



Original Research Article

Role of Vitamin D3 in fracture union in adults

Amrit Kumar Singh¹, Arunabh Arora^{1,*}¹Dept. of Orthopaedics, School of Medical Sciences and Research, Sharda University, Greater Noida, Uttar Pradesh, India

ARTICLE INFO

Article history:

Received 02-06-2021

Accepted 19-06-2021

Available online 24-06-2021

Keywords:

Vitamin D3

Calcium

Fracture

Osteoporosis

ABSTRACT

Introduction : Fractures play an important role in morbidity and often premature mobility among the elderly population. Because inactivity as a result of a fracture is harmful both to bone healing and health, it appears early or rapid fracture healing would be highly recommendable for returning fracture patients to come back to normal as soon as possible with minimal side effects. The literature remains unclear regarding supplementation required for promoting bone healing in fracture cases. Hereby we evaluated the advantages and disadvantages of vitamin D3 supplementation in fracture cases along with the quantitative analysis of vitamin D3 at the time of fracture and after fracture union.

Materials and Methods: A total of 200 patients were assessed clinically, biochemically (serum alkaline phosphatase, serum vitamin D3, and serum parathormone), and radiologically. All patients who satisfy inclusion criteria are followed up and vitamin D3 levels were measured up within 1 day of fracture and at the interval of 6 months after the orthopaedic intervention. The outcomes were monitored by the 5 points radiographic scoring system by Warden et al.

Results: With the majority of patients falling under the vitamin insufficiency group i.e. 53% of all patients were found to be vitamin insufficient at the time of fracture. 33% of patients found to be vitamin D deficient while 14% found to be insufficient stage. No patient was found to be in a toxicity state. According to Warden's scoring., 50% of patients were in grade 3, 15% in grade 4, 33% in grade 2, and only 2% in grade 1.

Conclusion: Regarding the prevalence of vitamin D deficiency or insufficiency in the general population, this study shows an alarming rate of vitamin D insufficient patients in a group of 200 patients, which indicates the need for attention towards vitamin D status not only for bone-related issues but for other issues related to vitamin D deficiency.

© This is an open access article distributed under the terms of the Creative Commons Attribution License (<https://creativecommons.org/licenses/by/4.0/>) which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

1. Introduction

Fractures play an important role in morbidity and often premature mobility among the elderly population.¹ Among adults, bone fractures due to trauma can seriously impair function and future activities.² In both elder persons as well as younger persons reducing the bone healing time while increasing bone strength at the fracture site during healing is important for better outcomes of the therapeutic process.^{3,4} Because inactivity as a result of a fracture is harmful both to bone healing and health, it appears early or

rapid fracture healing would be highly recommendable for returning fracture patients to come back to normal as soon as possible with minimal side effects.^{5,6}

Hip fractures represent the most frequent fractures in the patients presenting to the trauma center or orthopedics department.⁷ After these fractures, patients are at an increased chance of subsequent fracture or re-fracture. Patients with previous hip fractures have a 2.5 fold higher chance of re-fracture at the same site compared to normal patients especially, in the osteoporotic patients.^{8,9} This increases risk is associated with morbidity, mortality and therefore gives a dramatic increase to social and economic costs.¹⁰ All national and international societies' guidelines

* Corresponding author.

E-mail address: arunabharora1989@gmail.com (A. Arora).

on osteoporosis advocate evaluating patients presenting with a fracture to consider treatment to reduce the risk of subsequent fractures or re-fractures.^{11–13}

Adequate Calcium and Vitamin D3 intake are advised in guidelines of osteoporosis. However, the dosage needed to achieve an optimal calcium and vitamin D3 status is still a point of debate. The literature remains unclear regarding supplementation required for promoting bone healing in fracture cases.^{14–16} Even if the vitamin D3 hormone system is essential for calcium homeostasis, there is no consensus about vitamin D3 efficacy and safety concerning bone health. Hereby we evaluated the advantages and disadvantages of vitamin D3 supplementation in fracture cases along with the quantitative analysis of vitamin D3 at the time of fracture and after fracture union.

