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ORIGINAL ARTICLE

Correlation of High Dose of Vitamin D3 with Increased Hemoglobin in Patients under Mechanical Ventilation in Medical ICU

Sara Salarian[1], Seyed Pouzhia Shojaei[2], Mehran Kouchek[2], Mir Mohammad Miri[2], Mohamad Sistanizad[3,4], Amin Sahranavard shirazi[*1], Tahere Sorbi[5]

[1]*Anesthesiology Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran*

[2]*Anesthesia and Critical Care Department, Critical Care Quality Improvement Research Center, Imam Hossein Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran*

[3]*Department of Clinical Pharmacy, School of Pharmacy, Shahid Beheshti University of Medical Sciences, Tehran, Iran*

[4]*Prevention of Cardiovascular Disease Research Center, Imam Hossein Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran*

[5]*Anesthesiology Research Center, Iran University of Medical Sciences, Tehran, Iran*

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KEYWORDS

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ABSTRACT: Anemia is very common in critical illnesses. Around two-thirds of adults are anemic when admitted to the intensive care unit (ICU). Recently, Vitamin D deficiency has been identified as a potential cause of inflammatory anemia. In this study, we examine the relationship between the injection of a high dose of vitamin D3 and the hemoglobin level in patients undergoing mechanical ventilation in the ICU unit. The present study is a double-blind clinical trial. During a six-month period (June to November 2018), all patients admitted to the ICU department of Imam Hossein Hospital who met the study's inclusion criteria and were under mechanical ventilation were randomly divided into two groups. At first, the concentration of hemoglobin and the level of vitamin D3 were checked. In the control group, a placebo was used, while in the intervention group, patients were administered vitamin D3 via gavage (50,000 units for 5 days). The hemoglobin levels were measured and recorded once a week for a maximum duration of one month. No statistically significant difference was observed between the two groups in terms of demographic variables and SOFA. The average hemoglobin levels before and after the study in the vitamin D3 group were 9.9 ± 2.1 and 11.2 ± 2.5, respectively, and the difference was statistically significant (P=0.004). While in the control group, the average hemoglobin levels before and after the study were 9.9 ± 2.1 and 10.2 ± 1.8, respectively. However, the difference was not found to be statistically significant (P=0.102). In this study, it was found that increasing the level of vitamin D3 in patients hospitalized for 6 months in the ICU significantly increased their hemoglobin levels.

INTRODUCTHION

The measurement of hemoglobin levels in hospitalized patients holds significant importance. The intervention not only demonstrates high efficacy in promoting cardiopulmonary function, but also assumes a crucial

*Corresponding author: aminm5571@yahoo.com (A. Sahranavardshirazi)
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role in the management of infections within the intensive care unit (ICU). Most notably, correcting the decrease in hemoglobin concentration in the intensive care unit, a frequent occurrence due to frequent blood draws, can significantly reduce the necessity for transfusion, which carries a high risk of mortality and morbidity [1, 2].

Low levels of hemoglobin can lead to the development of Anemia, a condition that is frequently observed in individuals with critical illnesses. Approximately two-thirds of adults admitted to the intensive care unit (ICU) experience anemia, with an even higher prevalence observed during the initial week of admission [2].

Anemia in critical illness can arise from various factors including frequent blood sampling, hemorrhaging, renal dysfunction, inflammation, and deficiencies in essential nutrients such as iron, folate, and vitamin B12. Recently, there has been growing recognition of the association between vitamin D deficiency and anemia, particularly inflammatory anemia [3, 4].

The occurrence of anemia has been linked to a heightened mortality risk, cardiovascular disease, and reduced oxygen-carrying capacity, which may lead to a prolonged requirement for mechanical ventilation. This issue may be particularly linked to the occurrence of premature cardiovascular diseases.

Traditional interventions for anemia in critical illness encompass blood transfusions, erythropoiesis-stimulating agents, and iron supplementation. However, these interventions are not devoid of risks, and their efficacy in enhancing patient survival remains a subject of debate [5, 6].

When anemia is attributed to iron deficiency, which refers to the depletion of iron stores, it is commonly assessed by measuring the concentration of ferritin in the blood. Consequently, there is a decrease in circulating iron levels. Inflammatory anemia occurs when there is a decrease in the iron levels within the blood vessels, falling within the normal concentration range, or an increase in the ferritin levels, which leads to the sequestration of iron within the cells [7].

Considering the significant prevalence of anemia and its potential adverse consequences, it is imperative to conduct research on alternative and complementary therapies that are both safe and effective in enhancing hemoglobin levels in adults experiencing the condition.

