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Changes of serum trace elements in early stage trauma and its correlation with injury severity score

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Abstract

Background Severe trauma can cause secondary multiple organ dysfunction syndrome and death. The absolute and relative concentrations of trace elements in both critical care and conventional treatment, which can lead to acute trace element deficiency, constitute an important mechanism of multiple organ dysfunction syndrome (MODS)/multiple organ failure (MOF).

Methods We investigated the changes in serum Cu, Zn, and Fe in early stage trauma of patients with the high injury severity score (ISS) and correlated the change in trace elements with ISS. Blood samples were collected within an hour of admittance and the patients were scored according to ISS. We collected clinical data records and ISS score values, and determined serum Fe, Zn, and Cu by inductively coupled plasma mass spectrometry.

Results Compared with the control group, the serum Zn and Fe values of trauma patients were decreased. There was no significant difference in serum Cu between the patients and the control group. In the trauma group, the serum Zn and Fe were lower than that of the minor injury group, and the difference of Cu concentration was not statistically significant.

Conclusions Serum Zn and Fe levels in patients with multiple trauma fractures were significantly different than those in the normal group, suggesting that Zn and Fe need to be monitored in the early stage of trauma.

Abbreviations: ATED = acute trace element deficiency, ISS = injury severity score, MODS = multiple organ dysfunction syndrome, MOF = multiple organ failure, SIRS = systemic inflammatory response syndrome, TEs = trace elements.

Keywords: copper (Cu), iron (Fe), trauma, zinc (Zn)

1. Introduction

World wide, 1 million individuals fall victim to different types of trauma every year.[1] Multiple organ dysfunction syndrome/multiple organ failure (MODS/MOF),secondary to severe injury, is the most common and serious complication.[2] However, the mechanism of MODS/MOF is not clear, making it a serious complication with high incidence and high mortality clinically. At the same time, it is also a common problem in the mechanism of death in forensic pathology.

In vivo, there are more than 500 enzymes which incorporate trace elements (TEs) in the active center or a prosthetic group.[3] Of note, Zn2+ and Fe are 2 of the cofactors of many important DNA polymerase and repair enzymes, basically indispensable in the normal function of DNA repair polymerase.[4] What's more, this may be the important reason that Cu shows different changes compared with Fe and Zn after trauma, which will be fully discussed later.

So to speak, trace elements are essential nutrients, as important as proteins, lipids, carbohydrates, and vitamins. However, the medical community is still concerned about prevention and cure of chronic trace element deficiency while the lack of acute trace elements in critically injured patients has not been given sufficient attention. In recent years, the decrease of trace elements caused by severe trauma has begun to be paid attention to, and have demonstrated that changes in trace elements are different in different degrees and damage from brain injury, fracture, and burn injury.[5,6]

At present, the concept of "acute trace element deficiency" has not been extensively studied. Moreover, the extent and type of damage in clinical patients and animal models is not uniform. It has not been associated with the mechanism of the occurrence and death of MODS/MOF. Previous studies confirm that severe trauma induces acute trace element deficiency and its redistribution of the imbalance, which may be an underlying mechanism for biochemical metabolism, pathophysiology, and pathological anatomy of secondary SIRS, MODS/MOF, and death.[7–14] The absolute and relative concentrations of TEs in both critical care

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and conventional treatment, which can lead to acute trace element deficiency (ATED), constitute an important mechanism of MODS/MOF, SIRS, and death.[15,16] In this study, we investigate the early acute changes of blood zinc, iron, and copper in patients with multiple fractures, with the intent to verify the theory of acute trace elements from the clinical point of view.

2. Material and methods

2.1. Ethics statement

The study protocol was approved by the ethics committee of our hospital, an informed, written patient's consent was obtained both for the cases and the controls.

2.2. Clinical data and methods

Between September and December in 2015, 120 patients (aged 23–69 years old, averaging 42 years old) were assessed using the injury severity score (ISS). The sampling time is from 2 to 5 hours after the injury, an average of 3 hours. The type of fracture in these patients included comminuted tibial fractures, comminuted fibula fracture, dislocation of the ankle joint, fracture of the medial malleolus, fracture of the surgical neck of humerus, comminuted fracture of the radius, fracture of the rib, distal radius fracture and avulsion fracture of the distal ulna, inferior radioulnar joint dislocation, medial and lateral malleolus fracture, dislocation of the ankle joint, comminuted femur fracture, tibial insertion avulsion fracture, fracture of the right patella and femoral subtrochanteric fracture. By reviewing previous history, all the patients in the trauma group had no metabolic disease, acute and chronic wasting disease, or diseases closely related to the metabolism of trace elements. Blood test data were collected from the Emergency Department, which included blood routine examination, liver and kidney function, heart function, and C-reactive protein. Other 100 cases (60 men, 40 women; 28–50 years old) who go to the hospital for a health checkup were included as controls.

2.3. Collection and treatment of blood sample

Blood samples were taken within an hour from the admission of hospitalization of the patients. Meanwhile, patients were assessed using the ISS. All laboratory ware and equipment were cleaned thoroughly with detergent and tap water, soaked in dilute nitric acid, and then rinsed thoroughly with deionized distilled water. Blood samples were collected into tubes containing lithium heparin (Wujiang, China), and were frozen at −30 °C until analysis. Blood levels of Cu, Zn, and Fe were measured by inductively coupled plasma atomic emission spectrophotometry (Beijing BoHui Technology, Beijing, China). To reduce the nitric acid level, and nebulized in argon plasma, the colorless, homogeneous digests were diluted with water. For the analysis, the reference wavelength was 193.091.

