg, $P = 0.001$), BMI (− 0.4 ± 0.7 vs. + 0.1 ± 0.3 kg/m^2, $P = 0.002$), fasting glucose (β − 11.03 mg/dL; 95% CI, − 18.97, − 3.09; $P = 0.007$), insulin (β − 1.33 μIU/mL; 95% CI, − 1.90, − 0.76; $P < 0.001$), and insulin resistance (β − 0.44; 95% CI, − 0.62, − 0.25; $P < 0.001$) and significantly increased insulin sensitivity (β 0.007; 95% CI, 0.003, 0.01; $P < 0.001$) compared with the placebo. In addition, taking chromium led to a significant reduction in serum high-sensitivity C-reactive protein (hs-CRP) (β − 0.49 mg/L; 95% CI, − 0.91, − 0.06; $P = 0.02$) and plasma malondialdehyde (MDA) levels (β − 0.22 μmol/L; 95% CI, − 0.35, − 0.10; $P = 0.001$); also, a significant rise in total antioxidant capacity (TAC) (β 84.54 mmol/L; 95% CI, 31.05, 138.02; $P = 0.002$) was observed in comparison with placebo. Additionally, chromium administration significantly reduced diastolic blood pressure (DBP) (β − 5.01 mmHg; 95% CI, − 9.04, − 0.97; $P = 0.01$) compared with the placebo. Overall, the 12-week supplementation of chromium to diabetic patients with CHD had beneficial impacts on weight, BMI, glycemic control, hs-CRP, TAC, MDA, and DBP.

Trial Registration www.irct.ir: http://www.irct.ir: IRCT20170513033941N30.

Keywords Chromium · Coronary heart disease · Metabolic status · Type 2 diabetes mellitus

Introduction

Type 2 diabetes mellitus (T2DM) is a global health concern, with high morbidity and mortality rates [1]. The predictions are indicator of a growing burden of diabetes, particularly in developing countries [1]. T2DM is characterized by hyperglycemia, insulin resistance, and dyslipidemia resulting in the occurrence of chronic inflammation, atherogenesis, and cardiac complications [2]. Based on the available evidence, coronary heart disease (CHD) is highly prevalent among diabetic patients and considered as the major cause of death [3]. In T2DM complicated with CHD, multiple approaches such as lifestyle modification and pharmacological therapy are used for the management of glycemic status, atherosclerosis, and prevention of cardiovascular events [4].

It is proposed that subclinical chromium deficiency may contribute to glucose intolerance, insulin resistance, and cardiovascular disease particularly in an aging population [5]. Some observational studies have shown that diabetic and cardiac patients have reduced chromium levels compared with healthy individuals [6, 7]. In patients with coronary artery disease, serum chromium levels were inversely correlated with glucose levels [8]. In addition, it is indicated that lower chromium levels in T2DM were associated with insulin resistance and dyslipidemia [9]. Previous evidence demonstrated that chromium supplementation decreased the risk of T2DM [10]. Moreover, in a meta-analysis study by Huang et al. [11], chromium supplementation to diabetic patients improved

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glycemic control and lipid profiles. In addition, we have previously reported that an 8-week supplementation with chromium significantly reduced biomarkers of inflammation and oxidative stress in women with polycystic ovary syndrome (PCOS) [12]. Documented evidence suggested that chromium supplementation to overweight and obese people significantly decreased body weight [13]. However, some studies failed to find any significant improvement in body weight or parameters related to inflammation, glycemic, and lipid control in patients with metabolic syndrome after chromium supplementation [14, 15]. In addition, in several meta-analyses, chromium supplementation did not affect or had little effect on serum lipids or glycemic control was found in people without diabetes [16], patients with T2DM [17], and diabetic patients [18].