Several studies have demonstrated the potential of vitamin D in reducing inflammatory cytokines, enhancing iron efflux from cells, and increasing circulating iron levels to facilitate erythropoiesis. Furthermore, based on research findings, it has been demonstrated that vitamin D has the ability to suppress the expression of antimicrobial peptides (HAMP), such as hepcidin. This suppression leads to an elevation in inflammatory diseases and the accumulation of iron in cells, ultimately resulting in the development of anemia [8, 9]. The association between vitamin D deficiency and anemia in the intensive care unit (ICU) has been established through numerous studies. One notable study, the VITdAL-ICU study, demonstrated that the group receiving vitamin D treatment exhibited a higher serum hemoglobin concentration after 28 days of intervention compared to the placebo group [10-12].

Given the exorbitant expenses associated with blood transfusion in patients and the numerous complications that can arise from such procedures, it is plausible to explore alternative methods of managing anemia in ICU patients. One potential approach involves utilizing vitamin D to elevate hemoglobin levels, thereby potentially obviating the need for blood transfusion.

MATERIALS AND METHODS

We designed a randomized controlled trial study on 100 patients who were hospitalized in the medical ICU for 6 months (from June to November 2019) at Imam Hossein Hospital and were subjected to mechanical ventilation. The participants were carefully chosen and subsequently allocated into two groups consisting of 50 individuals each: the intervention group receiving vitamin D and the control group receiving a placebo. The ward nurse gave vitamin D3 or placebo to the patient with the knowledge and prescription of Medical ICU Attend. Also, the concentration of hemoglobin was recorded by the flow section.

All the patients with the age 18 years' old who did not have anemia, chronic kidney disease, chronic liver disease, deficiency and abnormal increase of vitamin D3 that more than 12 days have been hospitalized in the medical ICU, included in this study.

After registering the demographic information, including age, sex, and underlying diseases, the objectives of the

study were explained to the patient, and they entered the study if they wished and obtained written consent. At first, hemoglobin concentration and vitamin D3 level were checked. Then placebo was administered to patients in the control group, and vitamin D3 was gavaged to patients in the intervention group with a dose of 50,000 units for 5 days. Therefore, the patient's hemoglobin level was less than 12 grams per deciliter (9.9 ± 2.1) and hemoglobin was measured and recorded once a week for a maximum duration of one month.

Study variables

In addition to sex and age, we also measured vitamin D3, hemoglobin level and SOFA score (sequential organ failure assessment score).

Sample size

To ascertain the appropriate sample size, the hemoglobin (Hb) level was utilized as a crucial variable for comparison between the two groups. To estimate the standard deviation, a pilot sample of 10 was selected from both the treatment and control group and the pooled variance was calculated as 1.21. The formula for determining the sample size for comparing the average of a variable between two groups considering its parameters is as follows:

$$n = 2 \times \sigma^2 \times \frac{(Za + Zb)^2}{d^2}$$

If the acceptable error value for the significance of the difference is considered as 0.5 and the values of Za and Zb, which are used to include the significance level and the power of the test, respectively, are 1.96 and 0.84, the total sample size equal to:

$$n = 2 \times (1.21)^2 \times \frac{(1.96 + 0.84)^2}{(0.5)^2} \cong 100$$

Therefore, including totally the number of 100 samples in study, 50 patients should be included in each group.

Statistical analysis

To describe data, we used frequency (percent) and mean ± SD. After examining the hypothesis of normal data, using the Shapiro test, we used an independent t-test to compare Age, SOFA and hemoglobin levels between the two groups also Chi-square tests were utilized to compare qualitative variables such as sex. A P - value less than 0.05 was considered statistically significant. All statistical analyses were performed by SPSS software (IBM Corp. Released 2018. IBM SPSS Statistics for Windows, Version 26.0. Armonk, NY: IBM Corp.).

RESULTS

A total of 100 patients, who were admitted to the medical ICU at Imam Hossein Hospital, underwent mechanical ventilation for a duration of 6 months, specifically from June to November 2019. The participants were carefully chosen and subsequently allocated into two groups consisting of 50 individuals each: the intervention group receiving vitamin D and the control group receiving a placebo.

We recruited a total of 100 patients who were admitted to the medical Intensive Care Unit (ICU) for a duration of 6 months. Among them, 50 patients were assigned to the intervention group receiving vitamin D, while the remaining 50 patients were allocated to the control group. In the group receiving vitamin D, 33 individuals (66%) were male and 17 individuals (34%) were female. The age distribution in this group was 60.1±13.3 years. In the control group, 29 individuals (58%) were male and 21 individuals (42%) were female. The age distribution in the control group was 59.0±13.7 years. The age and sex differences were found to be statistically insignificant (P-value age= 0.49, P-value sex=0.109). Furthermore, there was no significant relationship observed between the treatment group and the level of SOFA in patients, as indicated by a P-value of 0.693. The hemoglobin levels of the patients in the control group before the intervention were recorded as 9.9 ± 2.1, while the hemoglobin levels in the vitamin D group were also 9.9 ± 2.1 (P-value=0.269). However, after the intervention, there was an increase in hemoglobin levels in both groups. Specifically, the control group showed a hemoglobin level of 10.2 ± 1.8, while the vitamin D group exhibited a hemoglobin level of 11.2 ± 2.5. It is evident from our study that the administration of vitamin D has a substantial impact on the hemoglobin levels of our patients (P-value <0.001) (Table 1).

