

Original Article

The Effects of Selenium Supplementation on Clinical Outcomes in Mechanically Ventilated, Non-Surgical/Traumatic Critically Ill Patients

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Abstract

Background: Selenium presents anti-inflammatory and antioxidant properties which plays a critical role in nutrition of patients following devastating conditions. Furthermore, several lines of evidence reported that most of patients who admitted to intensive care unit (ICU) have lower plasma levels of selenium. Therefore, this study was designed to define the impact of selenium supplementation on clinical outcomes of mechanically ventilated non-surgical/traumatic critically ill patients.

Materials and Methods: This study was conducted on 105 subjects hospitalized in ICU of Shohadaye Haft-e Tir Hospital, Tehran, Iran. Here the acute physiologic assessment and chronic health evaluation (APACHE) II score of patients was documented on the day of their ICU admission. The patients were divided to two groups based on block randomization technique and were assigned to receive selenium or placebo. Then the effect of selenium supplementation was evaluated based on the APACHE II score, the occurrence of ventilator associated pneumonia (VAP), length of ICU stay and the rate of mortality.

Results: The acquired data revealed no significant difference between two experimental groups based on the demographical information. Also it was demonstrated that selenium supplementation of critically ill patients was associated with better APACHE II score, fewer length of ICU stay and fewer mortality rate. Incidence of VAP indicated no significant difference between groups.

Conclusion: The obtained data of this single center clinical trial showed that selenium supplementation could improve clinical outcomes of critically ill patients.

Keywords: Selenium supplementation; APACHE II score; ventilator associated pneumonia; mortality rate; length of ICU stay

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Introduction

Critical illnesses are characterized by a life-

threatening production of reactive oxygen species (ROS) and other radical species that lead to oxidative stress. Oxidative stress is related to release of metalloproteins, copper and iron ions, production of nitric oxide and activation of phagocytes (1). It established that critical illnesses are accompanied by immunosuppression which is correlated with the role of ROS (2). Since oxidative stress is associated with the severeness of diseases which occurs following the elevated level of ROS or declined in antioxidant defenses, therefore managing production of ROS is a crucial strategy in treating illnesses (3).

An essential element, selenium, which is found in a bunch of proteins calls selenoproteins presents anti-inflammatory and antioxidant properties. It has been proposed that antioxidant properties of selenium are mediated via glutathione peroxidase enzymes activation which results in products with less toxicity to protect organism against free radicals causing oxidative stress (4). Hence, selenium probably plays fundamental roles to improve devastating condition (5). Nevertheless, in several parts of the world such as the Europe and Australasia it has been reported that owing to low soil content, peoples are prone to low baseline selenium status (6). In addition, a number of studies reported that selenium deficiency is common among Iranian people (7-10). Furthermore, reduced dietary intake, which occurs during critical illnesses, can further impair the selenium status. In such situation, acute illness combined with selenium deficiency might worsen oxidative stress and related damages (5, 6).

Several lines of evidence reported that most of patients who admitted to intensive care unit (ICU) have lower plasma levels of selenium and glutathione peroxidase activity. Moreover, plasma selenium concentrations are inversely associated with the severity disease (5, 6). Therefore, the aim of the present study was to investigate the effects of selenium supplementation on clinical outcomes in mechanically ventilated, non-surgical and non-traumatic critically ill adult patients.

Methods

This study was a prospective single center clinical trial conducted on 105 subjects hospitalized in ICU, Shohadaye Haft-e Tir Hospital (teaching hospital of Iran University of medical sciences, Tehran, Iran). Patient who signed the written informed involved in the study. The investigation was carried out in accordance with the declaration of Helsinki and approved by the ethics committee of Shohadaye Haft-e Tir Hospital.

The inclusion criteria were patients with age of more than 18 years who received mechanical ventilation more than 3 days and were admitted to ICU due to internal diseases not related to trauma or surgery. On the other hand the exclusion criteria were patients with renal failure, pancreatitis, short bowel syndrome and those that already have pressure ulcers and were HIV positive and also had bone marrow, lung, kidney and liver transplantation. Also all patients who were extubated within two days of establishment of mechanical ventilation or those died during the study period were excluded from this study.