Chromium possibly improves glucose homeostasis and insulin sensitivity through the effects on insulin receptors, glucose transporters (GLUT) translocation, and the activity of different enzymes involved in the insulin signaling cascade [19]. The increase in energy expenditure and insulin sensitivity by chromium may involve in weight management [20]. In addition, chromium exerts anti-inflammatory and antioxidative roles by inhibiting nuclear factor kappa B (NF-kB) activation and attenuating insulin resistance [21]. Therefore, we postulated that chromium supplementation may have beneficial effects in subjects with diabetes and CHD. The purpose of this study was to examine the effects of chromium supplementation on weight management, glycemic control, lipid profiles, biomarkers of inflammation, and oxidative stress in subjects with diabetes and CHD.

Methods

Study Population

The current study was a randomized, double-blind, placebo-controlled trial, registered in the Iranian registry of clinical trials (http://www.irct.ir: IRCT20170513033941N30), and was performed at a cardiology clinic affiliated to Kashan University of Medical Sciences (KAUMS), Kashan, Iran, between January 2018 and July 2018. The investigation was conducted based on the Declaration of Helsinki principals. The protocol of this study was approved by Research Ethics Committee, KAUMS, and Iran. Written informed consent was taken from all patients. Inclusion criteria were as follows: patients with T2DM, aged 40–85 years old with 2- and 3-vessel CHD. Diagnosis of T2DM was made according to the criteria of American Diabetes Association [22]. Furthermore, diagnosis of CHD was done according to the criteria of American Heart Association [23]. Patients who had one or more of the following criteria was considered as having CHD status: document of at least 50% stenosis in one or more coronary vessels upon cardiac catheterization assessed by the angiography, record of myocardial infarction, document of the exercise-induced ischemia by treadmill electrocardiogram or nuclear perfusion stress imaging, and a history of coronary revascularization [23]. Exclusion criteria were consuming chromium 3 months prior to the intervention, taking antioxidant and/or anti-inflammatory supplements such as vitamin E, vitamin C, and omega-3 fatty acids, change in type and dosage of antidiabetic and antilipidemic agents, and having an acute myocardial infarction, a cardiac surgery in the past 3 months, or renal or hepatic failure.

Study Design

Participants in each stratum were randomly allocated into two treatment groups to take either 200 μg chromium as chromium picolinate (21st Century, AZ, USA) or placebo (Barij Essence, Kashan, Iran) (n = 32 in each group) for 12 weeks. Due to the lack of evidence about the appropriate dosage of chromium for patients with T2DM and CHD, we used the abovementioned dose of chromium based on previous studies in T2DM elderly patients [24] and patients with women with polycystic ovary syndrome [25]. Color, shape, size, and package of placebos and chromium supplements were identical. Randomization assignment was conducted using computer-generated random numbers. Randomization and allocation were concealed from the investigators and participants until the final analyses were completed. The randomized allocation sequence, enrolling of participants, and their allocation to interventions were performed by trained staff at the cardiology clinic. Compliance with the consumption of placebos and chromium supplements was performed by examining the capsule containers. To increase compliance, all participants received brief daily cell phone reminders to take the supplements. All patients completed 3-day dietary intake records at weeks 1, 6, and 12 of treatment. For obtaining patients' nutrient intakes according to 3-day food records, Nutritionist IV software (First Databank, San Bruno, CA), which was adapted for Iranian food pattern, was applied. Anthropometric measures (Seca, Hamburg, Germany) recorded at baseline and also after the 12-week intervention in the cardiology clinic. All anthropometric measures were conducted by a trained nutritionist. In addition, nutritionist was blinded to the randomization assignments.

