The alteration of plasma's zinc and copper levels in patients with burn injuries and the relationship to the time after burn injuries

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ABSTRACT

Introduction: Burn injury is a medical problem as well as a social burden on the national health services in developing countries. Trace elements have important roles in wound healing and act as antioxidants. In this study, zinc (Zn) and copper (Cu) levels in plasma of burned patients and their relationship with the burn surface area and time-related pattern are determined in the admitted patients after burn injury.

Methods: 37 patients were divided into two groups: Group 1 consisted of 16 patients with burn injuries less than 20 percent of the total burn surface area, and Group 2 consisted of 21 patients with burn injuries between 20 and 40 percent of the total burn surface area. The control group consisted of 20 subjects. The Zn and Cu levels were determined one, three, seven and 14 days after the occurrence of burn injury. These trace elements were determined using atomic absorption spectrophotometer.

Results: These trace elements in plasma significantly decreased on all days after admission and the levels were lower than those of the control group. There was no significant relationship between Groups 1 and 2 in Cu and Zn concentrations on different days. We did not find any difference between burn surface area and Zn and Cu concentrations in these groups.

Conclusion: Based on the critical role of plasma's Zn and Cu rate in wound healing and their relationship in decreasing the burn injury, it is important that patients having burn types II and III take Zn and Cu supplements continuously as micronutrients after burn injury.

Keywords: burn injury, copper supplement, trace elements supplementation, wound healing, zinc supplement

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INTRODUCTION

Burn injury changes metabolic and immune responses. The immune system is depressed overall.[1] Some of these changes can be related to alterations in trace elements metabolism. Trace elements, especially zinc (Zn) and copper (Cu), have important roles in human growth, development and immune function.[2] It is also considered that some of these elements are essential in wound healing.[3] These trace elements act as major antioxidant enzymes' cofactors. Variation in Zn and Cu is important.[4] There is evidence that infection affected the plasma's Zn concentration.[5] Some reports showed the alteration of trace elements' metabolism in patients with burn injuries.[6-8] The deficiencies of Zn and Cu have been reported in burn injuries,[9,10] but the relationship between burn surface area and its time after burn injury remains unclear.

Boosalis et al showed that nutritional support improved health conditions in patients.[11] To determine the beneficial effects of nutritional support in patients' medication, it is necessary to find out when the levels at trace elements decrease. The purpose of the study was to determine the alteration of the levels of trace elements (Zn and Cu) in plasma, and to identify the relationship between the burn surface area and the time after burn injury in patients. These results can help to understand the pathophysiology of the burn syndrome related to the change of trace elements after burn injury and to use trace elements supplementation in patients with burn injury considering the surface area and time period after the burn incident.

METHODS

After approval by the Mazandaran University Medical Sciences Ethics Committee, patients admitted to the Burns Centre of Zare Hospital in Sari, Iran, were enrolled in this study in 2006. The patients had thermal burns of types II and III. The severity of the burn injury was assessed by using the total body surface area (TBSA). Patients were excluded if they had chronic disease or

Table I. Profile of patients with burn injuries.

Parameter	TBSA	
	< 20%	20%–40%
No. burn injury	16	21
Age (years)	29.6 ± 14.45	40.3 ± 18.78
Gender (%)		
Female	2 (12.5)	1(4.8)
Male	14 (87.5)	20 (95.2)
Mean of TBSA (%)	12.46 ± 4.9	25.78 ± 4.9

renal failure. 37 patients were included in two groups, 16 patients with TBSA < 20%, and 21 patients with TBSA between 20% and 40%. The control group contained 20 subjects. The patients were routinely managed and treated. The patients consumed food according to hospital management protocol, and no micronutrient supplements were administrated.

Blood samples were collected on days one, three, seven and 14 of admission. Blood samples were taken from the antecubital veins using stainless steel needles and trace element-free vacutainers. Plasma was separated by centrifugation at 2,000 g for 10 minutes. All samples were stored in plastic containers and frozen until the time of analysis. Trace elements concentrations in samples were determined using flame atomic absorption spectrophotometry (BRIAC FX-130, Beijing, China) with Zn and Cu hollow cathode lamp at wavelengths 213.9 nm and 327.9 nm, respectively. 0.5 ml of plasma was mixed with 4.5 ml of acidic glycerol (HNO_3 1% and glycerol 5%). The absorption of solution was directly measured by atomic absorption spectrophotometer. The standard curves were prepared using 50, 100, 150, 200, 250 µg/dL solution of Cu and 10, 30, 40, 50 µg/dL solution of Zn in acidic glycerol. All chemical reagents and solutions were from Merck Company (Darmstadt, Germany).