2. Materials and Methods

After obtaining the institutional ethical clearance, the patients with traumatic fractures who attend the orthopedics OPD were taken up for the study. A total of 200 patients, who were enrolled for the study after obtaining informed and written consent, were assessed clinically, biochemically (serum alkaline phosphatase, serum vitamin D3, and serum parathormone), and radiologically. All patients who satisfy inclusion criteria are followed up and vitamin D3 levels were measured up within 1 day of fracture and at the interval of 6 months after the orthopaedic intervention. The outcomes were monitored by the 5 points radiographic scoring system by Warden et al^{17,18} (Table 1).

Table 1: Modified warden's score (To assess the stage of fracture healing)^{17,18}

Score	Description
0	No evidence of healing
1	Callus formation evident but fracture gap not bridged
2	Callus formation evident with bridging of the fracture gap but fracture line evident
3	Callus formation evident with bridging of the fracture gap with an only faint fracture line
4	Fracture union

Patients greater than 18 years of age with traumatic fractures and willing for the orthopaedic intervention were included in the study. Patients less than 18 years of age, inflammatory arthritis (rheumatoid arthritis, psoriatic arthritis, and gouty arthritis), pathological fractures, pediatric fractures, metastasis, tumor lysis syndrome, calcium-phosphorus disorders, on treatment with bisphosphates, on dialysis and total parenteral nutrition and crush injury along with comminuted fractures were excluded from the study.

All the patients were analyzed for fractures and samples were drawn for serum vitamin D3 estimation within 1 day of fracture. Serum levels of vitamin D3 were analyzed

using the CLIA technique is a fully automated standard machine in labs certified by NABH. Patients were given various options for fracture management. Regardless of treatment options, the patients were given 60,000 IU vitamin D3 orally weekly once for six months. After three months of orthopaedic management, serum vitamin D3 and radiographs were obtained and assessed as per modified Warden's score.

3. Results

Our study includes 200 Patients with traumatic fractures who attend the OPD of orthopedics, from September 2019 to August 2020. Our study showed female preponderance (55%) with the majority of patients belong to 31 – 40 years (26%) followed by 41 – 50 years (19%) and 51 – 60 years (18%).

As discussed earlier all the 200 patients were classified and fit in the groups as per their vitamin D status at the time of fracture. With the majority of patients falling under the vitamin insufficiency group i.e. 53% of all patients were found to be vitamin insufficient at the time of fracture. 33% of patients found to be vitamin D deficient while 14% found to be insufficient stage. No patient was found to be in a toxicity state.

Case distribution showed lower limb fractures were in majority of the study with 63% of total cases and the remaining 37% cases belong to the upper limb. The patients were given 60000 IU vitamin D3 orally and assessed with X-rays after a six-month duration. According to Warden's scoring., 50% of patients were in grade 3, 15% in grade 4, 33 percent in grade 2, and only 2% in grade 1.

4. Discussion

After getting an informed and written consent from patients, the status of vitamin D3 has been obtained as per the study protocol. Patients were given 60,000 IU weekly once of vitamin D orally for 3 months. The radiographs were taken after 6 months and graded as per modified Warden's score.^{17,18}

Around 98% of patients of the study were having radiological signs for fracture union as they were in grades 2, 3, or 4 after 6 months of follow-up. Four patients had grade 1 modified Warden's score and both the patients were vitamin D3 deficient state (i.e. <20.00 ng/ml) at time of fracture. Three patients had floating knee injury and the other refused operative intervention even after failure to reduce fracture in a satisfactory position after three attempts.

The patients with modified Warden's score grade 2 comprises 1/3rd of the study population [i.e. 66 patients - 38 were a deficient state, 26 were insufficient to state, and 2 persons were insufficient state at the time of fracture]. The sufficient patient had a floating knee injury. The majority of patients had sustained a lower limb fracture here i.e femur

shaft fracture or both bone leg fracture.

The group with a grade 3 score includes almost 50% of the study population [i.e. 96 patients – 24 were a deficient state, 64 were insufficient to state and 12 were sufficient to state at the time of fracture]. The majority of them were having undisplaced and small bone fractures i.e. metacarpals, metatarsals, and distal end radius. 12 patients belonging to sufficient category at time of fracture were also in this group mainly sustained fracture of long bones i.e. femur and tibia and reduction was not satisfactory after operative intervention. Among the overall grade, 3 groups almost equal distribution of upper and lower limb fractures were noted.