Outcomes

The homeostasis model of assessment-insulin resistance (HOMA-IR) and insulin levels were considered as the primary outcomes, but fasting plasma glucose (FPG), the quantitative insulin sensitivity check index (QUICKI), serum lipids, and biomarkers of inflammation and oxidative stress were considered as secondary outcomes. Fasting blood (10 mL) was taken at baseline after the 12-week intervention at Kashan Reference

Laboratory. Insulin levels were measured by ELISA kit (DiaMetra, Milano, Italy) with inter-assay and intra-assay coefficient variances (CVs) below 5%. HOMA-IR and QUICKI were assessed in accordance with the standard formula [26]. Enzymatic kits (Pars Azmun, Tehran, Iran) were used to estimate fasting plasma glucose (FPG) and lipid variables with inter- and intra-assay CVs below 5%. Hs-CRP levels were assessed by an ELISA kit (LDN, Nordhorn, Germany) with inter- and intra-assay CVs below 7%. Total nitrite by the Griess assay [27], total antioxidant capacity (TAC) using the method reported by Benzie and Strain [28], total glutathione (GSH) by Beutler et al. method [29], and MDA concentrations were determined by the spectrophotometric test [30] with inter- and intra-assay CVs below 5%. Systolic (SBP) and diastolic blood pressure (DBP) was determined using a sphygmomanometer (ALPK2, Zhejiang, China). Blood pressure values were reported in millimeters of mercury (mmHg).

Statistical Methods and Sample Size

Sample size formula for randomized clinical trial were used, where type 1 (α) and type 2 errors (β) were 0.05 and 0.20 (power = 80%), respectively. In a previous study [25], 1.61 as the SD and 1.18 as the change in mean (d) of HOMA-IR were used. According to the power calculation, in each group, 29 individuals were needed; after allowing for 5 dropouts in each group, the final sample size was 35 persons in each group.

The Kolmogorov-Smirnov test was used for checking the normality of data. To determine the differences in anthropometric measures and dietary intakes between treatment groups, the independent-samples t test was used. Paired-samples t test was used to detect within-group differences. Differences in proportions were evaluated by Fisher's exact test. Multiple linear regression models were used to evaluate treatment impacts on study outcomes after adjusting for confounding parameters, including baseline levels of each biochemical variable, age, and baseline BMI. The effect sizes were presented as the mean differences with 95% confidence intervals. The Pearson chi-square test was applied for comparison of categorical variables. P values < 0.05 were considered significant. The Statistical Package for Social Science version 18 (SPSS Inc., Chicago, Il, USA) was used for statistical analyses of this trial.

Data Availability The primary data for this study is available from the authors on direct request.

Results

Among patients in chromium and placebo groups, three participants were withdrawn due to personal reasons (Fig. 1). Finally, sixty-four patients (chromium (n = 32) and placebo (n = 32)) completed the trial. The compliance rate was high; two groups took more than 90% of capsules during the trial. No adverse effects were reported in T2DM patients with CHD while consuming chromium supplements.

No significant differences were seen between groups regarding mean of age, height, baseline, and end-of-trial weight and BMI (Table 1). Chromium supplementation significantly reduced body weight (− 0.9 ± 1.6 vs. + 0.1 ± 0.8 kg, P = 0.001) and BMI (− 0.4 ± 0.7 vs. + 0.1 ± 0.3 kg/m^2, P = 0.002) compared with the placebo. Furthermore, a significant within-group reduction in weight (P = 0.003) and BMI (P =

