ORIGINAL ARTICLE

SERUM CONCENTRATION OF CHROMIUM IN HEAD INJURY PATIENTS

Hossein Eskandary MD[•], Nader Nowbari MD

Department of Neurosurgery, Neuroscience Research Center, Kashan, Iran

Background- Certain trace elements such as zinc and copper have been studied in head injury patients. In this study, we decided to determine whether serum chromium concentrations were affected by the severity of a head injury.

Methods- The study was conducted on 30 male patients aged from 10 to 30 years. Patients were divided into three groups based on the Glascow Coma Scale; 1-mild, 2-moderate and 3-severe head injury. Serum samples for chromium were obtained during the first four hours after head injury and analyzed by neutron activation analysis technique. Two independent sample t test was used to compare the mean serum concentration of chromium in different groups.

Results– Mean \pm SD of serum concentration of chromium was 1.41 \pm 0.2 mg/L in the first, 1.58 \pm 0.23 mg/L in the second and 1.42 \pm 0.23 mg/L in the third group of patients. There was no significant difference among the three groups with respect to the serum concentration of chromium.

Conclusion- To define the time-related changes of chromium and severity of the head injury, the total intake of chromium and other relevant factors should be considered in future studies.

Keywords • brain chromium • head injury • trace element

Introduction

hromium is an essential trace element for both humans and animals.¹⁻⁴ • Trivalent chromium is an integral part of the dinicotinic acid glutathione complex, (glucose tolerance factor) which is known to potentiate the action of insulin. $^{1-6}$ Studies of runners indicate increased plasma zinc and chromium (Cr) concentrations and acute urinary excretion of these trace elements after exercise.⁴ More severe signs of Cr deficiency, such as nerve and brain disorders that are reversed by supplemental Cr have been reported in patients receiving total parenteral nutrition (TPN).^{5,7} Trauma or severe injury leads to increased level of plasma catecholamines, cortisol, growth hormone and glucagon and inhibition of insulin secretion. Cr is also involved in glucose metabolism and the factors that affect glucose metabolism, often affect Cr metabolism and excretion.⁶ The acute response to injury and

infection is manifested as increased synthesis of acute-phase proteins by the liver, an increased blood cell count, fever, a negative nitrogen balance and altered serum mineral levels (zinc, iron, copper).⁸ Alterations of some of the trace elements such as $zinc^{9,10}$ and copper⁸ have been studied in head injury patients. Intracellular magnesium has also been shown to decrease after experimental traumatic brain injury.^{11,12} To our knowledge there are only four studies which have managed to isolate the trace element in trauma patients; one in burns ¹³ and three in brain injury patients.^{8–10} None of these three studies consider the severity of injury as a problematic factor affecting serum level of Cr. The present study was performed to determine whether severity of head injury affects serum concentrations of chromium.

Patients and Methods

Patients

In a time period of one year from August 1999, 30 head injury patients who met our selection

[•]Correspondence: H. Eskandary MD, Department of Neurosurgery, Jomhoory Islami Blvd, Kerman, Iran. P.O.Box: 76175-113, Fax: +98–0341–211010, E-mail: h_eskandary@yahoo.com

criteria were admitted to the Bahonar Hospital, an affiliation of Kerman University of Medical Sciences. Patients were included in the study based on the following criteria:

1. Presence of pure head injury without space occupying lesion on brain computer tomography (CT) scanning and no evidence of injury to other parts of the body.

2. Male sex in the age range of 10 to 30 years.

3. Absence of previous underlying diseases such as diabetes mellitus, hypertension and cardiovascular disease and habits such as addiction or alcohol consumption.

4. Having no history of using any drug or solution before or after trauma.

Workers of tanneries, mines and industries for metal plating, welding, photography, paint, industries of dyes and explosives were excluded from the study.¹⁴

Patients were divided into three groups based on the Glascow Coma Scale (GCS):

1- Severe head injury patients; GCS = 3-8

- 2- Moderate head injury patients; GCS = 9-12
- 3- Mild head injury patients; GCS = 13-15

Sample Collection 6,14

All samples were obtained within the first 4 hours of the trauma.

- The blood samples were collected using a plastic catheter placed in a vein.

- The collected blood was transferred to an acidleached (10% nitric acid for 48 hr) plastic centrifuge tube.

– Targeted samples were obtained prior to taking further blood samples.

- Contact with steel, dust and ordinary glassware was avoided.

– All samples were protected from dust particles and instantly stored in refrigeration.