The information of eligible patients consisting the age, gender, cause of hospitalization, diagnosis and the acute physiology and chronic health evaluation II (APACHE II) score was recorded on the day of their admission in the ICU. Moreover, in this study the ventilator associated pneumonia (VAP) was diagnosed based on Clinical Pulmonary Infection Score ≥ 6 (11). In this experiment, patients were divided to two groups using block randomization technique (12) and assigned to receive selenium (group A) or placebo tablets (group B). Patients of group A, received one mg selenium as sodium selenite pentahydrate at the first day and 0.5 mg selenium daily for the following 13 days.

APACHE II score was calculated in all patients of both groups twice: one on the day of their ICU admission and, on the 14th day following selenium treatment, to define the influence of the selenium supplementation at APACHE II score and final prognosis. To calculate web based APACHE II score, age and 12 relevant physiological variables and 2 disease related variables used consisting: Glasgow Coma score, white blood cell count, hematocrit, heart

and respiratory rate, mean arterial pressure (MAP), FiO_2 and PaO_2 , body temperature, arterial pH, serum creatinine, serum potassium, serum sodium, the occurrence of acute renal failure or severe organ system insufficiency and immunocompromised state (13).

Pearson Chi-square test or Fisher's exact test was used to compare categorical data. In addition, Student's t test or Mann-Whitney U test was applied to compare continuous variables. A $P < 0.05$ was considered statistically significant.

Results

Among 250 patients admitted in the ICU, 105 subjects were eligible to evaluation in this study. Here, 55 patients were male while 50 individuals were female which randomly divided in two experimental groups. One group treated with selenium (group A) and the other one received placebo (group B) while there was no significant difference between two groups based on the age and gender of patients. In this investigation, the underlying causes of hospitalization in ICU and mechanical ventilation evaluated and identified by the medical practitioners. In this regard, pulmonary diseases were the main reason of hospitalization in ICU in both groups that its incidence was about 70%. Sepsis was the second cause of these critically ill patients' condition with the prevalence of 14% and 16% group A and B, respectively. Also based on acquired data, 13% of subjects group A and 10% group B were admitted to ICU due to central nervous system (CNS) disorders (Table 1). Here, the severity of illness was defined using APACHE II scoring system at the time of their entrance to the ICU.

In this study statistical analysis of the acquired data from the point of interfering factors such as age, gender, the cause of hospitalization and illness severity revealed no significant difference between two experimental groups. According to obtained data the average APACHE II score of patients at the beginning of their admission to ICU was 20.6 ± 7 and 21 ± 8 in group A and B, respectively ($P = 0.1$). Following the employed nutritional treatment, the APACHE II score of group A reached to 18 ± 3 while this score in group B was 19.1 ± 4 ($P < 0.05$), which shows a significant difference between two groups.

Based on the APACHE II score, non-operation and post-operation predicted mortality percentage of patients in both groups were similar; however actual mortality in group A was 9 subjects (16.3%) and 12 subjects (24%) in group B which revealed the selenium supplemented nutrition resulted in a significant difference in the rate of death between groups ($P < 0.05$). The incidence of VAP was another factor that has been evaluated between two groups that acquired data demonstrated 6 (10.9%) subjects in group A were infected while 5 (10%) patients in group B developed VAP which indicated no significant difference between groups ($P = 0.3$). Also, there was a meaningful difference in duration of patients' stay in ICU among groups, as the number of days in ICU was 10.1 ± 8 and 11.2 ± 8.2 in group A and B, respectively ($P < 0.05$) (Table 2).

Discussion

Incidence and cause of malnutrition in ICU are multifactorial (14) and loss of essential micronutrients is common among critically ill patients who admitted to critical care wards. This situation can be worse in patients who suffer from micronutrient deficiency prior to the illness. Selenium is one of these essential trace elements which becomes reduced remarkably following devastating conditions (6). Hence, in these patients selenium supplementation could be a valuable strategy to prevent multi organ dysfunction due to severe oxidative stress. The result of this prospective randomized and placebo-controlled, single-center trial revealed selenium supplementation is a critical adjuvant therapeutic approach to improve outcome of patients in ICU who were admitted due to pulmonary diseases, sepsis or CNS disorders. We found that selenium supplementation in mechanically ventilated, non-surgical/traumatic adult patients during the first days in the ICU was associated with better APACHE II score, shorter stay in the ICU and fewer rate of death.

