Hypocholesterolemic Effects of Nicotinic Acid and Chromium Supplementation

Martin Urberg, MD, Judith Benyi, DO, and Reynold John, MD, PhD
Detroit and New Baltimore, Michigan

During the course of a study of the hypoglycemic effects of nicotinic acid and chromium on humans, two hypercholesterolemic subjects were found to experience clinically significant decreases in serum cholesterol levels. These subjects have now been followed for one year. The first subject had a cholesterol level of 10.33 mmol/L (399 mg/dL). Daily supplementation for four weeks with 100 mg of nicotinic acid (niacin) and 200 μg of chromium chloride led to a decrease in serum cholesterol to 8.86 mmol/L (342 mg/dL). Further supplementation for four months led to a further decrease in serum cholesterol to 7.25 mmol/L (280 mg/dL). The second subject had a cholesterol level of 8.73 mmol/L (337 mg/dL). Four weeks of supplementation lowered the level to 6.73 mmol/L (260 mg/dL). When supplementation was discontinued, the cholesterol level rose slightly. When supplementation was reinstituted, the cholesterol level decreased to 6.68 mmol/L (258 mg/dL).

During the course of a study of the hypoglycemic effects of dietary supplementation with nicotinic acid (niacin) and chromium on humans, two hypercholesterolemic subjects were found to experience clinically significant decreases in serum cholesterol levels after four weeks of supplementation. When the hypocholesterolemic effects of supplementation became known, the subjects were asked to take the supplements again for a longer period. These subjects have now been followed for one year. These cases suggest that supplementation with dietary levels of nicotinic acid and chromium has a clinically significant hypocholesterolemic effect.

METHODS

The two subjects were known hypercholesterolemic patients who had no acute illness and were not diabetic. They both had histories of untreated hypercholesterolemia, which had been documented by automated chemistry screening (SMA-12) measurements on their charts. They were informed of the nature of the study and were requested to sign an informed consent form.

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From the Department of Family Medicine, Wayne State University, Detroit, Michigan. Requests for reprints should be addressed to Dr. Martin Urberg, 4J University Health Center, 4201 St. Antoine, Detroit, MI 48201.

Chromium supplements (200 μg as chromium chloride) were purchased locally. Nicotinic acid tablets (100 mg) were supplied by a pharmaceutical company (E. R. Squibb and Sons). Each subject was given dated envelopes containing one nicotinic acid tablet and one chromium chloride capsule to take daily for four weeks for the first supplementation period. For the subsequent supplementation period, subjects were given bottles of 100 niacin tablets and 100 chromium capsules. Fasting serum cholesterol was measured before starting supplementation and at intervals thereafter. Cholesterol levels were measured by the cholesterol oxidase method at the Detroit Receiving Hospital laboratory. Measured cholesterol levels are known to vary widely from laboratory to laboratory and from method to method,[1] so cholesterol levels from the SMA-12 autoanalyzer that document the preexisting hypercholesterolemia are identified as such. Subjects agreed not to make any dietary changes during the supplementation periods. The study was approved by the Human and Animal Investigations Committee of Wayne State University.

RESULTS

Case 1

The first patient, a moderately obese 55-year-old woman, was being treated for hypertension with one hydrochlo-

