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THE EFFECT OF SINGLE DOSE VITAMIN D3 INTRAMUSCULAR INJECTION DURING INTENSIVE CARE UNIT ON RENAL FUNCTION IN PATIENTS WITH TRAUMATIC INJURIES: A DOUBLE-BLINDED, RANDOMIZED, AND CONTROL TRIAL STUDY

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Abstract

Background: Vitamin D deficiency is an independent risk factor for cardiovascular disease and a predictor of chronic kidney disease, especially in traumatic patients admitted to the intensive care unit. This study aims to investigate the effect of single-dose intramuscular injection of vitamin D3 on renal function in patients with traumatic injuries.

Methods: This was a randomized clinical trial with a control group in a parallel, double-blind, randomized study that enrolled patients from 2023-08 to 2023-10. The patients were divided into intervention (receiving vitamin D) and control groups. During the first 24 hours of hospitalization, both groups received either an intramuscular dose of the drug (300,000 units of vitamin D) or a placebo (which was identical to the original drug). Demographic information of patients (age, sex, underlying disease, height, and weight), trauma severity score (revised trauma score and new trauma score), the number of days requiring ventilation, anthropometric indices (BMI, abdominal circumference, and the ratio of abdominal circumference to hip circumference), length of hospital stay, blood urea nitrogen, and creatinine levels, were checked and recorded.

Results: Finally, 60 patients were included in this study. Most of the patients (85%) were male. The mean age of the patients (35.2 ± 13.96 years), the average new trauma score and revised trauma score showed no any significant differences between two groups ($P > 0.05$). Statistical analysis showed that the differences of average number of hospitalization days, the days requiring ventilation and the increase in blood urea nitrogen and creatinine levels between intervention and control groups were not significant ($P > 0.05$).

Conclusion: Administration of vitamin D in patients hospitalized in intensive care unit does not have a significant and beneficial effect on blood urea nitrogen, creatinine, the number of hospitalization days and the days requiring ventilation.

KEYWORDS: traumatic injuries, renal insufficiency, chronic kidney disease, intensive care unit, vitamin D.

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INTRODUCTION

Acute renal failure is one of the common symptoms in critical patients admitted to the intensive care unit (ICU) [Weisbord S, Palevsky P 2016]. Some studies have associated acute renal failure with a rapid decrease in glomerular filtration rate within several hours to several weeks, retention of excess nitrogen products, and disturbances in extracellular fluid volume, and acid-base and electrolyte balance [Makris K, Spanou L. 2016]. Acute renal failure is usually asymptomatic and is diagnosed when an increase in plasma urea and creatinine concentration is detected in the biochemical tests of hospitalized patients [Akçay A et al., 2010].

Acute renal failure affects 5-25% of patients in the ICU, increases mortality rate by 15-60%, and brings about many problems by increasing treatment costs and length of stay in hospital [Korkeila M et al., 2000]. Epidemiological studies have shown that acute renal failure can be an independent factor for death [Weisbord S, Palevsky P, 2006]. However, therapeutic interventions to prevent the occurrence of acute renal failure are limited, and there is no effective drug for its treatment [Kasper D 2015]. The level of vitamin D in people with sepsis hospitalized in ICU is lower than that in other ICU patients, but it is not different from the level of vitamin D in healthy individuals [Quraishi S, 2016]. On the other hand, lack of serum vitamin D levels in patients hospitalized in ICU causes a 1.5-fold increase in the likelihood of disease development and up to a 2-fold increase in the likelihood of a bad prognosis [Guan J, 2017]. Moreover, there were 86% of patients in the intensive care unit who did not have enough serum vitamin D, which was associated with a 2-fold increase in the likelihood of death [Amrein K, 2014]. Furthermore, lack of vitamin D levels in patients hospitalized in ICU is associated with an increase in the likelihood of disease and mortality caused by it, which lack of vitamin D level worsens the prognosis of ICU patients [Izadpanah M, Khalili H 2013].