2.4. Data analysis

Statistical evaluation involved use of SPSS v. 16.0 for Windows (SPSS Inc., Chicago, IL). The data represent $\overline{x} \pm SD$. $P < .05$ was considered statistically significant. All data were analyzed by a one-way analysis of variance, and Duncan's multiple range test determined the differences between means.

3. Results

Severe injury is defined as having an ISS ≥15 points, and mild injuries <15. In the 120 cases of multiple fractures, 36 cases were serious injury, with scores ranging from 17 to 26, and an average score of 21.6 points. There were 84 cases of mild injury, with the ISS ranging from 4 to 10, and the average being 7.6 points. Compared with the control group, the serum Zn and Fe in the trauma group were decreased ($P < .05$). The difference of serum Cu was not statistically significant ($P > .05$). In the trauma group, the serum Zn and Fe values of the severe injury group were lower than that of the mild trauma group ($P < .05$), and the changes of Cu were not statistically significant ($P > .05$) (Table 1). Serum Zn and Fe were negatively correlated with ISS score (Zn: $r = -0.39$ $P < .05$, Fe: $r = -.68$ $P < .05$).

4. Discussion

In this study, based on the ISS, among the 120 patients assessed, 36 cases were seriously injured (average 21.6 points), and 84 cases were mildly injuries (average 7.6 points). In the trauma group, decreases in serum zinc and iron are negatively correlated with ISS score, whereas there is no correlation between serum copper and ISS score.

Our results show that serum zinc within 5 hours after the injury in patients with multiple fractures is lower than the control group. This decrease is caused by trauma, and this reduction may affect the early repair of wound tissue.[17] The mechanism for the change in zinc levels is not very clear. It may be due to the increase in ACTH secretion in the blood in response to trauma, and the redistribution of zinc due to systemic inflammation, tissue edema, and blood flow. It has been suggested that the decrease of serum zinc and zinc content in the wounds and livers increases after trauma.[18,19] In addition, the possible causes of the loss may also include traumatic hemorrhage, extensive tissue damage, and a large amount of effusion.

Feidthusen and Lassen were the first to report a reduction in blood iron following fracture.[20] They found that the blood iron decreased most significantly within 5 days after fracture, and the severity of the fracture was more serious. In the present study, blood iron was decreased in the early stage after injury in patients with multiple fractures. The reason may be the generation of

Table 1

Blood Cu, Zn, and Fe concentrations in trauma and control groups.

Trace element	Mild trauma (n = 84)	Severe trauma (n = 36)	Control (n = 100)	Reference value
Cu, mg/L	1.00 ± 0.13	0.98 ± 0.16	1.05 ± 0.18	0.75–2.86
Zn, mg/L	5.66 ± 0.61	5.09 ± 0.21	5.99 ± 0.98*	5.05–11.22
Fe, mg/L	384 ± 34.69	345.44 ± 25.58	439.19 ± 59.97**	350–620

Data are xx00AF;x00B1;SD.
* $P < .05$.
** $P < .01$.

hemoglobin and myoglobin in tissue caused by blood loss after trauma. The synthesis of hemoglobin and myoglobin requires the participation of iron, which leads to a decrease in serum iron content. In addition, the regulation of plasma iron is also related to the reticuloendothelial system. In acute and chronic infectious diseases, the reticuloendothelial system function change caused by the decrease of serum iron.

Copper is also an important component of many enzymes such as superoxide dismutase and cytochrome oxidizes.[21] At the same time, it is also essential for free radical detoxification, heme, wound healing, antioxidant activity, immune function and collagen synthesis.[22] A large amount of copper is stored in the liver, so the lack of symptoms is rare, but it still can be lacking in long-term total parenteral nutrition malnutrition.[23] Zofkova et al[24] observed that plasma copper is reduced within 24 hours after injury in fracture patients, and picks up in 2 weeks after surgery. The authors attributed the decrease in blood copper to the transfer of copper to the liver. However, we find no significant early change in blood copper in patients with multiple fractures. The reason may be the ability of bile duct to regulate copper. In addition, only a small amount of copper is in the blood, loosely bound to albumin, and most copper together with ceruloplasmin. Therefore, this reduction is usually not evident. Only in stressful situations such as infection, acute blood copper can be increased gradually with the increase of ceruloplasmin.

5. Conclusion

Serum Zn and Fe levels in patients with multiple trauma fractures were significantly different compared with those in the normal group, suggesting that Zn and Fe needed to be vigilant and be monitored in the early stage of trauma.

Author contributions

Junyao Lv and Guanghuan Wang designed the research, performed experiments, analyzed and interpreted data, and wrote the manuscript. Kaihong Chen and Xiaojun Yu assisted with analyzing data, and with writing the manuscript. Xiaohu Xu, Guanghui Zhu, Zhuying Shao performed experiments, and assisted with analyzing and interpreting data, and editing the manuscript. Dian Wang assisted with interpreting data and editing the manuscript. Chang Tang and Shanqing Cai designed the research, and assisted with interpreting data and editing the manuscript.

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