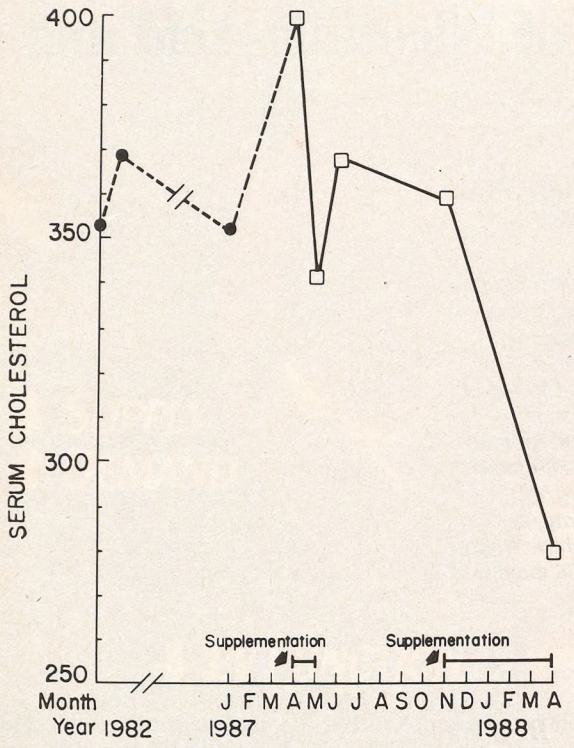

Figure 1. Serum cholesterol response to supplementation with nicotinic acid and chromium in subject No. 1. Horizontal bars indicated by two arrows on graph show the supplementation period. Solid dots indicate cholesterol measurements done in the SMA-12 multianalyzer

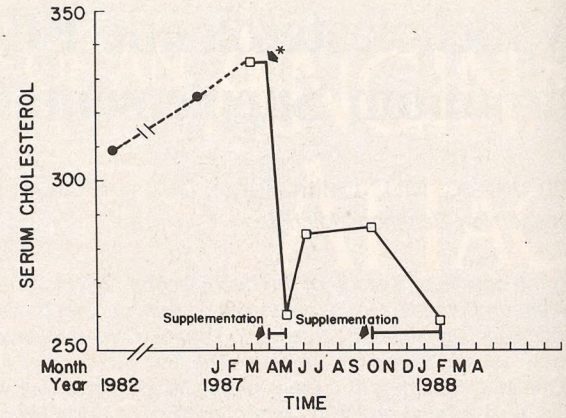

Figure 2. Serum cholesterol response to supplementation with nicotinic acid and chromium in subject No. 2. Horizontal bars indicated by two arrows on graph show the supplementation period. Asterisk with arrow indicates that cholesterol was taken in March but supplementation begun in April. Solid dots indicate cholesterol measurements done in the SMA-12 multianalyzer

rothiazide-triamterene capsule daily and was otherwise in good health. She was first noted to have elevated cholesterol 9.14 mmol/L (353 mg/dL) in 1982 on routine SMA-12 screening. In April 1987, her cholesterol level was found to be 10.33 mmol/L (399 mg/dL). After supplementation for four weeks, her cholesterol level dropped to 8.86 mmol/L (342 mg/dL). After supplementation was discontinued, her cholesterol level rose slightly but did not reach the earlier level. Supplementation was restarted in November 1987, and her cholesterol level dropped to 7.25 mmol/L (280 mg/dL). Her cholesterol data are displayed in Figure 1.

Case 2

The second patient was a 62-year-old woman, also moderately obese, who was being treated for mild hypertension with a hydrochlorothiazide-triamterene combination. She was also taking low-dose amitriptyline (10 mg twice a day) and haloperidol (0.5 mg daily) for an earlier nervous breakdown. In 1982 her cholesterol level was found to be 7.98 mmol/L (308 mg/dL) on the SMA-12. In March 1987, she had a cholesterol level of 8.73 mmol/L (337 mg/dL). After supplementation, her cholesterol level dropped to 6.73 mmol/L (260 mg/dL). When supplementation was discontinued, her cholesterol rose slightly. After supplementation was restarted, the cholesterol level again declined. Her cholesterol data are displayed in Figure 2.

DISCUSSION

The cases presented here demonstrate a clinically significant and persistent improvement in serum cholesterol levels during simultaneous supplementation with dietary levels of chromium chloride and nicotinic acid in patients with abnormally high cholesterol levels. Serum cholesterol levels were seen to decrease in both cases during periods of supplementation. When supplementation was stopped, the cholesterol levels began to rise slowly. When supplementation was restarted, the cholesterol levels again decreased. This finding suggests that in these patients hypercholesterolemia was due, at least in part, to a nutritional deficiency of chromium and nicotinic acid.