Vitamin D deficiency is known to be an independent risk factor for cardiovascular disease, and a predictor of chronic kidney disease [Lee M 2019]. Kidney dysfunction is associated with an increase in the concentration of uric acid and a decrease in its renal excretion [Ejaz A 2007]. Parathyroid hormone has a strong biological effect on uric acid concentration. Vitamin D deficiency or

insufficiency can activate the release of parathyroid hormone [Peng H 2013]. However, vitamin D may exert its paracrine function through local activation of 1-hydroxylase and thus preserve immunity and vascular function and reduce inflammation has received less scholarly attention. In kidneys, the importance of vitamin D may be attributed to maintaining the health of podocytes, preventing epithelial-to-mesenchymal transformation, and suppressing the renin gene expression and inflammation [Agarwal R. Vitamin D, 2009]. Researchers have shown that the development of end-stage renal disease in people with serum levels of 25-hydroxyvitamin D less than 15 ng/ml was 2.6 times more than in people with higher levels [Melamed M 2009]. Also, the association between vitamin D deficiency and reduced glomerular filtration rate and the inverse relationship between uric acid and 25-hydroxyvitamin D have been reported [Alemzadeh R, Kichler J 2016].

Aim of the work: According to the studies as mentioned above, the vitamin D level has a relationship with kidney function and body mass index (BMI). Reports also state that the level of vitamin D in ICU patients is low, and this vitamin is associated with the recovery rate and the length of hospital stay of these patients. Therefore, the present study aimed to investigate the effect of single-dose D3 intramuscular injection during ICU on renal function in patients with traumatic injuries.

MATERIAL AND METHODS

This study was based on the Consolidated Standards of Reporting Trials (CONSORT) guideline [Cuschieri S 2019].

Study design and participants: This was a randomized clinical trial with a control group in a parallel, double-blind, randomized study that enrolled patients from 2023-08 to 2023-10. The ethical approval under the code IR.AJUMS.HGOLESTAN.REC.1401.171 from the Research and Technology Deputy at Jundishapur Ahvaz University of Medical Sciences. Additionally, the trial was registered with the code IRCT20221121056570N2 at the International Clinical Trials Registry Platform of Iran (<https://www.irct.ir/>).

Inclusion criteria: Trauma patients with a revised trauma score greater than or equal to 6 and over 18 years of age have been hospitalized in the

ICU for at least 24 hours and Revised trauma score revised trauma score ≥ 6 New trauma score ≥ 8 were included.

Exclusion criteria: Having chronic kidney disease, autoimmune disease or cancer were excluded.

Intervention: Trauma patients in the ICU of Ahvaz Golestan Hospital, if they met the inclusion criteria, after obtaining written consent, they randomly divided into two groups A and B based on blocks of 4 random numbers. Blood urea and creatinine levels are recorded daily, and anthropometric indices (BMI, abdominal circumference) are recorded on arrival and at the end of the 28th day or day of discharge. Both groups received an intramuscular dose of 300,000 units of vitamin D or placebo during the first 24 hours of hospitalization. Demographic information of patients (age, sex, underlying disease, height, and weight), trauma severity score (revised trauma score and new trauma score), the number of days requiring ventilation, anthropometric indices (BMI, abdominal circumference, and the ratio of abdominal circumference to hip circumference), length of hospital stay, blood urea nitrogen, and creatinine levels, and were checked recorded.

Randomization: Randomization was done by individually assigning random numbers with blocks of 4. The tool generated random numbers with blocks of 4 is the online software of the www. Sealedenvelope.com website. Every new patient who was admitted to the ICU, if he met the inclusion criteria for entering the study, was placed in one of the A or B groups in the order of arrival and based on the order of randomly generated numbers.

Blinding: For allocation concealment, except for the hospital pharmacist who prepares the drugs for injection and is not present in the study, no one else knows which of the placebo or vitamin D groups referred to each of the A and B groups. Patients (or the patient's family), nurses (care providers), research assistants (who are in charge of data collection), and the statistical analyst did not know about the drug groups (intervention or control) and delivery of medication was done by a person selected from outside the department (hospital pharmacist).

Statistical analysis: Data was imported into SPSS software version 25 for analysis. Chi-square was employed to compare categorical variables.

TABLE 1.

