

# Chromium Picolinate Supplementation for Diabetes Mellitus

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Chromium picolinate is a widely available nutritional supplement marketed for a plethora of afflictions. There is some evidence, including results from human studies, that it has a role in glucose homeostasis. We report the case of a 28-year-old woman with an 18-year history of type 1 diabetes mellitus whose glycosylated hemoglobin (Hb A<sub>1c</sub>) declined from 11.3% to 7.9% 3 months after initiation of chromium picolinate, 200 µg 3 times daily. Chromium picolinate continues to fall squarely within the scope of "alternative medicine," with both unproven benefits and unknown risks. It deserves closer scrutiny with additional prospective, randomized, double-blind, placebo-controlled trials to evaluate its efficacy in improving outcomes in patients with diabetes. A brief review of the literature was done to assist physicians who are being called upon to counsel and treat patients who are engaging in alternative therapies.

**KEY WORDS.** Diabetes mellitus; chromium; alternative medicine; dietary supplementation. (*J Fam Pract* 1998, 46:83-86)

The hypothesis that chromium is involved as a factor in glucose tolerance dates to studies done in the 1950s and 1960s demonstrating its role in the restoration of glucose tolerance in rats.<sup>1,2</sup> Subsequently, it has been proposed that chromium is an essential micronutrient in humans and that its deficiency state causes abnormalities in carbohydrate metabolism. Although glucose intolerance has been the most consistently observed effect of chromium depletion, whether pharmacologic chromium supplementation improves clinical control in patients with diabetes mellitus has been more controversial.<sup>2</sup> We report the case of a patient with type 1 diabetes mellitus who appears to have benefited from chromium picolinate supplementation.

## CASE REPORT

A 28-year-old white woman had an 18-year history of type 1 diabetes mellitus. She had a reasonable diet, good hygiene and self-care, and kept her appointments regularly; she also appeared compliant with medical recommendations. She had a family history of diabetic retinopathy, for which she was being followed by an ophthalmologist, but had

no evident macrovascular, renal, or neurologic disease. In addition to adhering to a diet recommended for patients with diabetes, she used intermediate-acting insulin (Humulin N), 20 units in the morning and 10 units in the evening. She used a home monitor to take blood glucose measurements 3 times a day and was faithful in recording the values in a log book. She never smoked and never drank alcoholic beverages. Her family history was remarkable for diabetes mellitus among multiple siblings and other relatives.

On physical examination, the patient's vital signs were within normal limits. She weighed 120 lb. and was 65 in. tall. The remainder of the physical examination was unremarkable. Laboratory evaluation showed creatinine, 1.2 mg/dL; thyroid-stimulating hormone, 0.73 µU/mL; complete blood count, within normal range; serum albumin, 4.0 g/dL; glycosylated hemoglobin (Hb A<sub>1c</sub>) 11.3%; and urinalysis, negative for protein. Screening studies for microalbuminuria were normal.

The patient's Hb A<sub>1c</sub> was 11.3%; the lowest of several successive prior values was 9.9%. The patient began chromium picolinate, 200 µg 3 times per day with meals. Three months after initiating this supplementation, the patient reported improved home glucose values, which appeared to be about 30 to 60 mg/dL lower than corresponding values before she took chromium picolinate. Repeat Hb A<sub>1c</sub> value was 7.9%. During this period, there were no other elicitable substantive changes

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in medical or other circumstances to explain her improved glucose control.

## ■ DISCUSSION

This case indicates that there might be a subset of patients with diabetes that shows improvement in blood glucose control when taking chromium picolinate as a supplement. Especially when only one patient is involved, there are many other potential explanations. Even if improved glucose control were to be definitively shown through further study, it would remain to be shown that this would improve patients' outcomes with respect to both overall and diabetic morbidity and mortality.