Warden's score grade 4 includes 14 patients from the insufficient group and 16 patients from the sufficient group at the time of fracture. No patients with the deficient group was having a grade 4 score. The majority of the fractures here were undisplaced and upper limb fractures. In some cases where the reduction was not satisfactory even though grade 4 radiological healing is obtained in sufficient group,

None of the patients had nerve injury or vascular injury at the time of fracture. No patient had a post-operative infection till the follow-up of 6 months after surgery. No patients had implant failure or repeat fracture at same or another site till 6 months. No patients were having any epileptic disorders, lipid disorders, or GERDS. Hence there were fewer chances of drug-drug interaction with vitamin D3 in patients in the study.

All patients' serum vitamin D3 levels were increased after three months of supplementation. Even no patient had serum vitamin D3 levels higher than 55 ng/ml even after supplementation of vitamin D for three months. No patient had shown any symptoms of vitamin D3 toxicity at any time of the study. Although the amount of vitamin D3 levels gap between three months was not suggestive of anything conclusively regarding bone healing or modified Warden's grade.

Among the prevalence of vitamin D3 deficiency or insufficiency in the general population, this study showed an alarming rate of vitamin D3 insufficient patients in a group of 200 patients, which indicate the need for attention towards vitamin D3 status not only for bone-related issues but for other issues related to vitamin D deficiency.

5. Limitations of study

The sample size for the study was low to obtain a precise idea regarding the prevalence of vitamin D3 deficiency and its more specific roles in bone healing. The age group of this study includes a huge proportion of adults compared to the elder population, hence the study won't be able to show accurate vitamin D3 status in the population. As bone healing is multifactorial, many factors other than vitamin D are responsible for the healing of bone-like fracture reduction, patient compliance with doctors' advice, the role

of magnesium and calcium in bone healing, infection status, and general bone condition at the time of fracture. Very little literature was available on the role of vitamin D3 in fracture unions. Hence it was difficult to compare the study with other studies. Modified Warden's score includes bridging of fracture gap as a prime factor. As different patients had different fracture gaps at the time of fracture, hence the results may vary accordingly. The study has not divided fracture on basis of displacements or small/large bones, as healing time varies according to fracture type, results may vary accordingly. Many calcium supplements available on market and also taken by patients in a study that includes 600-1000 IU of vitamin D3. Hence this study can't comment on the required dosage of vitamin D3 required for bone healing. As a standard study, oral formulations were only prescribed to patients but for unknown reasons few patients (4 patients) went for syrup formulations hence accurate dosage of vitamin D3 intake is a questionable point along with the bioavailability of vitamin D3 in such patients. Sunlight plays an important role for Vitamin D in humans hence lower limb fracture patients due to immobilization following surgery have less exposure compare to upper limb fractures. Also, sun exposure changes the lifestyle of different patients. The study includes follow-up for 3 months only for the patients. Longer follow-up was also required to study the rate of union and advantages of vitamin D3.

6. Conclusion

Vitamin D3 plays an important role in calcium absorption and maintenance of calcium-phosphorus balance which plays a significant role in fracture union particularly in the early days of union. As the study indicated vitamin D efficacy and safety (no toxicity state was found) is too good that it helps to get an early union. As the sample size for the study is low and vitamin D3 assessment techniques are not so cheap and technologically demanding, more studies have to be done to find a more precise role of vitamin D3 in bone healing. Regarding the prevalence of vitamin D deficiency or insufficiency in the general population, this study shows an alarming rate of vitamin D insufficient patients in a group of 200 patients, which indicates the need for attention towards vitamin D status not only for bone-related issues but for other issues related to vitamin D deficiency.

7. Acknowledgments

None.

8. Conflict of Interest

The authors declare that there are no conflicts of interest in this paper.