Demographic information of the studied patients			
Variable		Mean \pm SD	P-Value
Age (year)	Int	35.27 \pm 14.161	0.993
	C	35.30 \pm 14.015	
Sex (female%)	Int	16.66	0.100
	C	13.33	
BMI (kg/m^2)	Ad	27.08 \pm 3.92	0.690
	Dis	27.18 \pm 3.70	
	Ad	26.61 \pm 3.38	0.964
	Dis	27.08 \pm 3.64	
The ratio of abdomen/hip circumference	Ad	0.87 \pm 0.42	0.612
	Dis	0.89 \pm 0.51	
	Ad	0.87 \pm 0.04	0.998
	Dis	0.88 \pm 0.05	
24-hour urine volume (ml)	Ad	2369.67 \pm 1148.66	0.163
	Dis	2327.00 \pm 1327.84	
	Ad	2793.33 \pm 1124.00	0.833
	Dis	2872.33 \pm 1089.85	

NOTES: Ad - Admission, Dis - Discharge, Int - Intervention group, C - Control group.

Also, one-way ANOVA was used to compare the means of independent groups. $P < 0.05$ was considered statistically significant.

RESULTS

In the final report of this study, 60 patients were studied (51 (85%) were males, and 9 (15%) were females). The average age of the participants was 35.2 ± 13.96 and ranged between 18 and 75 years. The patients' demographic characteristics are presented in Table 1.

As to their age, gender, height, weight, 24-hour urine volume, and anthropometric indices, there were no substantial differences between the two groups ($P > 0.05$).

According to the results, the length of stay in ICU was more extended in the intervention group, while patients in the control group experienced a longer period of mechanical ventilation. However, these differences were not statistically significant ($P > 0.05$) (Table 2). Revised trauma score was higher in the intervention group, whereas a higher new trauma score was observed in the control group. Of course, these differences were not statistically significant ($P > 0.05$). As shown in Table 3, no statistically significant difference was observed between the two groups regarding increased or creatinine levels ($P > 0.05$).

TABLE 2.

The average number of hospitalization days and the need for a ventilator in the studied patients.

Variable		Mean ± SD	P-Value
Length of ICU admission (days)	Int	10.07 ± 7.59	0.827
	C	10.77 ± 7.10	
Length of mechanical ventilation (days)	Int	10.07 ± 7.59	0.066
	C	10.77 ± 7.10	

Notes: ICU -intensive care unit, **Int** - Intervention group, **C** - Control group.

TABLE 3.

Trauma severity scale, and changes in blood urea nitrogen and creatinine levels in the studied patients in the studied patients.

Variable		Mean ± SD	P-Value
New trauma score	Int	11.20 ± 0.961	0.162
	C	11.53 ± 0.860	
Revised trauma score	Int	10.67 ± 1.44	0.547
	C	10.53 ± 1.30	
Increased blood urea nitrogen, N (%)	Int	11 (36.6)	0.199
	C	7 (23.3)	
Increased creatinine, N (%)	Int	9 (30)	0.209
	C	4 (13.3)	

Notes: ICU -intensive care unit, **Int** - Intervention group, **C** - Control group.

DISCUSSION

This study was conducted to examine the effect of vitamin D3 on renal function in patients who were being treated at an intensive care unit. Overall, our studies have shown that vitamin D3 supplementation had no significant effect on these patients' critical condition. The vitamin D3 supplementation and placebo groups did not differ significantly in length of stay at the Intensive Care Unit or duration of days that had to be mechanically ventilated. In addition, no statistically significant difference was observed between the two groups in terms of the mean revised trauma score and new trauma score.

The results of the present study are generally consistent with those of a meta-analysis by Lan et al. [Lan S et al., 2020]. Their results showed that vitamin D supplementation did not reduce mortality, length of stay in the ICU length of hospital stay, or the length of mechanical ventilation. However, our results showed that vitamin D3 supplementation reduced the length of ICU stay.

In line with our research, Shen et al [Shen H et al., 2020] reported that the administration of vita-

min D supplements reduced the length of stay in the ICU and the length of mechanical ventilation.

Our results are consistent with the meta-analysis of Langlois et al [Langlois P et al., 201], which stated that vitamin D did not reduce mortality rate, length of stay in an intensive care unit and hospital stay or mechanical ventilation time. The second meta-analysis, conducted by Putzu et al. [Putzu A et al., 2017], concluded that vitamin supplementation was associated with a reduction in mortality as opposed to placebo.