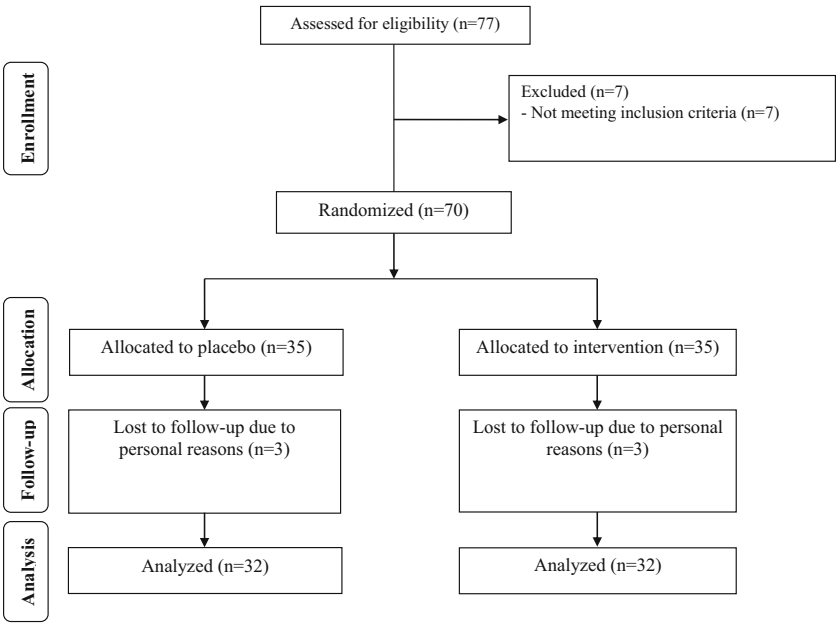

Fig. 1 Summary of patient flow diagram

Table 1 General characteristics of study participants at baseline study

	Placebo group (n = 32)	Chromium group (n = 32)	P^1
Age (years)	60.9 ± 7.7	58.0 ± 8.0	0.14
Height (cm)	160.8 ± 7.5	162.0 ± 9.8	0.58
Gender			
Female	15 (46.9%)	17 (53.1%)	
Male	17 (53.1%)	15 (46.9%)	0.61†
Weight (kg)			
Baseline	77.4 ± 11.9	79.7 ± 13.2	0.45
End-of-trial	77.5 ± 11.9	78.8 ± 12.8	0.68
P^2	0.30	0.003	
BMI (kg/m^2)			
Baseline	29.9 ± 3.8	30.4 ± 4.3	0.61
End-of-trial	29.9 ± 3.8	30.0 ± 4.1	0.92
P^2	0.29	0.006	
Aspirin 80 mg (%)	32 (100)	32 (100)	1.00†
Statin (%)	32 (100)	32 (100)	1.00†
Insulin therapy (%)	10 (31.3)	8 (25.0)	0.57†
Antidiabetic drugs (%)			
Monotherpy	17 (68.0)	16 (61.5)	
Combination therapy	8 (32.0)	10 (38.5)	0.62†

Data are means ± SDs

[1] Obtained from independent t test

[2] Obtained from paired-samples t test

[†] Obtained from Fisher's exact test

0.006) was seen in the chromium group. The mean smoking, taking antidiabetic and antilipidemic agents, hypertension rate, consumption of angiotensin-converting enzyme inhibitors (ACEI), aldosterone receptor blocker (ARB) drugs, and blocker drugs (β-blocker and calcium channel blocker) of the study participants were not statistically different between the two groups.

Macronutrient and micronutrient supplementation calculated based on the 3-day food record was not significantly different between the chromium and control groups (data not shown).

After the 12-week intervention, chromium supplementation significantly reduced FPG (β − 11.03 mg/dL; 95% CI, − 18.97, − 3.09; P = 0.007), insulin (β − 1.33 μIU/mL; 95% CI, − 1.90, − 0.76; P < 0.001), and HOMA-IR (β − 0.44; 95% CI, − 0.62, − 0.25; P < 0.001) and significantly increased QUICKI (β 0.007; 95% CI, 0.003, 0.01; P < 0.001) compared with the placebo (Table 2). In addition, taking chromium led to a significant reduction in serum hs-CRP (β − 0.49 mg/L; 95% CI, − 0.91, − 0.06; P = 0.02) and plasma MDA levels (β − 0.22 μmol/L; 95% CI, − 0.35, − 0.10; P = 0.001); also, a significant rise in TAC (β 84.54 mmol/L; 95% CI, 31.05, 138.02; P = 0.002) was observed in comparison with placebo. Additionally, chromium administration significantly reduced DBP (β − 5.01 mmHg; 95% CI, − 9.04, − 0.97; P = 0.01) compared with the placebo. Chromium supplementation did not affect triglycerides, VLDL-cholesterol, total cholesterol, LDL-cholesterol, HDL-cholesterol, and total cholesterol/HDL-cholesterol ratios, total nitrite, GSH levels, and SBP.