9. Source of Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

References

1. McPhee JS, French DP, Jackson D, Nazroo J, Pendleton N, Degens H, et al. Physical activity in older age: perspectives for healthy ageing and frailty. *Biogerontology*. 2016;17(3):567–80. doi:10.1007/s10522-016-9641-0.
2. Soubra R, Chkeir A, Novella JL. A Systematic Review of Thirty-One Assessment Tests to Evaluate Mobility in Older Adults. *BioMed Res Int*. 2019;p. 1354362.
3. Clark D, Nakamura M, Miclau T, Marcucio R. Effects of Aging on Fracture Healing. *Curr Osteoporos Rep*. 2017;15(6):601–8. doi:10.1007/s11914-017-0413-9.
4. Karpouzou A, Diamantis E, Farmaki P, Savvanis S, Troupis T. Nutritional Aspects of Bone Health and Fracture Healing. *J Osteoporos*. 2017;doi:10.1155/2017/4218472.
5. Taormina DP, Shulman BS, Karia R, Spitzer AB, Konda SR, Egol KA, et al. Older Age Does Not Affect Healing Time and Functional Outcomes After Fracture Nonunion Surgery. *Geriatr Orthop Surg Rehabil*. 2014;5(3):116–21. doi:10.1177/2151458514532811.
6. Bishop JA, Palanca AA, Bellino MJ, Lowenberg DW. Assessment of Compromised Fracture Healing. *J Am Acad Orthop Surg*. 2012;20(5):273–82. doi:10.5435/jaaos-20-05-273.
7. Castronuovo E, Pezzotti P, Franzo A, Lallo DD, Guasticchi G. Early and late mortality in elderly patients after hip fracture: a cohort study using administrative health databases in the Lazio region, Italy. *BMC Geriatrics*. 2011;11(1):37. doi:10.1186/1471-2318-11-37.
8. Unnanuntana A, Gladnick BP, Donnelly E, Lane JM. The Assessment of Fracture Risk. *J Bone Joint Surg Am*. 2010;92(3):743–53. doi:10.2106/jbjs.i.00919.
9. Balasubramanian A, Zhang J, Chen L, Wenkert D, Daigle SG, Grauer A, et al. Risk of subsequent fracture after prior fracture among older women. *Osteoporos Int*. 2019;30(1):79–92. doi:10.1007/s00198-018-4732-1.
10. Bahl S, Coates PS, Greenspan SL. The management of osteoporosis following hip fracture: Have we improved our care? *Osteoporos Int*. 2003;14:884–8. doi:10.1007/s00198-003-1492-2.
11. Cosman F, de Beur S, LeBoff MS, Lewiecki EM, Tanner B, Randall S, et al. Clinician's Guide to Prevention and Treatment of Osteoporosis. *Osteoporos Int*. 2014;25(10):2359–81. doi:10.1007/s00198-014-2794-2.
12. Sözen T, Özişik L, Başaran NÇ. An overview and management of osteoporosis. *Eur J Rheumatol*. 2017;4(1):46–56.
13. Kanis JA, Cooper C, Rizzoli R, Reginster JY. on behalf of the Scientific Advisory Board of the European Society for Clinical and Economic Aspects of Osteoporosis (ESCEO) and the Committees of Scientific Advisors and National Societies of the International Osteoporosis Foundation (IOF). European guidance for the diagnosis and management of osteoporosis in postmenopausal women. *Osteoporos Int*. 2019;30(1):3–44.
14. Gorter EA, Hamdy NAT, Appelman-Dijkstra NM, Schipper IB. The role of vitamin D in human fracture healing: a systematic review of the literature. *Bone*. 2014;64:288–97. doi:10.1016/j.bone.2014.04.026.
15. Loi F, Córdova LA, Pajarinen J, Lin T, Yao Z, Goodman SB, et al. Inflammation, fracture and bone repair. *Bone*. 2016;86:119–30. doi:10.1016/j.bone.2016.02.020.
16. Malhotra K, Baggott PJ, Livingstone J. Vitamin D in the Foot and Ankle: A Review of the Literature. *J Am Podiatric Med Assoc*. 2020;110(3). doi:10.7547/18-087.
17. Warden SJ, Komatsu DE, Rydberg J, Bond JL, Hassett SM. Recombinant human parathyroid hormone (PTH 1-34) and low-intensity pulsed ultrasound have contrasting additive effects during fracture healing. *Bone*. 2009;44(3):485–94. doi:10.1016/j.bone.2008.11.007.
18. Mohamad S, Shuid AN, Mohamed N, Fadzilah FM, Mokhtar SA, Abdullah S, et al. The effects of alpha-tocopherol supplementation on fracture healing in a postmenopausal osteoporotic rat model. *Clin*. 2012;67(9):1077–85. doi:10.6061/clinics/2012(09)16.

Author biography

Amrit Kumar Singh, Junior Resident  <https://orcid.org/0000-0002-7601-3815>

Arunabh Arora, Junior Resident  <https://orcid.org/0000-0003-0501-0665>

Cite this article: Singh AK, Arora A. Role of Vitamin D3 in fracture union in adults. *IP Int J Orthop Rheumatol* 2021;7(1):38–41.