The difference in the size of the sample, dose of vitamin D injection and length of follow-up may be related to these differences.

A prior study has shown that, compared to healthy subjects, the concentration of plasma 25OH(12) D in patients with sepsis is strongly related to a decreased plasma cathelicidin level. A low level of 25(OH)D was a predictive biomarker for Acute Kidney Injury and had a significant impact on length of stay, organ dysfunction, infection rate, and survival in critically ill patients [Bouillon R et al., 2019]. Another study evaluated the effects of vitamin D on clinical outcomes (consciousness, ICU length of stay, mechanical ventilation, and serum cytokines (IL-6, TNF- α , IL-2, IFN- γ)) of patients. The results showed that vitamin D improved the level of consciousness and shortened the period of mechanical ventilation in these patients and that the level of consciousness and Glasgow Outcome Scale score were significantly higher in patients receiving vitamin D compared to those receiving placebo [Sharma S et al., 2020].

Lee et al. reported that most of the studied trauma patients were deficient in vitamin D, and that administration of vitamin D in these patients improved the serum level of vitamin D in three months. According to their results, the Glasgow Outcome Scale – Extended score of patients receiving vitamin D was higher in the control group [Lee J et al., 2019]. In a study in Austria on 655 patients, Amrein et al. found that 86% of patients referred to the ICU had a deficiency of serum vitamin D levels, which was associated with a 2-fold increase in mortality [Amrein K et al., 202].

In a clinical trial, Abbasi et al investigated the effect of vitamin D on the prognosis of trauma patients admitted to ICU. The results of the study showed that the administration of vitamin D to

trauma patients admitted to the ICU who are deficient in this vitamin significantly increases the rate of discharge from the ICU. Also, body mass index was lower in the group receiving vitamin D compared to the control group [Abbasi S et al., 2020]. The results of Dickerson et al. showed that trauma patients admitted to the ICU with vitamin D deficiency had a longer length of stay [Dickerson R et al., 2016].

The two groups of patients have been compared about increased blood urea nitrogen and creatinine levels which, to the very best of our knowledge, had not been assessed before this study. The results showed an increase in blood urea nitrogen and creatinine levels in the patients of the intervention group compared to the control group, but the difference was not statistically significant.

Some previous studies have shown a decrease in e glomerular filtration rate with 1,25 OH₂D analogues, such as paricalcitol, which may be due to a change in creatinine metabolism rather than a real decrease in glomerular filtration rate. However, there were no reports of any effects on creatinine metabolism with cholecalciferol. Although several observational studies have demonstrated an association between low circulating 25-hydroxyvitamin D concentrations and kidney disease, only a limited

number of studies were conducted to investigate the effects of vitamin D supplementation on renal function [Kim S et al., 2021]. Acute kidney injury is a significant decrease in kidney function that affects the normal enzyme activity of the kidney, thereby disrupting vitamin D function. Vitamin D deficiency is usually caused by decreased kidney function. A progressive decline in kidney function during acute kidney injury leads to phosphate retention and accumulation due to the inability to excrete it. Phosphate acts as a negative regulator of 1-hydroxylase, an enzyme of 1,25 (OH)₂D synthesis, and thus negatively contributes to vitamin D metabolism [Graidis S et al., 2020].

CONCLUSION

The results of the present study showed that the administration of vitamin D in patients admitted to the ICU does not have a significant and beneficial effect on the number of days of hospitalization and the need for ventilator. Despite the absence of statistically significant results regarding the increase in blood urea nitrogen and creatinine levels in patients receiving vitamin D, it is necessary, from a clinical point of view, to conduct more similar studies with a larger sample size and a longer follow-up period.