This finding is in agreement with other single and multi-center trials which reported the important role of this essential trace element in nutrition plan of ICU admitted patients. In this regard, Heyland et al. in a systematic review on antioxidant supplementations reported that enhanced selenium (alone or in combination with other antioxidants) can be

Table 1: Patient characteristics on admission with detail of the diagnostic categories.

Variable	Group A (selenium)	Group B (placebo)	P value
Number	55	50	
Age (mean± SD)	47±9	49±8	P>0.05
Gender			P>0.05
Male	31	28	
female	24	22	
Illness causing hospitalization			
Pulmonary diseases	38 (69%)	36 (72%)	
Sepsis	8 (14%)	8 (16%)	
CNS disorders	7 (13%)	5 (10%)	
Others	2 (4%)	1 (2%)	

Table 2: The effects of selenium supplementation on clinical outcomes of critically ill patients.

Variable	Group A (selenium)	Group B (placebo)	P value
Admission APACHE II score	20.6±7	21±8	P<0.05
Predicted mortality	40/30 %	40/30 %	
Final APACHE II score	18±3	19.1±4	
Actual Mortality (%)	9 (16.3%)	12 (24%)	P<0.05
Length of ICU stay (Days)	10.1±8	11.2±8.2	P<0.05
VAP Incidence (%)	6 (10.9%)	5 (10%)	P>0.05

correlated with decreased rate of mortality (15, 16). Also a multiple-center study demonstrated that enhanced level of sodium-selenite reduced rate of mortality in patients with septic shock or severe sepsis (17). In addition, Andrews et al. found that daily selenium administration for at least five days, reduced new infections (18). On the other hand, Berger et al. reported that antioxidant supplements (mixture of selenium, zinc, vitamin C and vitamin B₁) for 5 days did not reduce infectious complications, length of hospital stay, early organ failure and mortality; however remarkably decreased the inflammatory responses in trauma patients or following cardiac

surgery (19).

It has been assumed that antioxidant and anti-inflammatory properties of selenium are mediated through glutathione peroxidase and thioredoxin reductase which are crucial elements to maintain redox system in any types of cells in the body including the immune cells (20-22). These two enzymes reduce hydrogen peroxide, lipid, and phospholipid hydroperoxides and also diminish free radicals and ROS propagation (23). Following selenium supplementation the selenoprotein is rapidly generated which subsequently prevents endothelial cells from oxidative damage (24, 25).

To the best of our knowledge, although so many investigations reported the impact of selenium supplementation in clinically ill patients in other parts of the world, there is just one documented investigation in Iran about administration of this trace element and its influence on patients who admitted in the ICU due to trauma (26). Chelkeba et al. in 2015 reported the effects of parenteral selenium on outcomes of mechanically ventilated patients following sepsis, severe sepsis and septic shock and their study carried out in a center in Tehran, Iran; however, their findings and the target patients were different. This research group revealed selenium can reduce the occurrence of VAP in patients who mainly admitted in ICU due to trauma. Also their goal-directed therapy didn't change the mortality rate, significantly (26), while our supplementation resulted in reduction of mortality rate without significant effect on the incidence of VAP. Since VAP is the leading cause of death in the ICU, increases length of ICU and hospital stay and elevates mortality rate and costs, various treatments have been employed to reduce its incidence (27-29); however, in the present study, selenium supplementation did not affect VAP incidence.

Up until now there is no conclusive investigation to show where the balance should lie between therapeutic and toxic doses of selenium (6, 15). Therefore, the employed protocol of selenium administration can provide a useful insight about the required dose of this important trace element in the nutrition plan of patients with critical condition in our country. It is important to mention that our study was single-center trial that did not include patients from various geographical parts of Iran; therefore, it requires data of more centers to gain further validity. In addition, we did not measure selenium levels before and after the treatment, that is another limitation of the current investigation.

Conclusion

The obtained data of this single center clinical trial showed that selenium supplementation could improve clinical outcomes of critically ill patients.

Acknowledgment

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Conflicts of Interest

The authors declare that they have no conflict of interest.

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