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Original article

Trace element intakes should be revisited in burn nutrition protocols: A cohort study

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SUMMARY

Background & aims: Due to inflammatory and hypermetabolic responses and to extensive exudative trace element (TEs) losses, major burn patients have substantially increased nutritional requirements. To date, information is only available for Cu, Se, and Zn. We aimed at analyzing losses of 12 TEs and Mg through burn wound exudation and corresponding plasma concentrations during the first week after burn injury, and to evaluate the impact of current TE repletion protocols.
Methods: Burn wound exudate was collected under negative pressure in 15 adult patients burned 29 ± 20% of body surface (TBSA) for 8 days after injury. Two samples were collected daily. The TE concentrations were measured by inductively coupled plasma mass spectrometry (ICP-MS). Losses and serum concentrations were compared to intakes.
Results: For the majority of 12 TEs, the highest losses were observed on day 1, and declined thereafter. Despite Cu supplementation (4.23 mg/day) serum levels remained below reference values. Se supplements (745 µg/day) normalized and even increased serum levels to upper normal value. Despite large supplements (Zn 67.5 mg/day), serum Zn values remained below reference range. Large exudative losses of B, Br and Mg were found, as well as of Fe and I, with the latter being probably due to contamination.
Conclusion: Current nutritional Cu, Se, Zn repletion protocols in major burn patients which were based on measured exudative losses should be revised to include higher Cu and lower Se doses, as well as planned Mg administration. In burns <20% TBSA and for the other TEs the recommended parenteral nutrition TE doses appear sufficient.

1. Introduction

After major burns, hypermetabolic state induced by oxidative stress and extensive inflammation increases nutritional requirements. Burn patients frequently exhibit low circulating concentrations of several TEs that are explained by the combination of urinary excretion [1], fluid and micronutrient losses through burn wound exudation resulting in micronutrient deficiencies that complicate the clinical course and are, in part, responsible for infections and delayed wound healing [1]. Wound exudation was found to be a major route for TE losses in burn patients resulting in losses of 10–40% of overall body content of copper (**Cu**), 10% of zinc (**Zn**) and 10% of selenium (**Se**) during the first week after trauma

Abbreviation list: GPx, glutathione peroxidase; ICU, intensive care unit; IV, intravenous; TBSA, total body surface area; TE(TEs), trace element(s); on IV-TE, Patients receiving the intravenous TE repletion protocol; PN, parenteral nutrition; PN-needs, standard parenteral nutrition TE requirements.

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[2,3]. So far, only these three TEs were studied because of their particular role in wound healing [4,5], antioxidant defense [6] and immune function [5], which are all of extreme importance in the clinical course of burns [7]. Compensation of exudative losses of these TEs through early intravenous repletion has been associated with reduced infection and Intensive Care Unit (ICU) stays, improved antioxidant status and skin local protein metabolism along with wound healing [8–10]. They were therefore included in recommendations for major burn nutrition (ESPEN guidelines 2013 [11]).

Eleven TEs are essential for the activity of multiple enzymes involved in immune function, gene expression regulation and antioxidant defense [12], but the majority of them are not measurable in clinical settings. Current nutritional supplementation of TEs for burns also considers only Cu, Se, and Zn due to a lack of investigations on other elements. Furthermore, these recommendations are based on exudative losses that were measured with simple mass spectrometry in wound exudates collected indirectly from dressings that covered the burn wounds [2,3]. A reassessment of TE requirements in burn patients is required in order to up-date the local TE repletion protocols and to complete the recommendation for the other TEs that are currently missing in clinical practice. The present study aimed at quantifying and measuring kinetics of TE exudative losses using a new methodology with a direct and continuous collection system from burn wounds over the first week after burn injury.

2. Methods

The study was designed as a prospective observational study without intervention conducted with individual consent and after approval by the Institutional Review Board of the Centre Hospitalier Universitaire Vaudois and the Ethics Committee of the State of Vaud, Switzerland (Ethics # 488/13).

2.1. Patients

The inclusion criteria were admission to the Lausanne Burn Center ICU between February 2014 to April 2015, age >18 years with burns exceeding 10% total body surface area (TBSA) and involving one arm, or leg. Exclusion criteria were: aged <18 years, presence of comorbidity such as local infections, diabetes and HIV, and burns limited to head, neck and trunk areas.

