RESEARCH ARTICLE

The Effect of Selenium High Dose Intravenous on Rapid Shallow Breathing Index (RSBI) in Ill Patients: A Clinical Trial Study

Babak Alikiaii[1]*, Faezeh Khodabandeh[2], Masoumeh Ghane[3]

Background: Selenium (Se), mainly through its incorporation into selenoproteins, plays an important role in in ammation and immunity. Evidence has emerged regarding roles for individual selenoproteins in regulating in ammation and immunity: The aim of the study was to evaluate of the effect of selenium administration on rapid shallow breathing index (RSBI) in ill patients.

Methods: In this single blinded clinical trial study, 105 patients under mechanical ventilation were randomly divided into three groups, a received 1mg of Selenium, group B received 0/5 mg of selenium and group C received 2cc normal saline daily. Patients at the time of breathing spontaneously, and when receiving pressure support ventilation 8 and 5 cmH2o, and at the time of extubation were evaluated for Rapid Shallow Breathing Index and then compared between the groups.

Results: There were no significant differences in the three groups in terms of distribution of age, sex, and cause of hospitalization and the mean of RSBI index at breathing spontaneously and when ventilator setting were reached to pressure support ventilation 8 cmH2o, however the difference was significant between the three groups from the pressure support ventilation 5 cmH2o until the extubation time.

Conclusion: The results of the study showed a positive effect of selenium high dose (1mg) on the reduction of extubation time and RSBI, but due to the limitations of our study, further studies are recommended.

Keywords: Rapid Shallow Breathing Index; mechanical ventilation; selenium

Today, airway support and its maintenance are critical issues in the intensive care unit [1]. One of the important issues in this regard is the mechanical separation of ventilator from the patient and spontaneous breathing [1-2]. Determining the right time for this process is very important because any delay in ventilator separation can lead to various complications, including acquired pneumonia from the ventilator. Early separation also results in an increase in the number of hospital admissions and financial losses, or in some cases even leads to the death of patients [3-5]. One of the determinants of separation time is the Rapid Shallow Breathing Index (RSBI). This index was first introduced in 1991 in a study by Yang and Tobin as the most sensitive and most promising indicator (Respiratory frequency/Tidal volume) [6-7]. RSBI is measured by a spirometer attached to the endotracheal tube, while the patient breathes for a minute without mechanical ventilation. This ratio is normally 40-50, and in patients who cannot tolerate spontaneous respiration, it is often higher than 100. When the RF/ TV ratio is more than 105, 95% of attempts to stop the ventilator will fail. But when this ratio is less than 105, 80% of the strike will succeed. Therefore, the results of various studies have proven that the RF/ TV ratio is approximately 100.1 which predicts the success or failure of spontaneous breathing [8-12]. Due to the antioxidant and anti-inflammatory activity of selenium, this micronutrient plays a very important role in the treatment of patients, especially those admitted to the intensive care unit [13]. On the other hand, long-term mechanical ventilation can cause respiratory dysfunction and, with its diaphragm and its atrophy, can reduce respiratory rate [14-15]. Selenium, one of the body's essential minerals has antioxidant properties which improves immunity [9]. Selenoproteins are enzymes that have significant amounts of selenium in their active portions [13,18]. GPx-3 is an antioxidant of selenium that prevents peroxide in cells and prevents damage. 20-40% of all serum selenium is in GPx-3. Because this enzyme represents one of Selenium's main activities and is easy to measure, it is commonly used as one of the markers of selenium levels in the body. Therefore, the goal of giving selenium supplementation is to bring GPx-3 to its maximum activity level [13,16].

Selenium, as a regulator of T helper 2 responses, can justify the association between these micronutrients and respiratory diseases, especially immune-based diseases in allergic disorders such as asthma. According to researches

[1]Anesthesiology and Critical Care Research Center, Isfahan University of Medical Sciences, Isfahan, Iran.
[2]School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran.
[3]Alzahra Hospital, Isfahan University of Medical Sciences, Isfahan, Iran.
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*Corresponding author: Babak Alikiaii, MD. Anesthesiology and Critical Care Research Center, Isfahan University of Medical Sciences, Isfahan, Iran. E-mail: alikiaiib@med.mui.ac.ir

the causes of muscle atrophy are the mechanisms of protein oxidation and lipid peroxidation. Selenium inhibits these two mechanisms by increasing TNFα and IL6, and it has been shown that selenium deficiency causes muscle atrophy [18]. Therefore, the present study was performed to determine the RSBI in patients admitted to the intensive care unit with blood transfusion with and without selenium.

