

High Insulin Requirement Versus High Chromium Requirement in Patients Nourished With Total Parenteral Nutrition

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INTRODUCTION

Trivalent chromium, in contrast to the toxic hexavalent chromium, is an essential trace element required for insulin function, normal lipid metabolism, and nervous system function.^{1,2} Studies have shown that patients with type 2 diabetes mellitus (DM) do not retain chromium as well as healthy people and therefore may have a higher requirement for chromium.^{3,4} Glucocorticoid administration raises blood glucose levels and has been shown to increase chromium losses.⁵ The infusion of large amounts of glucose as in total parenteral nutrition (TPN) is known to increase renal excretion of chromium.⁶ Negative chromium balances in patients on short-term TPN have been reported.⁶

The commercially available multi-trace element formulation, designed for adult patients nourished solely by TPN, provides 10 μg of chromium per day. This amount may be inadequate in many patients.^{1,7} There is no standard normal blood chromium range established for patients on continuous TPN infusion. When blood glucose is high, chromium moves from body stores into the blood. The high blood chromium level during TPN infusion does not reflect body storage of chromium.⁸ Observing the effect of supplemental chromium can identify patients with high chromium requirements. Therefore, we conducted a study in patients nourished solely by TPN who required a substantial amount of exogenous insulin.

Recent cell culture and in vivo animal studies have shown that chromium picolinate generates oxidative stress and DNA damage,^{9,10} but there is no conclusive evidence on the toxic effects of chromium picolinate in humans. Chromium chloride, which is the form of chromium used in TPN, has no reported toxicity. Chromium, 200 to 250 $\mu\text{g}/\text{d}$ for a period of 2 wk or longer, has been given to TPN patients suspected to be deficient in chromium.^{1,2} We chose a small supplemental dose for a very short period as a test dose to identify patients with high chromium requirements. The duration of observation of chromium supplementation was planned at 5 d (2 d of chromium supplementation and 3 d of continued observation post-supplementation) based on the responses reported by previous studies.^{2,11}

MATERIALS AND METHODS

All acute-care patients meeting the following criteria were included: 1) anticipated need for TPN without oral or enteral intake for 7 or more consecutive days; 2) no renal or hepatic insufficiency; 3) not pregnant; 4) requiring more than 20 U of exogenous

insulin to keep blood glucose between 6.67 and 10.00 mM/L (120 to 180 mg/dL); and 5) informed consent provided by the patient or the patient's agent.

Chromium supplementation (in the form of chromium chloride) provided 1) the usual amount of chromium for 2 d (10 $\mu\text{g}/\text{d}$ in a multi-trace element formulation); 2) supplementation with 40 μg of chromium for 2 d (total amount of chromium, 50 $\mu\text{g}/\text{d}$); and then 3) the usual amount of chromium for 3 d.

RESULTS

Five patients completed (or partly completed) the study protocol. Two showed possible benefit from supplemental chromium, and three showed no or little possible benefit. No adverse effects from the supplementation could be identified. Summary case reports of the five subjects follow. TPN formulations were administered as a total nutrient admixture of amino acids, dextrose, lipid, electrolytes, and the usual amounts of vitamins and trace elements. Table I shows the responses to supplemental chromium by the two subjects who showed possible benefit.

Summary Case Report of Subject MR

A 79-y-old male was admitted with the chief complaint of aspiration pneumonia, possibly secondary to tube feeding. The medical history consisted of atrial fibrillation, congestive heart failure, hypertension, peripheral vascular disease, depression, and anemia. The surgical history consisted of bilateral above knee amputation and percutaneous endoscopic gastrostomy placement. The body mass index (BMI) was 20.5 kg/m^2 (Table I).

The patient showed possible benefit from supplemental chromium as shown by the decreased amount of insulin needed to control blood glucose while the infection increased (white blood cell count and temperature increased). The benefit lasted throughout the 3 d after the discontinuation of supplementation. Decreasing renal function (increasing serum creatinine) can prolong the half-life of insulin and may have resulted in reduced renal clearance of chromium. This might have contributed to this persisting effect. This patient had no pre-existing DM, but he was underfed for 10 d and then placed on TPN for 8 d before the beginning of the observation period. It is possible that the longer the time that a subject has been on TPN, the more likely it is that a chromium deficiency has developed.

Summary Case Report of Subject HR

A 72-y-old male was admitted with pneumonia, exacerbation of chronic obstructive pulmonary disease, congestive heart failure, severe anemia, and benign prostatic hypertrophy. The medical and surgical histories consisted of chronic obstructive pulmonary dis-

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TABLE I.