All data was analysed by the Statistical Package for Social Sciences software version 13.0 (SPSS Inc, Chicago, IL, USA). Zn and Cu levels on the days of admission were compared using the analysis of variance (ANOVA). The analysis for the difference between times was done by the repeated measurement test.

RESULTS

The profile of patients with burn injuries is shown in Table I. The patients were of both gender, with a mean age of 29.6 ± 14.45 years and 40.3 ± 18.78 years for Groups 1 and 2, respectively. The TBSA mean was 12.46% ± 4.9%, ranging from 4% to18% for Group 1; and 25.78% ± 4.9%, ranging from 20% to 38% for Group 2. The status of Zn and Cu levels in plasma in the different groups are shown in Figs. 1 and 2. The plasma Zn and Cu concentrations were 65.90 ± 3.87 µg/dL and 81.07 ± 0.45 µg/dL, respectively, in the control group. The plasma Zn concentration was

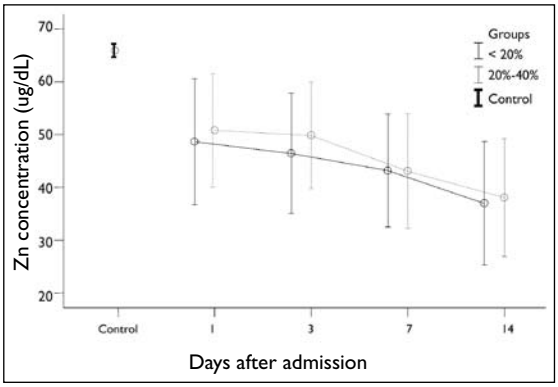

Fig. 1 Mean plasma Zn concentration in patients with TBSA > 20% (Group 1) and 20%–40% (Group 2) and control subjects on 1–14 days after burn injury.

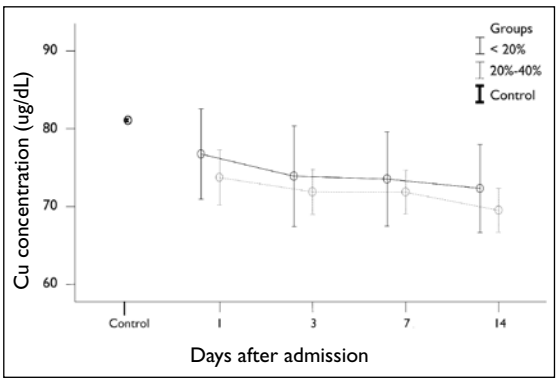

Fig. 2. Mean plasma Cu concentration in patients with TBSA > 20% (Group 1) and 20%–40% (Group 2) and control subjects on 1–14 days after burn injury.

48.6 ± 22.3 µg/dL and 50.8 ± 23.6 µg/dL, respectively, in Groups 1 and 2 on the first day after admission. These levels were statistically lower than the control levels of Zn ($p < 0.01$). The average Zn level of plasma was 46.4 ± 21.4 µg/dL, 43.1 ± 20 µg/dL, 36.9 ± 21.1 µg/dL, respectively, on days three, seven and 14 after admission for Group 1, and 49.8 ± 22.1 µg/dL, 43 ± 23.9 µg/dL, 38 ± 22.4 µg/dL, respectively, on days three, seven and 14 after admission for Group 2 (Fig. 1). There was no correlation between Groups 1 and 2 in Zn concentration on different days. Also, there was no correlation between TBSA and Zn concentration in Groups 1 and 2. Zn concentrations showed a significant trend of decrease on different days after admission in Groups 1 and 2, and the Zn levels were statistically different among the different days after admission in each group.