Methods

This is a single-blinded clinical trial study undertaken in a single center from October 2016 to December 2017. The study population consisted of consecutive patients admitted to the Intensive Care Unit (ICU) of Alzahra hospital (Isfahan, Iran), a tertiary-level university- affiliated hospital. The ethics committee of Isfahan University of Medical Sciences approved the study. Eligible patients were 15 to 80 years old and newly admitted to the ICU due to serious medical problems. Patients were excluded from the study if they had an expected stay or life expectancy of less than 48 hours. The sample size was calculated as 35 patients in each group according to the sample size formula and taking into account 95% confidence level, 80% test power, the standard deviation of the fast and average respiratory index which was estimated about 1.17 and the least significant difference between RSBI in the two groups which was considered as 0.8. In this study, 105 patients were randomly assigned in three groups; Patients in group B received 0/5 mg and in group A received 1 mg daily during the time of admission to the intensive care, Patients in group C received placebo (2 cc normal saline) daily at the time of admission to the intensive care unit. Patients at the time of breathing spontaneously, and the ventilator parameters were reduced according to the patient's comfort and tolerance, until minimum values were enrolled when receiving pressure support ventilation (PS= 8-5cm H2O; PEEP = 5 cm H2O). and at the time of extubation were evaluated for Rapid Shallow Breathing Index and that compared between the groups.

The duration of mechanical ventilation and intubation and admission to the intensive care unit was also determined and recorded in a questionnaire. The obtained data, along with demographic characteristics of patients, were analyzed using SPSS software version 24 and one-way ANOVA, Chi-square test and ANOVA with repeated observations.

Results

The demographic characteristics are shown (Table 1). There were no significant differences in the three groups in terms of distribution of age, sex, and cause of hospitalization. The mean of RSBI index are shown in the three groups from breathing spontaneously, to the time of Extubation (Table 2). According to the results, time breathing spontaneously and when were reached pressure support 8cmH2o, the mean of the mentioned index was not significantly different between the three groups however the difference was significant between the three groups from PSV 5 cmH2O to the extubation time.

The patients in group A (1 mg selenium) had lower mean of RSBI. based on Scheffe test, when patients reached PSV 5 cmH2O, the mean of RSBI between the two groups C and group A (1 mg selenium) was significant (P< 0.001), but there was no significant difference between the groups C and group B (500 mg selenium) (p= 0.046) (Figure 1). Table 3 shows the mean and standard deviation of the duration of stay in the intensive care unit, the duration of ventilation and ApacheII in the three groups. According to the results, the duration of hospitalization and ApacheII in the three groups did not differ significantly, but the duration of mechanical ventilation had a significant difference, while the group A had a shorter duration of mechanical ventilation than the group B, C (p< 0.001).

Table1- The main characteristics of patients in the study

Variable		Control	500 micgr	1000 micgr	P
Age, year		59/6±7	56/1±16/8	10/8±58/3	0.49
Sex	Male	17(48//6)	22(62/9)	22(62/9)	0.38
	Female	18(51/4)	13(37/1)	13(37/1)	
Cause of hospitalization	COPD	5(14/3)	5(14/3)	4(11/4)	
	Trauma	7(20)	10(28/6)	15(42/9)	
	CHF	5(14/3)	2(5/7)	3(8/6)	0.46
	CVA	4(11/4)	7(20)	5(14/3)	
	Tumor	9(25/7)	4(11/4)	3(8/6)	
	other	5(14/3)	7(20)	5(14/3)	

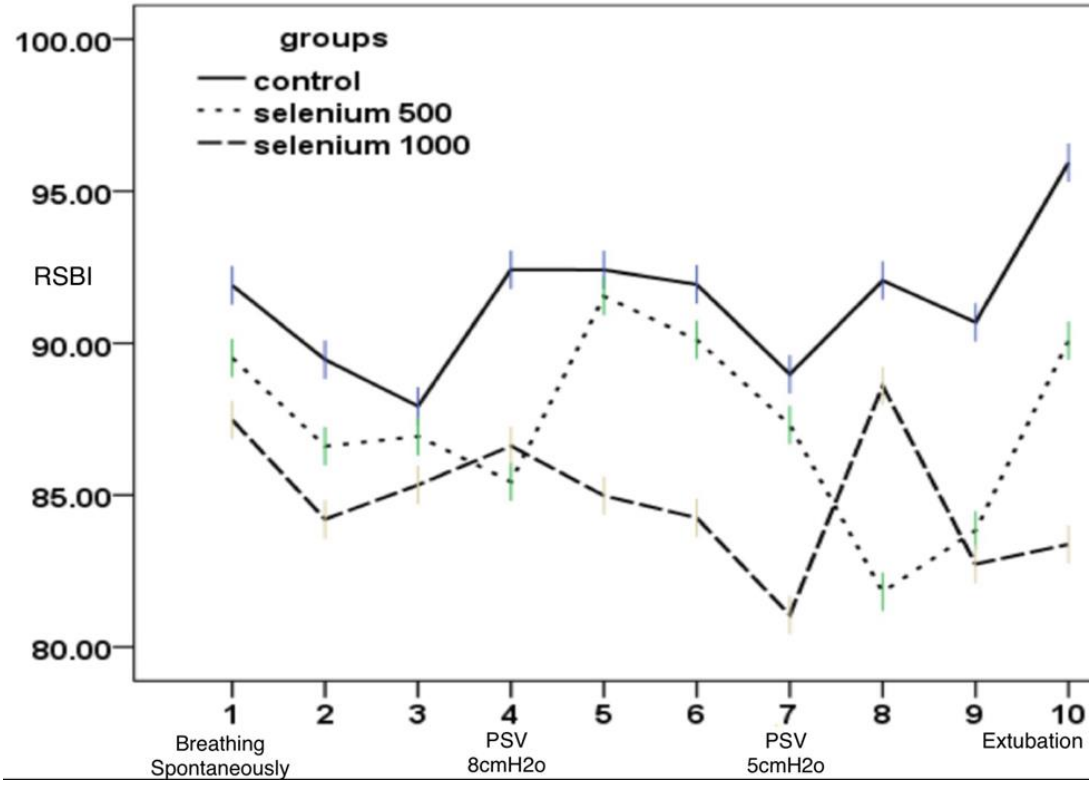
Table 2- The Mean of RSBI at breathing spontaneously until Extubation