Discussion

In the current study, which to the best of our knowledge is the first of its kind, we found that the 12-week supplementation of chromium to diabetic patients with CHD had beneficial impacts on weight, BMI, glycemic control, hs-CRP, TAC, MDA, and DBP, but did not affect other metabolic profiles. Chromium supplementation may have an indirect role in DBP due to its beneficial effect on glycemic control and lipid profiles. It must be kept in mind that taking antidiabetic and antilipidemic agents would not influence our findings because individuals in both intervention and non-intervention groups were taking antidiabetic and antilipidemic agents. This should be taken into account in the interpretation of our findings. However, in the current study, observed changes in glycemic control, hs-CRP, TAC, MDA, and DBP was statistically significant; it was not clinically significant. Long-term intervention and higher dosage of chromium might result in greater changes in these variables.

Table 2 The effect of chromium supplementation on metabolic status in type 2 diabetic patients with coronary heart disease

Variables	Placebo group (n = 32)		Chromium group (n = 32)		Difference in outcome measures between chromium and placebo treatment groups[1]	
	Baseline	Week 12	Baseline	Week 12	β (95% CI)	P[2]
FPG (mg/dL)	123.6 ± 36.5	125.6 ± 35.3	129.9 ± 42.5	119.9 ± 33.8	− 11.03 (− 18.97,− 3.09)	0.007
Insulin (μIU/mL)	11.1 ± 3.1	11.1 ± 2.8	11.6 ± 1.5	10.2 ± 1.7	− 1.33 (− 1.90,− 0.76)	< 0.001
HOMA-IR	3.4 ± 1.5	3.4 ± 1.5	3.8 ± 1.5	3.3 ± 1.4	− 0.44 (− 0.62,− 0.25)	< 0.001
QUICKI	0.32 ± 0.01	0.32 ± 0.01	0.31 ± 0.01	0.32 ± 0.01	0.007 (0.003, 0.01)	< 0.001
Triglycerides (mg/dL)	131.0 ± 45.7	133.5 ± 41.9	140.1 ± 42.9	133.4 ± 37.5	− 8.79 (− 18.71, 1.13)	0.08
VLDL-cholesterol (mg/dL)	26.2 ± 9.1	26.7 ± 8.4	28.0 ± 8.6	26.7 ± 7.5	− 1.75 (− 3.74, 0.22)	0.08
Total cholesterol (mg/dL)	160.4 ± 34.8	161.3 ± 35.9	164.5 ± 43.7	166.2 ± 47.5	5.21 (− 11.92, 22.34)	0.54
LDL-cholesterol (mg/dL)	90.6 ± 37.2	92.8 ± 38.0	91.9 ± 39.6	95.3 ± 46.0	5.11 (− 12.00, 22.23)	0.55
HDL-cholesterol (mg/dL)	43.6 ± 6.5	41.9 ± 5.3	44.7 ± 8.9	44.2 ± 8.3	1.43 (− 0.52, 3.40)	0.14
Total cholesterol/HDL-cholesterol ratio	3.7 ± 1.2	3.9 ± 1.1	3.7 ± 0.9	1.4	0.001 (− 0.40, 0.40)	0.99
hs-CRP (mg/L)	4.5 ± 1.9	4.4 ± 1.9	5.2 ± 1.8	4.5 ± 2.6	− 0.49 (− 0.91,− 0.06)	0.02
Total nitrite (μmol/L)	32.8 ± 4.5	32.9 ± 4.3	31.6 ± 4.9	30.8 ± 4.5	− 1.14 (− 2.68, 0.40)	0.14
TAC (mmol/L)	992.0 ± 207.2	998.3 ± 227.9	1064.6 ± 114.1	1146.7 ± 75.8	84.54 (31.05, 138.02)	0.002
GSH (μmol/L)	615.7 ± 136.0	635.5 ± 148.3	655.4 ± 115.5	672.4 ± 109.4	10.02 (− 38.85, 58.89)	0.68
MDA (μmol/L)	2.8 ± 0.5	2.8 ± 0.6	2.7 ± 0.3	2.5 ± 0.2	− 0.22 (− 0.35,− 0.10)	0.001
SBP (mmHg)	129.5 ± 19.1	130.9 ± 18.8	126.6 ± 14.4	125.6 ± 13.7	− 3.65 (− 9.51, 2.21)	0.21
DBP (mmHg)	78.2 ± 10.7	78.9 ± 10.1	76.9 ± 7.2	73.6 ± 7.4	− 5.01 (− 9.04,− 0.97)	0.01

