Beneficial Effect of Chromium Supplementation on Serum Triglyceride Levels in NIDDM

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OBJECTIVE — To investigate the effect of chromium picolinate supplementation on the lipid profile of the predominantly Hispanic population of non-insulin-dependent diabetes mellitus (NIDDM) patients in San Antonio, Texas.

RESEARCH DESIGN AND METHODS — A prospective, double-blind, placebo-controlled, crossover study was performed on 14 men and 16 women. Initially, each patient was randomly assigned to receive either chromium picolinate or placebo for 2 months. This initial treatment phase was followed by a 2-month washout period. Subjects were then crossed-over and received the alternate capsule for an additional 2 months. Fasting blood glucose, HbA_{1c}, and serum lipids were compared at the end of each treatment phase.

RESULTS — Twenty-eight of the originally enrolled 30 patients completed the study. There were no adverse reactions to chromium reported. There were no differences noted between the control and chromium-treated subjects in glucose control, high-density lipoprotein cholesterol levels, or low-density lipoprotein cholesterol levels. Triglyceride (TG) levels were reduced significantly (17.4%; $P < 0.05$) during the 2 months of chromium supplementation.

CONCLUSIONS — Ours is the first report of a significant reduction in serum TGs in a group of NIDDM patients treated with chromium. The low cost and excellent safety profile of chromium make it an attractive lipid-lowering agent for this population. Long-term studies are needed to determine if the short-term changes in plasma lipids can be sustained.

Insulin resistance is felt to play a key role in the pathogenesis of lipid abnormalities commonly seen in non-insulin-dependent diabetes mellitus (NIDDM) patients (1–3). The trace element chromium and two molecules of nicotinic acid form a biologically active complex referred to as "glucose tolerance factor" (4,5), which has been reported to enhance the action of insulin. Jeejeebhoy (6) confirmed the importance of chromium in humans when he successfully treated an insulin-resistant diabetic patient with only chromium supplementation after she had become chromium deficient while being given parenteral nutrition for 3 years. Chromium deficiency has been associated with lipid abnormalities and an increased risk of atherosclerotic disease (7). Newman et al. (7) measured serum chromium levels in 32 subjects referred for selective coronary arteriography. Patients with catheterization-proven coronary disease had significantly lower serum chromium levels and higher serum triglyceride (TG) than patients without coronary disease.

Chromium deficiency may be common in NIDDM patients. The 1980 National Research Council of the National Academy of Sciences recommends a chromium intake of 50–200 μg/day (8), yet the standard North American diet is estimated to contain <50 μg/day of chromium (9). Moreover, Morris et al. (10–12) have shown that plasma chromium concentrations are lower in diabetic patients than in nondiabetic control patients (10) and that the depressed plasma chromium levels are related to elevated glucose concentrations (11,12). Unfortunately, it is difficult to accurately estimate serum chromium levels in many patients, because mean serum concentration is between 0.1 and 0.3 μg/l in normal individuals and the lower limit of detection in commercially available assays is 0.2 μg/l. Moreover, chromium is widely distributed throughout the body and there is no established standard for assessing total body chromium stores.

The purpose of our study was to investigate the effect of chromium picolinate supplementation on the lipid profile of the predominantly Hispanic population of NIDDM patients in San Antonio, Texas.

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NIDDM, non-insulin-dependent diabetes mellitus; TG, triglyceride; FBG, fasting blood glucose; LDL, low-density lipoprotein; HDL, high-density lipoprotein.

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Table 1—*Baseline hypoglycemic and hypolipidemic medications used by patients*

Glucose-lowering therapy	*n*	Lipid-lowering therapy	*n*
Diet alone	2	No therapy	28
Oral agents	11	Lovastatin	6
Insulin	14	Gemfibrozil	4
Insulin + oral agents	3	Combination therapy	2

Small changes were made in hypoglycemic therapy to try to optimize glucose control throughout the study period, as discussed in RESULTS.