The plasma Cu concentration was 76.74 ± 22.3 µg/dL and 73.7 ± 7.8 µg/dL in Groups 1 and 2, respectively, on the first day after admission. These levels were statistically lower than the control level of Cu ($p < 0.01$). The average Cu level of plasma was 73.8 ± 12.1 µg/dL, 73.5 ± 11.3

μg/dL, 72.3 ± 10.2 μg/dL, respectively, on days three, seven and 14 after admission for Group 1; and 71.8 ± 6.3 μg/dL, 71.8 ± 6.1 μg/dL, 69.5 ± 5.6 μg/dL, respectively, on days three, seven and 14 after admission for Group 2 (Fig. 2). There was no correlation between Groups 1 and 2 in Cu concentration on different days. Also, there was no correlation between TBSA and Cu concentration in these groups. Cu concentrations showed a significant decreasing trend after admission in Groups 1 and 2 on different days, and the Cu level was statistically different among the days after admission.

DISCUSSION

The trace elements play important roles for antioxidant defence, inflammatory process and wound healing in burn injuries.[11-13] It is important to determine the levels of trace elements in relationship with time and burn surface area after burn injury in patients. This study showed that Zn and Cu levels were lower in the patients with burn injuries than in healthy individuals, and amounts of these trace elements decreased in a time-dependent manner. The average accumulations which decreased during the first week postinjury were approximately 190 mg and 33 mg for Zn and Cu, respectively. This included extensive losses, approaching 20%–40% of body content for Cu and 10% of body content for Zn.[11,12] On the first day after admission of patients, Zn and Cu levels respectively decreased by 29% and 5% in patients with TBSA < 20%, and 22% and 9% in patients with TBSA between 20% and 40%.

This study showed the loss of Zn to be more than that of Cu in patients with burn injury. There was no correlation between TBSA and the loss of Zn and Cu levels. Agay et al showed that Zn serum level decreased with six hours of burn injury to 20% and remained significantly lower on day one in plasma of rats and it was continued on day three and then returned near control levels.[6] The decrease of serum Zn concentrations was associated with accumulation of Zn in the liver.[4] Serum Cu concentration increased on days one and two, and remained elevated on day ten following the burn injury.[4] Previous studies of burn patients have reported that plasma levels of Zn and Cu were reduced,[14] but Zn urinary excretion was increased.[15,16]

There are some reasons for loss of plasma Zn and Cu levels in burn injuries. First of all, the greatest loss of Zn and Cu levels is through the wound exudates. The body distribution profile of these trace elements is changed following the burn injury, and it is possibly due to contribution of Zn and Cu in the inflammatory process.[17] The second reason is that the low levels of plasma Zn may be related to hypoalbuminaemia; this protein is known to transport about 70% of Zn to the cells.[18] In this study, the loss of Zn continued on day 14 after the burn injury and did not return to near control level in patients. Berger and Chiolero observed a positive relationship between burn area and the amount of Zn and Cu excretion through the urine.[19] Berger et al showed that administration of additional supplements of Cu, selenium and Zn for eight days resulted in the increase of plasma and tissue antioxidant in patients with major burn injuries. The number of infections was lower in the supplement treatment group compared to the placebo group. Wound healing was improved in patients with trace element treatment and these patients needed less regrafting.[20]

When the oxidative stress is elevated soon after the burn injury, Zn and Cu mobilise in the liver and contribute to antioxidant defences.[21] Cu/Zn-superoxide dismutase (SOD) enzyme containing Cu and Zn as cofactors, plays a key role to counteract the oxidative stress induced by thermal injury. The increase of Cu/Zn-SOD activity is known to limit the diffusion of reactive oxidative species released by injured tissue, and therefore avoid the extension of the oxidative injury.[22]

In this study, we have showed that plasma Zn and Cu levels are reduced in burn patients and they were time-dependent after the burn injury but independent to TBSA. Since Zn and Cu elements have a critical role in wound healing and antioxidant enzyme activity, the return of the reduced plasma trace element level to normal is important. The increased intake of trace elements, nutritional support, parenterally-administered fluids, plasma, albumin, and globulin and blood transfusions affect the blood levels of the elements. We proposed that these trace elements should be administrated as micronutrients to patients with types II and III thermal burn injury.

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