Analysis

Neutron activation analysis¹⁵ was the technique we used to measure Cr.

Statistical Methods

The analysis was based on group comparisons according to the selection criteria. Two independent sample t tests were used to compare the mean serum concentration of Cr in different groups.

Results

The mean age of patients in the three groups, were 20.4, 22.4 and 20.9 years respectively. Mean \pm SD of serum concentration of Cr (mg/L) in the groups was as follows: group 1: 1.42 ± 0.23 ; group 2: 1.58 ± 0.23 (SD); and group 3, 1.41 ± 0.2 (SD) (Table).

The comparisons between groups showed that there was no significant difference between serum concentration of Cr and severity of head injury, during the first 4 hours following injury.

Discussion

This study revealed that the serum concentration of Cr was increased in patients with head injury; however, the concentration of Cr in serum had no significant relation to the degree of head injury during the first 4 hours. Injury

Table. Serum concentration of chromium (Cr) in different groups of head injury patients.

Case No	Group 1: GCS / 3-8		Group 2: GCS / 9–12		Group 3: GCS / 13–15	
	Age (Yr)	Cr (mg/L)	Age (Yr)	Cr. (mg/L)	Age (Yr)	Cr. (mg/L)
1	20	1.60	16	1.42	22	1.83
2	12	1.50	21	1.90	14	1.42
3	18	1.49	16	1.54	15	1.49
4	30	1.24	20	2.50	20	1.31
5	21	1.60	30	1.85	19	1.38
6	21	1.06	20	1.40	25	1.35
7	30	1.80	11	1.20	25	2.37
8	30	1.50	30	1.80	27	1.12
9	10	1.20	30	1.50	30	1.40
10	12	1.20	30	1.60	12	4.70

induces extensive physiologic and biochemical responses throughout the body.¹³ Any trauma patient will develop an acute phase response, which is characterized by decreased levels of iron, selenium, zinc and increased levels of copper.^{8,9,13}

Trauma patients have been shown to possess negative trace element balances during the first week of injury. The alterations have been particularly marked for selenium. In brain injury patients, the magnitude of the changes has been shown to have a prognostic value.¹³

Based on an association with Glucose tolerance (GTF) factor, Cr3⁺ has been proposed to be a trace essential element in humans and animals, necessary for proper carbohydrate, protein and lipid metabolism.^{1,3,4,6,7,16–18} Cr3⁺ is transported in blood predominantly by transferrin.¹⁷ Some data suggest adverse interactions between Cr and iron. Cr supplementation significantly reduces iron excretion.^{4,17}

Cr deficiency has been proposed to lead to diabetes and cardiovascular disease. ^{2,17} It may also be possible that Cr has a role in lipid metabolism. ^{1–5} Cr3⁺ has been found to bind to DNA and induce abnormal synthesis of RNA *in vitro*. ^{1,3,4} In patients with such severe alterations of vital functions, trace elements have been shown to play a role as coadjuvant therapy. ¹³ Some authors have suggested that Cr4⁺ compounds are more toxic and carcinogenic than Cr3⁺. ^{18–20} Toxicity results in liver and kidney impairment, dermatitis, convulsion and coma. ^{19,21}

The reduction of hexavalent Cr to trivalent Cr outside the cell gives rise to stable trivalent chromium complexes, which are unlikely to react with other molecules. These extracellular complexes are likely to be eventually excreted.²²

The increased urinary Cr excretion of trauma patients appears to be related both to trauma and to the Cr intake via the intravenous fluids administered.⁶

Individuals participating in strenuous physical activity have increased acute loss of Cr.^{2,4} It is interesting to note that copper is the only trace element that correlated with Cr intake.¹

For many reasons, trace element studies are difficult to conduct in critically ill patients, which explains why the data in this field remain sparse. Contamination is inevitable and can limit the validity of the results. These problems arise especially with chromium and zinc.¹³ The mean value of Cr in plasma or serum in healthy adults lies somewhere between 0.18 and 0.47ng/mL (35–

90nmol/L, SI units) or less than 0.5mg/L (PPM).²¹ In one study, the Cr concentration in the first 4 hours urine sample for all severely traumatized patients was high.⁶ The study comprised seven patients with multiple injuries and all of the patients had received intravenous solutions.

In our study, conditions were optimized for Cr during the collection, homogenization and analysis of samples. The type of injury for all patients was similar and none of the patients had received any drug or intravenous solution before blood sampling.