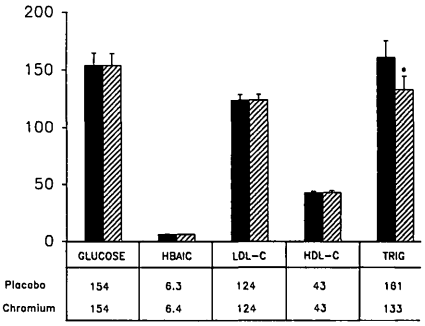

Figure 1—*Metabolic parameters measured at the end of each 2-month treatment phase (■, placebo vs. ▨, chromium). C, cholesterol. *TG levels were reduced significantly by 17.4% after chromium treatment (133 vs. 161 mg/dl; P < 0.05). Error bars (T) represent SE.*

RESEARCH DESIGN AND METHODS

— Thirty NIDDM patients between the ages of 32 and 65 were recruited from the diabetes clinics of Medical Center Hospital and the Audie Murphy Veterans Hospital in San Antonio, Texas. Exclusion criteria included untreated thyroid dysfunction, pregnancy, acute medical or psychiatric illness, renal insufficiency (serum creatinine >2.0 mg/dl), liver disease, ethanol or illicit drug use, steroid use, and poorly controlled diabetes (HbA_{1c} >10% or fasting blood glucose [FBG] >200 mg/dl). Patients who had been on a stable dose of lipid-lowering agent for 6 months were continued on that therapy. All studies were carried out in the General Clinical Research Center after obtaining informed consent. Approval of the study protocol was obtained through the institutional review board of the University of Texas Health Sciences Center at San Antonio.

This study used a prospective, double-blind, placebo-controlled, crossover design. Between June and November 1992, 14 men and 16 women were randomly assigned to receive a capsule of chromium picolinate (200 μg/day) or an identical placebo for 2 months. After completion of the initial treatment period, no medication was taken for 2 months (hence, a washout period). Subjects then were crossed-over and treated with the alternate capsule for an additional 2 months. Compliance with medication use was documented by pill count.

A physical examination was performed at study entry and at 2-month intervals thereafter. Laboratory analysis at each appointment included a fasting lipid profile, HbA_{1c}, serum chemistries, complete blood count, thyroid function tests, a pregnancy test (if indicated), and serum chromium concentration. Patients were asked to continue their pre-study dietary, smoking, and exercise routines during the investigation.

All specimens for chromium analysis were run in a single assay at Mayo Medical Laboratories at the termination of the study. Serum chromium concentrations were determined by the flameless atomic absorption spectrometry method. A Bio-Rad (Richmond, CA) urine metal control was used as a standard in this assay. The intra-assay coefficient of variation was <10%. Changes (chromium versus placebo) in total cholesterol, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, TGs, HbA_{1c}, and FBG levels were compared using paired Student's *t* tests.

RESULTS

— Twenty-eight of the originally enrolled 30 patients completed the study. One patient with known coronary disease was withdrawn after being hospitalized for unstable angina. A second patient was removed from the study because of worsening hypertension that occurred while taking placebo. The average age of the study population was 56 (range 32–65). As a whole, the group was moderately obese with a mean body mass index of 31.2 kg/m^2. The medications used to control blood glucose and lipids are listed in Table 1. During chromium therapy, insulin dosage was decreased slightly in one subject and increased in one subject, while oral hypoglycemic therapy was increased in two subjects. During placebo therapy, insulin dosage was decreased in one subject, increased in two subjects, and the dosage of oral hypoglycemic agents was increased in two subjects. Insulin was added to oral hypoglycemic therapy in one patient during the chromium period and one patient during the placebo period. Pharmacotherapy for hyperlipidemia was unchanged throughout the study.

There were no adverse reactions to chromium reported in this study. Compliance to therapy was excellent in both groups with all patients having <10 capsules remaining at the end of each study interval. All but two subjects had undetectable levels of serum chromium before study entry. At the end of 2 months of chromium supplementation, all patients had detectable serum levels with a mean concentration of 0.85 μg/l. During the placebo period, there was a 0.6% increase in mean body weight versus a 0.2% weight increase during chromium supplementation.