Table 1. Comparison of the two groups through patient's characteristics and hemoglobin lever before and after treatment

Items	Control	Vitamin D	P-value
Age	60.1±13.3	59.0±13.7	0.490
Sex (Male)	33(66.0%)	29(58.0%)	0.109
SOFA	6.9±3.8	6.7±3.6	0.693
Hemoglobin			
Before	9.9 ± 2.1	9.9 ± 2.1	0.269
After	10.2 ± 1.8	11.2±2.5	<0.001*
P-Within	0.102	0.004	

**p-value based on chi-square; **p-value based on T-test*

The mean Hemoglobin levels exhibited a significant difference before and after the study in the group receiving vitamin D3 (P-value=0.004). In the control group, there was no significant difference in the average Hemoglobin levels before and after the study (P-value=0.102). Figure 1 illustrates the fluctuations in the mean Hemoglobin levels within two distinct groups, both prior to and subsequent to the conducted study.

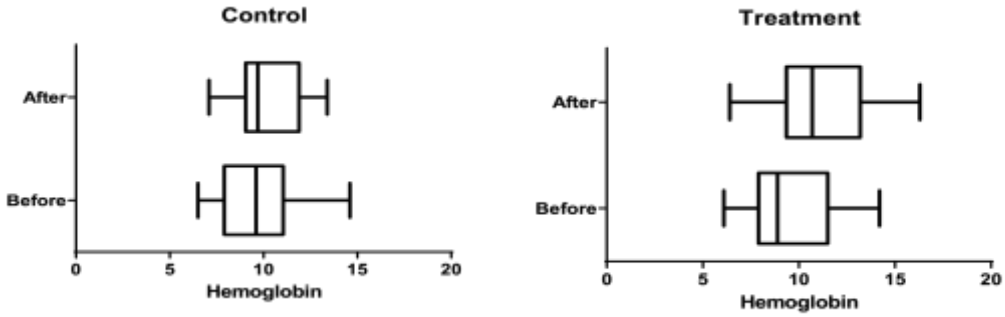

Figure 1. Average hemoglobin changes before and after the study in two groups.

DISCUSSION

Anemia is a prevalent condition observed in critically ill or injured patients. Approximately 66% of these patients exhibit hemoglobin levels below 12 grams per deciliter, and a staggering 97% of them experience the onset of anemia by the 8th day [13]. The impact of elevated doses of vitamin D on various diseases has been extensively investigated by numerous researchers. The administration of high doses of vitamin D has demonstrated significant efficacy in the management of various diseases [13-15].

In previous research, the potential impact of vitamin D on hemoglobin levels and its potential as a treatment for anemia has been investigated. The findings of these studies indicate that vitamin D levels do not have a significant impact on increasing hemoglobin levels in individuals with hypertension [16].

In previous research conducted on various populations, such as those with chronic obstructive pulmonary disease (COPD) and chronic kidney disease (CKD), the potential impact of vitamin D on hemoglobin levels has been extensively examined [16, 17].

We conducted an investigation to examine the impact of administering a high dosage of vitamin D to patients who were admitted to the hospital's ICU for a duration of six months. In light of this matter, we have made the decision to assess the hemoglobin levels in two groups of

patients: one group receiving 50,000 units of vitamin D3 every 5 days, and the other group receiving a placebo. The hemoglobin level exhibited a significant increase in the group that received a high dose of vitamin D3, suggesting its potential efficacy in the treatment of anemia. It has been discovered that the administration of a high dosage of vitamin D3 (50,000 units) can result in an elevation of hemoglobin levels, thereby offering a potential treatment option for anemia caused by frequent blood draws during hospitalization.

The elevation of vitamin D plasma levels provides enhanced preconditions for a better tissuenoxygenation on a cellular level [18].

The results showed that vitamin D could cause leukopenia (e.g., neutropenia and lymphopenia), therombocytopenia, as well as an increase in hemoglobin levels in the blood [19].

In conclusion, our study aimed to investigate the impact of increasing the level of vitamin D3 on the control and treatment of anemia in hospitalized patients. The results obtained from the study indicate a positive effect of the treatment, as it was found to increase hemoglobin levels in the patients.

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Conflict of interests

The authors declare that they have no conflicts of interest.

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