The results of this study show only the changes in Cr concentrations in the first 4 hours after injury. The changes are not related to the severity of head injury. Acceptance of the null hypothesis in this study may be due to the small sample size and power of the study. However, the lack of adequate samples is the problem of studies on trace elements. Further studies using a larger sample size is required to determine whether this elevated level of Cr is due to contamination or a normal occurrence in our population. If we want to consider the time-related changes and GCS, total intake of Cr as well as other relevant factors should be considered.

References

- Anderson RA, Kozolvsky AS. Chromium intake, absorption and excretion of subject consuming selfselected diets. *Am J Clin Nutri*. 1985; **41**: 1177–83.
- 2 Anderson RA. Essentiality of chromium in human. *Sci Total Environ*. 1989; **86:** 75–81.
- **3** Bunker VW, Lawson MS, Delves HT, et al. The uptake and excretion of chromium by the elderly. *Am J Clin Nutr.* 1984; **39:** 797–802.
- **4** Lukaski HC, Bolonchuk WW, Siders WA, et al. Chromium supplementation and resistance training: effects on body composition, strength, and trace element status of men. *Am J Clin Nutr*. 1996; **63**: 954–65.
- 5 Anderson RA. Effects of chromium on body composition and weight loss. *Nutr Rev.* 1998; **56:** 266–70.
- **6** Borel JS, Majerust TC, Polansky MM, et al. Chromium intake and urinary chromium excretion of trauma patients. *Biol Trace Elem Res.*1984, **6**:
- 7 Jeejeebhoy KN, Chu RC, Marliss EB, et al. Chromium deficiency, glucose intolerance, and neuropathy reversed by chromium supplementation, in a patient receiving longterm parenteral nutrition. *Am J Clin Nutr.* 1977; **30**: 531–8.
- 8 Young AB, Ott L, Beard D, et al. The acute-phase response of the brain-injured patient. *J Neurosurg.* 1988; 69: 375–80.
- 9 McClain CJ, Twyman DL, Ott L, et al. Serum and urine zinc response in head-injured patients. *J Neurosurg*. 1986; 64: 224–30.
- **10** Young B, Ott L, Kasavskis E, et al. Zinc supplementation is associated with improved neurological recovery rate and

visceral protein levels of patients with severe closed head injury. *J Neurotrauma*. 1996; **13**: 25–34.

- McIntosh TK, Vink R, Weiner MW. Alterations in free magnesium, high-energy phosphates, and lactate following traumatic brain injury: assessment by nuclear magnetic resonance spectroscopy. *J Cereb Blood Flow Metab.* 1987; 7 (suppl 1):
- 12 Shigemori N, Kikuchi T, Tokutomi T, et al. Coexisting diffuse axonal injury (CDI) and outcome of severe head injury. *Acta Neurochir Supll (Wien)*. 1992; **55**: 37.
- 13 Berger MM, Shenkin A. Trace elements in trauma and burns. *Curr Opin Clin Nutr Metab Care*. 1998; 1: 513-7.
- 14 Willie Glen R. *Trace Elements, Laboratory Test Book.* 4th ed, 1996: 585–8.
- **15** Versieck J, Hoste J, Barbier F, et al. Determination of chromium and cobalt in human serum by neutron activation analysis. *Clin Chem*.1978; **24**: 303–8.
- 16 Duckett S. Abnormal deposits of chromium in the pathological human brain. *J Neurol Neurosurg Psychiatry*.

1986; **49:** 296–301.

- 17 Stearns. DM. Is chromium a trace essential metal? *Biofactors*. 2000; 11: 149–62.
- 18 Sugiyama M. Role of physiological antioxidants in chromium (VI)-induced cellular injury. *Free Radic Biol Med.* 1992; 12: 397–407.
- **19** Gad SC. Acute and chronic systemic chromium toxicity. *Sci Total Environ.* 1989; **86:** 149–57.
- **20** Ueno S, Susa N, Furukawa Y, et al. Cellular injury and lipid peroxidation induced by hexavalent chromium in isolated rat hepatocytes. *Nippon Juigaku Zasshi*. 1989; **51**: 137–45.
- 21 Chernecky CC, Berger BJ. *Laboratory Tests and Diagnostic Procedures*. 2nd ed. Philadelphia: Saunders; 1997: 367–8.
- 22 Alexeeff GV, Satin K, Painter P, et al. Chromium carcinogenicity: California strategies. *Sci Total Environ.* 1989; 86: 159–68.