The metabolic parameters measured at the end of each 2-month treatment phase (chromium versus placebo) are shown in Fig. 1. The metabolic results were not affected by the order of chromium treatment as assessed by the two

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period crossover analysis of variance. There was no difference in glucose control between the chromium-treated and placebo groups as evidenced by similar FBG levels and HbA_{1c} concentrations. Additionally, LDL cholesterol and HDL cholesterol levels were identical in each group. TG levels were reduced significantly by 17.4% after chromium treatment (133 mg/dl versus 161 mg/dl; $P < 0.05$).

CONCLUSIONS — Our prospective, placebo-controlled, double-blind, randomized, crossover trial of 28 NIDDM patients showed that dietary supplementation with chromium picolinate (200 μg/day) for 2 months was associated with an average reduction in TG levels of 17.4% when compared with the placebo treatment phase. No differences were noted in LDL cholesterol or HDL cholesterol levels. FBG concentrations and HbA_{1c} levels were similar in both treatment phases. Compliance with the study was excellent and no side effects were reported.

Several studies have reported a beneficial effect of chromium on serum lipids. An increase in HDL cholesterol levels was observed after chromium treatment in 23 healthy volunteers (13) and in 72 hypertensive men on β-blockers (14). A significant reduction in LDL cholesterol and an increase in HDL cholesterol was seen in 27 patients treated with 20 g of a high chromium brewer's yeast for 8 weeks (15). Similarly, Press et al. (16) reported significant reductions in LDL cholesterol, apolipoprotein B, and an increase in apolipoprotein A-1 in 28 healthy volunteers treated with chromium picolinate for 42 days. Abraham et al. (17) treated 76 patients with established atherosclerotic disease with either chromium or placebo for 11 months. In this prospective, randomized trial, which included 25 diabetic patients, serum TGs were significantly lowered and HDL cholesterol significantly increased.

Ours is the first report of a significant reduction in serum TGs in a group of NIDDM patients treated with chromium. No change was seen in FBG, cholesterol, or TG levels when inorganic chromium trichloride and a brewer's yeast that contained chromium were administered to 43 diabetic men for 4 months each (18). Similarly, no change in serum total cholesterol, TGs, HDL cholesterol, or LDL cholesterol was noted in a placebo-controlled, double-blind, crossover study of 10 NIDDM patients given 200 μg of trivalent chromium daily for 6 weeks (19). The lack of improvement in diabetic dyslipidemia reported in these studies is surprising, considering that chromium has been shown to improve β-cell sensitivity to glucose (20) and decrease insulin resistance (13). It is possible that these earlier studies of chromium supplementation in diabetic patients failed to show any benefit because their study subjects were not chromium deficient. Our patient population is almost certainly chromium deficient with all but two patients having undetectable plasma chromium levels (<0.2 μg/l). Alternatively, the chromium salts, high chromium yeast, or other organic forms of chromium used in the above studies may have provided inadequate amounts of bioavailable chromium. Picolinic acid is present in intestinal cells and is felt to be a naturally occurring ligand that facilitates absorption of ions (16). Thus chromium, when bound to picolinate, forms an organic complex with improved bioavailability.

Atherosclerotic disease is responsible for over 75% of hospital admissions (21) and 80% of all mortality (22) in patients with NIDDM. Diabetic dyslipidemia is felt to be a major risk factor for coronary artery disease in this population and was found in 60% of NIDDM patients in the San Antonio Heart Study (23). The 17% reduction in plasma TG levels seen in NIDDM patients in this study with chromium supplementation should be associated with a reduction in their risk of atherosclerotic disease. Elevated TG levels are positively and independently associated with an increased risk of heart disease in this population (24,25). In the Paris Prospective Study, 943 middle-aged men with diabetes or impaired glucose tolerance were followed for a mean of 11 years. An elevated plasma TG level was the only independent risk factor for coronary heart disease identified on multivariate analysis (24).

The low cost (<$5.00/month) and lack of side effects of chromium (26) make it an attractive lipid-lowering agent for diabetic patients. Long-term studies of chromium supplementation in NIDDM patients are needed to determine if improvement in insulin sensitivity and diabetic dyslipidemia will be sustained and result in a reduction in atherosclerotic vascular disease.

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