Groups	Breathing spontaneously	Pressure support 8cmH2O	Pressure support 5cmH2O	Time extubation
A (1mg selenium)	91.9±13.7	91.7±12.7	82.3±10.06	83.4±10.4
B (0/5mg selenium)	89.5±13.8	88.9±11.7	92.4±11.65	93.23±11.86
C(placebo)	87.5±12	89.3±13.6	94.6±11.4	95.9±12.1
P value	p=0.45	P=0.53	P<0.001	P <0.001

Table 3- Mean and standard deviationAPACHE score, duration of mechanical ventilation, and length of stay in the study

	Group A Selenium1 mg	Group B Selenium 0/5 mg	Control	P value
APACHEII Score	15/83±3/89	16/83±3/14	15/76±3/89	0/28
length of stay in ICU(Day)	10/49±13/43	5/6±69/11	3/89±10/49	0/139
duration of mechanical ventilation (Day)	1/95±6/97	3/09±8/8	1/23±9/89	0/001<

Figure 1- Meanof RSBI at breathing spontaneously until Extubation



Discussion

In this randomized controlled trial, 105 patients were randomly assigned in three groups; Patients in group B received 0/5 mg and group A received 1 mg daily and those in group C received placebo at the time of admission to the intensive care unit.

We found that selenium(1mg) administration had effect on the RSBI, although compared to the control group, selenium (0/5 mg) administration had no effect in index, The results may be affected by limitations such as limited sample size as well as the effect of medications such as steroids, salicylates and non-steroidal anti-in ammatories, which can affect in ammatory factors, that are not considered in this study.

Heyland et al studied the effects of antioxidants and Glutamine in a heterogeneous ICU population (N = 1223). Patients were divided into four groups: placebo, glutamine (0.35 g/kg/24 h of body weight intravenously), antioxidants (selenium, zinc, beta carotene, vitamin E, and vitamin C), or antioxidants plus glutamine. Again, respiratory muscle function was not specifically evaluated but no difference in duration of mechanical ventilation was observed among the four groups. Although the effect of high-dose [22].

Antioxidant administration on respiratory muscle structure and function is encouraging in animal models, no data support the routine administration of antioxidants or other specific feeding strategies on respiratory muscle function in the critically ill ventilated patient [20].

But in a study which was conducted in the Czech Republic in 2006, it has been argued that blood selenium levels in patients in the intensive care unit are lower than the normal range of these micronutrients, so that they are not even compensated by conventional supplemental doses. Hence, these patients need high doses of selenium to correct their selenium levels [18]. Some studies have shown that the administration of selenium in patients who are in intensive care units with mechanical ventilation can contribute to respiratory symptoms in these patients [19]. However, in a study by Ali Kiaii et al. in 2017, it was observed that administration of selenium orally in patients admitted to the ICU was not accompanied by a reduction in extubation time [21]. The difference of this research with the present study was in oral and intravenous administration of selenium.

Conclusion

Although the results of our study suggest a positive effect of selenium on the reduction of duration mechanical ventilation and improve the patient's healing status, due to the acquisition of different progenies in our studies, as well as the limitations of our study, including a small sample size and the impossibility of a patients' follow-up; further studies in this regard are recommended. Selenium supplementation in critical illness and other disease states is promising; however, large randomized multi-center studies are needed to confirm the beneficial effects of selenium supplementation in critically ill patients.

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