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REFERENCES

1. Abbasi S, Alikiaii B, Kashefi P, Hatamzadeh B. (2020). [The effect of Vitamin D supplement on outcomes in patients with traumatic injuries hospitalized in intensive care unit: A clinical trial study], [Print in Farsi] Journal of Isfahan Medical School. 2020;38(590):649-54. DOI: 10.22122/jims.v38i590.13204
2. Agarwal R. Vitamin D, (2009). proteinuria, diabetic nephropathy, and progression of CKD. Clin J Am Soc Nephrol. 2009;4(9):1523-8. DOI: 10.2215/CJN.02010309
3. Akcay A, Turkmen K, Lee D, Edelstein CL. (2010). Update on the diagnosis and management of acute kidney injury. Int J Nephrol Renovasc Dis. 2010;3:129-40. DOI: 10.2147/IJNRD.S8641
4. Alemzadeh R, Kichler J. (2016). Uric Acid-Induced Inflammation Is Mediated by the Parathyroid Hormone:25-Hydroxyvitamin D Ratio in Obese Adolescents. Metab Syndr Relat Disord. 2016;14(3):167-74. DOI: 10.1089/met.2015.0099

5. Amrein K, Scherkl M, Hoffmann M, Neuwersch-Sommeregger S, Köstenberger M, Tmava Berisha A, et al. (2020). Vitamin D deficiency 2.0: an update on the current status worldwide. *Eur J Clin Nutr.* 2020;74(11):1498-513. DOI: 10.1038/s41430-020-0558-y
6. Amrein K, Zajic P, Schnedl C, Waltensdorfer A, Fruhwald S, Holl A, et al. (2014). Vitamin D status and its association with season, hospital and sepsis mortality in critical illness. *Crit Care.* 2014;18(2):R47.
7. Bouillon R, Marcocci C, Carmeliet G, Bikle D, White JH, Dawson-Hughes B, et al. (2019). Skeletal and Extraskelatal Actions of Vitamin D: Current Evidence and Outstanding Questions. *Endocr Rev.* 2019;40(4):1109-51. doi: 10.1210/er.2018-00126
8. Cuschieri S. (2019). The CONSORT statement. *Saudi J Anaesth.* 2019;13(Suppl 1):S27-s30. DOI: 10.4103/sja.SJA_559_18
9. Dickerson RN, Van Cleve JR, Swanson JM, Maish GO, 3rd, Minard G, Croce MA, et al. (2016). Vitamin D deficiency in critically ill patients with traumatic injuries. *Burns Trauma.* 2016;4:28. DOI: 10.1186/s41038-016-0054-8
10. Ejaz AA, Mu W, Kang DH, Roncal C, Sautin YY, Henderson G, et al. (2007). Could uric acid have a role in acute renal failure? *Clin J Am Soc Nephrol.* 2007;2(1):16-21. DOI: 10.2215/CJN.03420906
11. Graidis S, Papavramidis TS, Papaioannou M. (2020). Vitamin D and Acute Kidney Injury: A Two-Way Causality Relation and a Predictive, Prognostic, and Therapeutic Role of Vitamin D. *Front Nutr.* 2020;7:630951. DOI: 10.3389/fnut.2020.630951
12. Guan J, Karsy M, Brock AA, Eli IM, Ledyard HK, Hawryluk GWJ, et al. (2017). A prospective analysis of hypovitaminosis D and mortality in 400 patients in the neurocritical care setting. *J Neurosurg.* 2017;127(1):1-7. DOI: 10.3171/2017.1.JNS16169
13. Izadpanah M, Khalili H. (2013). Potential benefits of vitamin D supplementation in critically ill patients. *Immunotherapy.* 2013;5(8):843-53. DOI: 10.2215/CJN.10640820
14. Kasper D, Fauci A, Hauser S, Longo D, Jameson J, Loscalzo J. (2015). *Harrison's principles of internal medicine, 19e:* Mcgraw-hill New York, NY, USA.; 2015.
15. Kim SH, Brodsky IG, Chatterjee R, Kashyap SR, Knowler WC, Liao E, et al. (2021). Effect of Vitamin D Supplementation on Kidney Function in Adults with Prediabetes: A Secondary Analysis of a Randomized Trial. *Clin J Am Soc Nephrol.* 2021;16(8):1201-9. DOI: 10.2215/CJN.10640820
16. Korkeila M, Ruokonen E, Takala J. (2000). Costs of care, long-term prognosis and quality of life in patients requiring renal replacement therapy during intensive care. *Intensive Care Med.* 2000;26(12):1824-31. DOI: 10.1007/s001340000726
17. Lan SH, Lai CC, Chang SP, Lu LC, Hung SH, Lin WT. (2020). Vitamin D supplementation and the outcomes of critically ill adult patients: a systematic review and meta-analysis of randomized controlled trials. *Sci Rep.* 2020;10(1):14261. DOI: 10.1038/s41598-020-71271-5
18. Langlois PL, Szvec C, D'Aragon F, Heyland DK, Manzanares W. (2018). Vitamin D supplementation in the critically ill: A systematic review and meta-analysis. *Clin Nutr.* 2018;37(4):1238-46. DOI: 10.1016/j.clnu.2017.05.006
19. Lee JM, Jeong SW, Kim MY, Park JB, Kim MS. (2019). The Effect of Vitamin D Supplementation in Patients with Acute Traumatic Brain Injury. *World Neurosurg.* 2019;126:e1421-e6. DOI: 10.1016/j.wneu.2018.12.155
20. Lee MJ, Hsu HJ, Wu IW, Sun CY, Ting MK, Lee CC. (2019). Vitamin D deficiency in northern Taiwan: a community-based cohort study. *BMC Public Health.* 2019;19(1):337. DOI: 10.1186/s12889-019-6657-9
21. Makris K, Spanou L. (2016). Acute Kidney Injury: Definition, Pathophysiology and Clinical Phenotypes. *Clin Biochem Rev.* 2016;37(2):85-98. DOI: 10.33176/AACB-CBR-2016-0012
22. Melamed ML, Astor B, Michos ED, Hostetter TH, Powe NR, Muntner P. (2009). 25-hydroxyvitamin D levels, race, and the progression of kidney disease. *J Am Soc Nephrol.* 2009;20(12):2631-9. DOI: 10.1681/ASN.2009020216
23. Peng H, Li H, Li C, Chao X, Zhang Q, Zhang Y. (2013). Association between vitamin D insuf-