Data are mean ± SDs

[1] "Outcome measures" refers to the change in values of measures of interest between baseline and week 12. β (difference in the mean outcomes measures between treatment groups (chromium group = 1 and placebo group = 0))

[2] Obtained from multiple regression model (adjusted for baseline values of each biochemical variables, age, and baseline BMI)

DBP diastolic blood pressure, *FPG* fasting plasma glucose, *GSH* total glutathione, *HOMA-IR* homeostasis model of assessment-estimated insulin resistance, *hs-CRP* high-sensitivity C-reactive protein, *MDA* malondialdehyde, *QUICKI* quantitative insulin sensitivity check index, *SBP* systolic blood pressure, *TAC* total antioxidant capacity

Effects on Body Weight, Glycemic Control, and Lipid Profiles

T2DM is accompanied by insulin resistance and dyslipidemia. In addition, diabetic patients are susceptible for hyperglycemia-induced oxidative stress and inflammatory status which attributed to CHD [2]. Our study showed that chromium supplementation significantly decreased body weight and BMI in T2DM complicated with CHD. Consistent with the present data, in a meta-analysis study by Onakpoya et al. [13], chromium supplementation significantly reduced body weight in overweight and obese individuals. In addition, a 3-month chromium supplementation (1000 μg/day) to T2DM patients attenuated weight gain [31]. Also, chromium supplementation for 6 months (1000 μg/day) to women with PCOS led to a significant decrease in BMI [32]. However, another study did not show any significant effect on BMI after 8 weeks of chromium supplementation (500 μg/day) in patients with T2DM [33]. Overweight and obesity are associated with insulin resistance and T2DM which accelerate the progression of CHD and worsen its prognosis [34]. Weight loss in diabetic and coronary patients ameliorates insulin resistance and metabolic syndrome components, including dyslipidemia and hypertension [35, 36]. The beneficial effects of chromium on body weight may be related to the modulation of energy expenditure and the reduction of ghrelin response by increasing insulin sensitivity which regulates energy intake [20, 37].

In this research, we found that taking chromium supplements was associated with a decrease in FPG, insulin levels, and HOMA-IR and an increase in QUICKI without affecting lipid profiles in diabetic patients with CHD. Similar to our findings, chromium supplementation at a dosage of 400 μg/day for 3 months to T2DM patients decreased FPG, circulating insulin levels and HOMA-IR [38]. In addition, a 4-month chromium supplementation at a dosage of 600 μg/day to patients with poorly controlled T2DM improved FPG, while did not affect lipid variables [39]. Moreover, a 16-week chromium supplementation (400 μg/day) to patients with human immunodeficiency virus infection decreased insulin values and HOMA-IR and did not influence lipid parameters except for triglycerides [40]. In support with our study, a 2-week chromium supplementation (100 μg/day) followed by 6 weeks of chromium supplementation at dosage 200 μg/day did not affect lipid variables in T2DM patients [41]. However, 6 months