2.2. Clinical management including TE protocols

The Parkland formula was used for orientation of fluid resuscitation in patients with burns covering >20% TBSA. Chlorhexidine was used for wound disinfection. Iodine containing disinfectants were used during surgical procedures (Betadine®: povidone iodine). Enteral nutrition was provided in all mechanically ventilated patients.

In ICU patients with burns >20%TBSA, TE repletion was routinely performed using a combination of 3 products [11]: 1 amp Decan® (Laboratoires Aguettant Lyon France) that covers the standard parenteral nutrition requirements (PN-needs) [13,14] to which was added a special intravenous Cu–Se–Zn cocktail (total daily dose Cu = 4.23 mg, Se 445 mcg, Zn 47.5 mg, Co 1.47 mg, Cr 15 mcg, Fe 1 mg, F 1.45 mg, I 1.52 mg, Mo 25 mcg, Mn 200 mcg) diluted in 250 ml NaCl 0.9% (delivered over 6–12 h). Duration of this supply depended on burn size: 20–40%TBSA received 14 days, 40–60% TBSA and >60% 30 days. In parallel an enteral product Intestamin® (Fresenius Kabi, Stanz, Switzerland: 30 g Glutamine, 300 mcg Se, 20 mg Zn) is delivered for 14 days (20–60% TBSA) or 28 days (>60% TBSA). The patients with burns <20% TBSA receive an oral multi-micronutrient supplement (Supradyn®, Roche, Basel, Switzerland).

2.3. Burn wound exudate & blood collection

The exudate was collected from second degree superficial or deep burns. Sample collection was begun with the initiation of wound treatment upon admission to the burn center using a negative pressure dressing that collected the fluid into a reservoir bottle as described previously [15]. Exudate samples were collected twice daily (morning and evening) during the first week after trauma by changing the reservoir bottle. Sample collection was discontinued upon grafting of the wound site or natural arrest of exudation. The collection material was tested for TE contamination before the study. One blood sample was collected per day. All samples were kept at −80 °C until analysis.

2.4. TE analysis in exudate and serum samples

The concentrations of several TEs were measured in burn wound exudate and serum samples by inductively coupled plasma system coupled to mass spectrometry (ICP-MS; 7700 Series; Agilent, Palo Alto) for elementary quantification: boron (B), bromium (Br), chromium (Cr), copper (Cu), cobalt (Co), iodine (I), iron (Fe), manganese (Mn), molybdenum (Mo), selenium (Se), vanadium (V), zinc (Zn), as well as Magnesium (Mg). Prior to analysis, samples (200 μL) were diluted with 1.8 ml of HNO_3 1% solution containing 10 ng/mL Rh and 10 ng/mL as internal standards. In addition, each analytical batch of study samples was processed with laboratory controls, including method blanks and standard reference materials to continuously monitor method performance.

2.5. Statistical analysis

Independent 2-sided *t* test was used to evaluate statistical difference between daily exudative losses of TEs during the first week after trauma with the losses at the first day. Two-way ANOVA enabled analyzing the changes over time according to the delivery or not of IV supplements, or to burn size below or superior to 20% TBSA. A $P < 0.05$ was considered significant. Pearson's correlation coefficient was used to evaluate the association between intake and exudative losses for **Se**, **Zn** and **Cu**. $0 < r < 0.5$ was considered as not linearly correlated.

3. Results

3.1. Characteristics of patients

Out of 44 patients admitted to the Burn ICU during the study period, 20 were enrolled: 15 patients (13 men, 2 women) aged 46 ± 21 years (mean ± SD) and burned 27 ± 17% TBSA (0.5 ± 0.3 m^2) completed the study (details in Table 1). Four patients suffered from inhalation injury and two developed transient renal failure; an 86 year-old patient died. An intense inflammatory response was present in all patients as reflected by elevated C-reactive protein serum levels (average of all values during study 151 ± 46 mg/l). We observed an average exudation period of 5.5 days (range, 3–8 days) with maximum volumes during the first four days after trauma (10.7 ± 1 ml/collection surface percent); exudation decreased gradually (5.3 ± 2.1 ml/collection surface percent) during the second four days. The TE repletion protocol (on IV-TE) was applied to the 7 most severely burned patients.