Chromium deficiency has been shown to lead to impaired glucose tolerance,[2,3] increased cholesterol levels,

and advanced atherosclerosis[4] in animals, and to lead to insulin-resistant diabetes in humans.[5] It has also been associated with atherosclerotic disease in humans. Schroeder and colleagues[6] reported that patients who died with atherosclerotic heart disease were relatively chromium-depleted compared with patients who died of other causes. Furthermore, chromium levels in atherosclerotic plaque were found to be very low compared with other tissues.

The very encouraging animal studies linking chromium supplementation to decreased serum cholesterol levels and protection from atherosclerosis[7–9] have led to several studies attempting to demonstrate a hypocholesterolemic effect of chromium supplementation in humans. Results of these studies have been mixed. Elwood et al[10] reported that eight weeks of supplementation with 24 μg of chromium daily as chromium-rich brewer's yeast led to large changes in serum cholesterol both up and down. The net effect for 16 subjects was a decrease of 0.62 mmol/L (24 mg/dL). Offenbacker and Pi-Sunyer[11] reported a decrease in total cholesterol from 6.66 mmol/L (257 mg/dL) to 5.88 mmol/L (227 mg/dL) in 12 institutionalized elderly adults after eight weeks of supplementation with 200 μg of chromium daily. They repeated the study with a group of noninstitutionalized elderly patients and found no changes.[12] Riales and Albrink[13] reported a slight increase in high-density lipoprotein cholesterol after 12 weeks of supplementation with chromium chloride, but no changes in total cholesterol were found. Unfortunately, no long-term benefits of chromium supplementation have been reported, and the possible therapeutic potential of chromium supplementation in hypercholesterolemia has not been realized.

Schwarz and Mertz[3] demonstrated that nicotinic acid was involved in an active complex of chromium in mammalian systems, suggesting that nicotinic acid is necessary for the metabolic activity of chromium. Nicotinic acid reduces cholesterol levels in humans.[14] The doses required (1 to 4.5 g daily), however, are in the pharmacological range, not in the dietary range. Nicotinic acid at these levels has been shown to lead to impaired glucose tolerance because of insulin resistance.[15–17] The lowest daily dose of nicotinic acid that has been reported to be effective in lowering cholesterol is 750 mg.[18] Supplementation with dietary levels of nicotinic acid have been shown to have a short-lived hypoglycemic effect,[19] but hypocholesterolemic effects have not been reported, although there are no reports that demonstrate that 100 mg of nicotinic acid daily is without effect.

Previous reports from Wayne State University,[20,21] on the other hand, showed that nicotinic acid in dietary amounts potentiated the hypoglycemic effects of chromium supplementation in humans. Elderly subjects given 100 mg of nicotinic acid and 200 μg of chromium as chromium chloride daily experienced an improvement of 14.8 percent in glucose tolerance as measured by the area under the glucose tolerance curve.[20] No effect was seen from nicotinic acid or chromium alone. Furthermore, adding nicotinic acid and chromium in levels of 10 parts per billion to the assay medium improved insulin binding to transformed monocytes in vitro.[21] No effect was seen when either nicotinic acid or chromium alone was added to the medium. Animal feeds are routinely supplemented with nicotinic acid as the niacin source, so the animal chromium supplementation studies were in fact carried out in the presence of adequate nicotinic acid. The nicotinic acid content of the human diet is unknown but probably small.

The cases reported here demonstrate that dietary supplementation with nicotinic acid and chromium led to a clinically significant decrease in total serum cholesterol in two subjects. That no persistent lowering of cholesterol levels has been demonstrated with either nicotinic acid or chromium alone at these levels suggests that both are required simultaneously for optimal benefit. Further controlled studies are needed to determine the independent effects of these two nutrients on cholesterol control in humans.

Acknowledgment

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