of chromium supplementation at dosage 500 μg or 1000 μg/day did not affect FPG, insulin levels, and HOMA-IR in individuals at risk for diabetes mellitus [42]. In contrast to our findings, an 8-week chromium supplementation (200 μg/day) improved triglycerides and HDL-cholesterol levels [43]. In patients with T2DM, insulin resistance and glucose disturbances are correlated with vascular stiffness and atherosclerosis [44]. Chromium is a central part of chromodulin, which involved in the insulin action [45, 46]. It also enhances beta cell sensitivity and increases the number of insulin receptors [45]. Moreover, chromium decreases protein tyrosine phosphatase 1B activity, increases mitogen-activated protein kinase function and insulin receptor phosphorylation, and promotes the translocation of GLUT4 in cell membrane, which in turn improves insulin sensitivity and glucose uptake [19, 47].

Effects on Biomarkers of Inflammation and Oxidative Stress

The findings of present study showed that consuming chromium supplements for 12 weeks led to a significant decrease in hs-CRP and MDA levels and a significant increase in TAC in diabetic individuals with CHD. In accordance with our findings, several animal investigations have shown that chromium administration led to a significant decrease in MDA and CRP concentrations [48–50]. In addition, we have previously reported that an 8-week chromium supplementation at a dosage of 200 μg/day to women with PCOS candidate for in vitro fertilization increased TAC and reduced MDA levels [51]. Moreover, supplementation with chromium, zinc, and magnesium for 24 weeks decreased CRP levels in patients with metabolic syndrome [52]. In contrast to the results of present study, a 16-week chromium supplementation (100 μg/day) to non-diabetic adults with obesity did not affect CRP and other inflammatory markers [14]. In diabetic patients, oxidative stress and elevated inflammatory mediators such as CRP are associated with endothelial dysfunction and the progression of macrovascular disease [53]. In addition, a significant positive correlation has been reported between circulating MDA levels and FPG in T2DM complicated with CHD [54]. Chromium may act as an indirect antioxidant via decreasing insulin levels and preventing the auto-oxidation of glucose [55]. In vitro exposure with chromium decreased lipid peroxidation in red blood cells exposed to high glucose, which in turn reduced oxidative stress [56]. It also contributes in anti-inflammatory process by modulation the activity of NF-kB [21].

The limitations of this study were few. Due to funding limitations, we did not measure chromium and HbA1c levels before and after the intervention. The next limitation was that gene expression related to lipid, insulin, inflammation, and oxidative damage in patients with diabetes who underwent CHD was not evaluated.

Conclusions

Overall, the 12-week supplementation of chromium to diabetic patients with CHD had beneficial impacts on weight, BMI, glycemic control, hs-CRP, TAC, MDA, and DBP, but did not affect other metabolic profiles.

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Author Contributions ZA: Conception, design, and statistical analysis, drafting of the manuscript, and supervision of the study.
AF, MM, FB, EA, and RS: Data collection and manuscript drafting.

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Compliance with Ethical Standards

The investigation was conducted based on the Declaration of Helsinki principals. The protocol of this study was approved by Research Ethics Committee, KAUMS, and Iran. Written informed consent was taken from all patients.

Ethics Approval and Consent to Participate All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki declaration and its later amendments.

Competing Interests The authors declare that they have no competing interests.

Abbreviations ACEI, angiotensin-converting enzyme inhibitors; ARB, aldosterone receptor blockers; FPG, fasting plasma glucose; GSH, total glutathione; HOMA-IR, homeostasis model of assessment-insulin resistance; HDL-cholesterol, high-density lipoprotein-cholesterol; Hs-CRP, high-sensitivity C-reactive protein; LDL-cholesterol, low-density lipoprotein-cholesterol; MDA, malondialdehyde; NO, nitric oxide; QUICKI, quantitative insulin sensitivity check index; VLDL-cholesterol, very low–density lipoprotein-cholesterol; TAC, total antioxidant capacity

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