It is generally accepted that chromium is an essential trace element in human nutrition. However, study of chromium deficiency, even in animals, has been hampered because (1) chromium is so ubiquitous in the environment that it is extremely difficult to eliminate from the diet; (2) chromium assays are difficult to perform accurately because incidental and unrecognized contamination may result in reporting many times the amount of chromium contained in the original sample; and (3) there is no direct biologic measure of chromium depletion or repletion. Some authors feel that all studies prior to 1978 are unreliable because of unrecognized dietary chromium and contamination of assays.<sup>3</sup> Although chromium levels in blood, urine, and hair can be accurately assessed, none of these levels accurately reflects body chromium stores.<sup>4</sup> Because of these factors, the role of chromium is still being elucidated.

## LITERATURE REVIEW

We reviewed some of the literature that addresses what is known about the potential relationship between chromium picolinate and glucose homeostasis. In animals, researchers linked trivalent chromium and glucose metabolism as early as the 1950s.<sup>1,5,6</sup> The first reports in humans regarding a possible link between chromium and carbohydrate metabolism were in patients on long-term, chromium-deficient total parenteral nutrition. After unexplained loss of good glucose control in these patients, supplementation with chromium restored normal glucose tolerance.<sup>7,9</sup> In these cases, within a few days of supplementation with chromium, supplemental insulin that had been required for glucose control could be discontinued.

Subsequent studies of chromium supplementation in other patient groups were conflicting, with some investigators concluding that chromium supplementation improves glucose tolerance<sup>10</sup> and others finding no evidence of benefit.<sup>11-14</sup> In one study that did not find evidence that chromium benefits glucose tolerance, chromium was found to enhance insulin secretion.<sup>11</sup> In another, after 6 months of chromium picolinate supplementation, there was a decline in mean serum triglycerides of 84 mg/dL (221.4 to 177.1 mg/dL), in mean blood glucose on the three determinations during a 2-hour glucose tolerance test of 12 mg/dL (136.9 to 124.9 mg/dL), and in the mean 2-hour glucose value of 16 mg/dL (147.7 to 131.5 mg/dL).<sup>12</sup> However, there was a statistically significant weight loss in the chromium group (body mass index 29.9 to 29.1 kg/m<sup>2</sup>), to which the authors ascribed to these changes in glucose and lipids. There were 13 subjects in the chromium group and 11 subjects in the placebo group, increasing the likelihood of failing to find a true difference (type II error). Support for this thesis is provided by two prospective, double-blind, placebo-controlled, crossover studies demonstrating statistically significant favorable effects of chromium picolinate supplementation on lipids in patients with type 2 diabetes mellitus.<sup>15,16</sup>

In more recent human studies, Ravina and colleagues<sup>17</sup> compared chromium picolinate (200 µg per day) with a placebo in 48 patients with type 1 diabetes and 114 patients with type 2 diabetes. In contrast to the placebo, chromium supplementation reduced the need for insulin and oral hypoglycemic medications in about 70% of diabetic patients.<sup>17</sup> Perhaps the most promising study, sponsored by the US Department of Agriculture and published only in preliminary form, was reported at the 1996 meeting of the American Diabetes Association.<sup>18,19</sup> Conducted in China, this randomized, double-blind, placebo-controlled study, involving 180 patients with type 2 diabetes mellitus, found that patients had significant improvements in lipids and Hb A<sub>1c</sub> levels within 4 months of beginning supplementation with chromium picolinate. After 4 months, Hb A<sub>1c</sub> was 8.5% in the placebo group; 7.5% in the 200-µg/day supplementation group; and 6.6% in the 500-µg twice-daily group. The differences in the Chinese and American diet may partly account for these findings. It is more likely that the Chinese diet is deficient in chromium, and therefore the results of



supplementing the Chinese diet may produce results in that population that would not be reproducible in the US population.

In a randomized trial of pregnant women with gestational diabetes, supplementation with chromium picolinate (4 µg/kg/day) resulted, after 8 weeks, in lower fasting plasma glucose and insulin levels and lower peak glucose and insulin responses to 100-g oral glucose load. However, in women with severe glucose intolerance, these doses of chromium appeared to have no beneficial effect on glucose metabolism.<sup>2</sup> There were no side effects evident from this supplementation in any of these studies.