	RESPONSE TO SUPPLEMENTAL CHROMIUM BY SUBJECTS MR AND HR											
	Subject MR on days							Subject HR on days				
	1	2	3 (+Cr)	4 (+Cr)	5	6	7	1	2	3 (+Cr)	4 (+Cr)	
Energy (kJ)	5292	5175	5091	5091	5091	5091	5091	6972	6972	6972	6972	
Glucose (g)	196	196	196	196	196	196	196	220	220	220	220	
Insulin (U)	50	50	50	40	40	40	30	55	60	60	45	
Glucose from drips (g)	Nil	Nil	Nil	Nil	Nil	Nil	Nil	20.7	18.05	20.3	20.6	
Average FSBS (mM/L)	7.27	8.21	7.10	6.63	5.85	4.72	7.27	9.29 (8)*	10.88 (15)*	7.73 (4)*	6.72 (5)*	
WBC (1000/mm ³)	24.4	NA	NA	24.9	24.0	NA	23.5	10.0	10.1	10.3	10.0	
Maximum temperature (°C)	36.83	36.89	37.00	37.67	37.11	36.22	37.11	37.11	37.00	37.72	36.67	
Serum creatinine (μM/L)	106.1	123.8	115.0	132.7	150.4	159.2	150.4	WNL	WNL	WNL	WNL	

* Sliding scale units of insulin units given appear in parentheses.

FSBS, fingerstick blood glucose level; NA, not available; WNL, within normal limit

ease, coronary artery disease (status post coronary bypass), congestive heart failure, arteriosclerotic peripheral vascular disease, type 2 DM, postoperative pulmonary embolus (status post inferior vena caval filter placement), and peptic ulcer disease with *Helicobacter pylori* infection. The BMI was 21.5 kg/m² (Table I).

The patient showed possible benefit from supplemental chromium as demonstrated by the decreased amount of sliding scale insulin needed to control blood glucose while infection worsened (white blood cell count and temperature increased) on the first day of supplementation. It is not clear whether the benefit persisted because the patient started eating significantly after the period of chromium supplementation. This patient had pre-existing DM, was given a short course of glucocorticoid to treat worsened dyspnea, was undernourished for 10 d and then placed on TPN for 5 d before the beginning of the observation period. It is likely that this patient had chromium deficiency.

Summary Case Report of Subject MF

A 56-y-old male was admitted with acute myocardial infarction (status post cardiopulmonary resuscitation), ventricular fibrillation (status post cardioversion to sinus rhythm), and hypoxic encephalopathy. The medical history consisted of hypertension, hyperlipidemia, borderline type 2 DM on a controlled diet, and asthma. There was no surgical history. The BMI was 31.5 kg/m².

After infusion of TPN for 5 d, TPN was discontinued as requested by the patient's family based on the patient's terminal status. The patient showed no benefit from the supplemental chromium. This patient had only borderline DM and was not underfed for a long period before starting TPN. In addition, he was placed on TPN for only 2 d before the beginning of the observation period. He probably had little or no chromium deficiency.

Summary Case Report of Subject LH

A 58-y-old female was admitted with intermittent small bowel obstruction and recurrent ovarian carcinoma. The medical and surgical histories consisted of hypertension, hyperlipidemia, type 2 DM, diastolic dysfunction with increased left ventricular diastolic pressure, multiple laparotomies for ovarian carcinoma, cholecystectomy, and appendicitis. The BMI was 32.1 kg/m².

She showed a possible, slight benefit from the supplemental chromium as demonstrated by the slight decrease in average fingerstick blood sugar, despite the increases in body temperature and white blood cell count on day 6 of the 7-d observation period. The patient had pre-existing DM but was on TPN for only 1 d before

the beginning of the observation period. She probably had some chromium deficiency.

Summary Case Report of Subject JE

A 20-y-old male was admitted for pancreatitis and mild diabetic ketoacidosis. The medical history showed type 1 DM. The patient smoked marijuana occasionally (last use was approximately 4 to 5 d before admission). The BMI was 40.12 kg/m².

The patient showed a possible, slight benefit from supplemental chromium as shown by the slight decrease in the average fingerstick blood sugar level, despite the increase in body temperature on day 6 of the 7-d observation period. The increase in temperature may have been caused by discontinuation of the antibiotic. Unfortunately, we did not have adequate white blood cell count data to confirm the worsening of infection. The patient had pre-existing DM and was placed on nothing per oral for 3 d and then on TPN for 7 d before the beginning of the observation period. He likely had chromium deficiency, but for some reason responded only slightly to the supplementation.

DISCUSSION

The benefit of chromium was not dependent on the patient having pre-existing DM or chronicity of disease. Any self-administration of an oral chromium supplement before hospitalization was unknown. The two who showed possible benefit from supplemental chromium had lower BMIs than did those three who showed no or only slight benefit. All subjects, regardless of their body weights, received the same amount of vitamins and trace minerals. Most nutrient requirements increase as body weight increases. Obese patients may need more micronutrients to form adequate biologically active chromium compounds (chromium-binding oligopeptide chromodulin or holochromodulin) from chromium. These holochromodulins are needed for insulin action to transport glucose into the cell. The more available the holochromodulins are, the lower the insulin resistance becomes.⁹ One report has suggested that the inability to respond to chromium supplementation may be due to suboptimal levels of nicotinic acid.¹²

Future research should 1) use a standardized test for insulin sensitivity such as the Homeostasis Model Assessment test; 2) carry out daily white blood cell counts during the 7-d observation period for febrile patients to determine the progress of infection; and 3) give nicotinic acid plus chromium supplementation in place of chromium supplementation alone.

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