- iciency and elevated serum uric acid among middle-aged and elderly Chinese Han women. *PLoS One*. 2013;8(4):e61159. DOI: 10.1371/journal.pone.0061159
24. Putzu A, Belletti A, Cassina T, Clivio S, Monti G, Zangrillo A, et al. (2017). Vitamin D and outcomes in adult critically ill patients. A systematic review and meta-analysis of randomized trials. *J Crit Care*. 2017;38:109-14. DOI: 10.1016/j.jcrc.2016.10.029
25. Quraishi SA, McCarthy C, Blum L, Cobb JP, Camargo CA, Jr. (2016). Plasma 25-Hydroxyvitamin D Levels at Initiation of Care and Duration of Mechanical Ventilation in Critically Ill Surgical Patients. *JPEN J Parenter Enteral Nutr*. 2016;40(2):273-8. doi:10.1177/0148607114566276.
26. Sharma S, Kumar A, Choudhary A, Sharma S, Khurana L, Sharma N, et al. (2020). Neuroprotective Role of Oral Vitamin D Supplementation on Consciousness and Inflammatory Biomarkers in Determining Severity Outcome in Acute Traumatic Brain Injury Patients: A Double-Blind Randomized Clinical Trial. *Clin Drug Investig*. 2020;40(4):327-34. DOI: 10.1007/s40261-020-00896-5
27. Shen H, Mei Y, Zhang K, Xu X. (2020). The Effect of Vitamin D Supplementation on Clinical Outcomes for Critically Ill Patients: A Systemic Review and Meta-Analysis of Randomized Clinical Trials. *Front Nutr*. 2021;8:664940. doi: 10.3389/fnut.2021.664940
28. Weisbord SD, Palevsky PM, editors. (2006). Acute renal failure in the intensive care unit. *Seminars in respiratory and critical care medicine*; 2006: Published by Thieme Medical Publishers, Inc., 333 Seventh Avenue, New York.
29. Weisbord SD, Palevsky PM. (2016). Acute renal failure in the intensive care unit. *Semin Respir Crit Care Med*. 2006;27(3):262-73. DOI 10.1055/s-2006-945527. ISSN 1069-3424.



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