### BIOLOGICAL EFFECTS OF CHROMIUM PICOLINATE

Regarding the specific role of the chromium and the picolinate components, chromium picolinate increased glucose uptake by skeletal muscle cells in cultures but other chromium complexes were ineffective. In an *in vivo* assay, dietary supplements of chromium picolinate decreased hemoglobin glycation in aging rats, but none of the other chromium complexes demonstrated such activity.<sup>20</sup> Insulin internalization and glucose uptake were markedly increased in muscle cells cultured in a medium that contained chromium picolinate. The effect was specific for chromium picolinate; neither zinc picolinate nor any other form of chromium tested was effective.<sup>21</sup> Therefore, it appears that it is neither specifically the chromium nor the picolinate, but the combination that possesses the ability to alter glucose metabolism. Some purported actions of chromium picolinate may result from the actions of picolinic acid on the central nervous system. Analogues of picolinic acid have been shown to induce profound alterations in the metabolism of serotonin, dopamine, and norepinephrine in the brain.<sup>22</sup> There is no evidence that the reported central effects of picolinate influence glucose metabolism.

**Side Effects** Little is known about the potential long-term toxicity of chromium picolinate, a trivalent form of chromium. In high-exposure industrial use, the hexavalent form of chromium (VI) is a known human respiratory tract carcinogen. There is no evidence of any carcinogenesis in humans from the trivalent form of chromium (III) found in chromium picolinate.<sup>23,24</sup> There is one anecdotal report of cognitive disturbance in a patient who

used chromium picolinate supplementation. The patient, engaged in psychotherapy because of a marital separation, experienced on several occasions within an hour after taking the supplement mild, brief episodes of "feeling funny," a "disruption" of his thinking, "short-circuiting," and mental slowness. He had difficulty completing routine tasks, but experienced no concurrent anxiety or autonomic symptoms. With each episode, symptoms subsided within 2 hours of onset.<sup>22,25</sup>

### CHROMIUM PICOLINATE AS ALTERNATIVE THERAPY

Patients are using alternative therapies; some sources claim 50% of the American population use dietary supplements.<sup>22</sup> Often, patients feel unable to communicate with their physicians about these practices.<sup>29</sup> "Alternative" and "herbal" are not synonymous with "inactive" and "harmless"; such simple things as taking medication with a glass of acidic fruit juice can dramatically alter absorption and serum levels. Marketing chromium picolinate as a nutritional supplement complicates any claim made for it. In addition to glucose metabolism and lipid profiles, it has been reported to improve mood, sleep, energy level, vision, and acne; reduce body fat content and addictive behaviors; and increase lean body mass and longevity. Because of its status as a nutritional supplement, there is little rigorous scientific data supporting these claims.<sup>22</sup> Furthermore, in the United States, one company holds the exclusive patent rights for its manufacture.<sup>23</sup> Moreover, the company's vice president for research and development has published several articles about chromium picolinate in which there are no clear disclaimers disclosing his potential conflict of interest.<sup>26-28</sup> However, combined with such trials as those of Ravina and coworkers<sup>17</sup> and Anderson and colleagues,<sup>18</sup> the accumulating data lend sufficient credibility to claims that chromium picolinate may influence diabetic control to warrant further, more definitive investigation.

### CONCLUSIONS

It remains to be determined if any patients with diabetes truly respond to chromium picolinate and, if so, which ones. If there is benefit, it is important to demonstrate benefit not only in improved glucose control, but also for more definitive, patient-oriented outcomes (for example, retinopathy, renal



preservation, and life expectancy). In the meantime, there is at least equally scant scientific evidence of harm from chromium picolinate. Physicians may encounter patients with diabetes who have learned about chromium picolinate from alternative sources and who cannot afford medications such as troglitazone (\$5 per day), for which long-term risk and patient-oriented data are also sparse, but who can afford chromium picolinate (\$5 to \$10 per month). If these patients, by taking chromium picolinate supplements, demonstrate quantifiable reductions in blood glucose measurements and reductions in hemoglobin A<sub>1c</sub> without apparent toxicity, they would meet recently published criteria for continued use of this alternative therapy.<sup>29</sup>

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