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Research Article



Novel Fracture Improvements Via Vitamin D Supplementation

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Abstract

Background: Distal radius fracture (DRF) is one of the most common upper limb fractures, which is associated with osteoporosis and vitamin D deficiency, especially in old adults.

Objectives: The aim of this study was to evaluate the effect of supplementary vitamin D on grip strength, pinch power, pain intensity, and DASH score in post-menopausal females after distal radius fractures.

Methods: Fifty-two post-menopausal women with distal radius fractures were enrolled in a randomized single-blinded multicenter trial from January 2015 to January 2016 (IRCT registration number: IRCT20160830029603N7). Patients with pre-operative serum vitamin D level of 30 to 100 ng/mL were enrolled in the study. Patients were divided to two randomized groups including groups with and without supplementation of vitamin D [25 women in intervention group (50,000 IU supplementary vitamin D, every 4 weeks for 6 months) and 27 women in placebo group]. Grip strength, pinch power, pain intensity, and DASH score pre-operatively and at three and six months after the surgery were measured; the obtained data were analyzed using SPSS version 16.

Results: The subjects' mean age in vitamin D supplemented and placebo group was 57.98 \pm 7.15 and 59.15 \pm 8.03, respectively. The mean grip strength of patients in vitamin D supplemented group was significantly higher than the placebo group on both the third and sixth month (P = 0.011 and P = 0.003, respectively). The pinch power was significantly increased on the sixth month compared to the third month in patients revised vitamin D supplementation (1.32 \pm 2.14 and 0.67 \pm 0.96 respectively, P = 0.0001). There was no statistically significant difference between the two groups in terms of mean VAS and DASH scores at the end of the study (P = 241, P = 0.665, respectively).

Conclusions: Vitamin D supplementation was significantly helpful in improving grip strength recovery in post-menopausal women after distal radius fracture, however, no significant differences were observed in supplementation of vitamin D on pinch power and pain intensity after distal radius fractures.

Keywords: Vitamin D, Distal Radius, Fracture, Post-Menopausal, Wrist Function

1. Background

Distal radius fracture (DRF) is one of the most common upper limb fractures that occurs in all age groups, which is associated with osteoporosis and vitamin D deficiency, especially in older adults (1, 2). Hand grip strength has an important role during the performance of daily activity and is considered as an critical measurement of recovery in upper extremity injuries specially for DRFs and for the evaluation of treatment outcomes (3, 4).

Vitamin D is known to be a lipophilic hormone, which, in addition to its major effects on calcium and phosphorus homeostasis, affects growth, bone mineralization, and remodeling (5, 6). Other studies have also emphasized on

the role of vitamin D and its receptors in muscle strength. In addition, some other studies have shown that supplementation of vitamin D can increase muscle strength in adults with vitamin D deficiency (7-10). In addition, vitamin D deficiency is a common worldwide issue (11), and Iran is one of the countries with a high prevalence of vitamin D deficiency. Despite the estimation that about 70% of the Iranian population have vitamin D deficiency (12), a few studies have evaluated the effect of vitamin D supplementation on power strength and physical ability (13-16). The increase in grip strength can provide a return to activity and thereby improve the quality of life in individuals with fractures.

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2. Objectives

The aim of this study was to evaluate the effect of supplementary vitamin D on grip strength, pinch power, and DASH score in post-menopausal women after distal radius fractures.

3. Methods

The local medical Ethics Committee approved the protocol. All patients provided written informed consents. This multi-center single blind trial was conducted on fifty-two post-menopausal women with distal radius fractures referred to Imam Khomeini and Boali-Sina hospitals of Sari and Shahid Beheshti Hospital of Babol during January 2015 to January 2016 (IRCT registration number: IRCT20160830029603N7). Patients with pre-operative serum vitamin D level of 30 ng/mL to 100 ng/mL were enrolled in the study. Patients with vitamin D levels less than 30 and more than 100 ng/mL, gastrointestinal diseases, renal failures, mal-nutritional conditions, additional surgeries on hands and males were excluded from the study.

Patients were divided to two randomized groups based of random number tables, including the groups with and without vitamin D supplementation (25 women in case groups received supplementary vitamin D and 27 women in placebo group). The control group consisted of agematched postmenopausal females invited to participate in the current study. Supplementary vitamin D was added at a dose of 50,000 IU in case groups every four weeks for six months post-operatively (since the dose of vitamin D supplementation is between 600 and 800 IU per day, and there is no drug toxicity). After the operation of injured hands, all patients were seen in an outpatient follow-up clinic two weeks for wound check and suture removal and subsequent follow-up was at months three and six.

Pre-operative grip strength of contralateral hand was measured with hand dynamometer and was adjusted according to the hand dominance based on the simple rule that the dominant hand is about 10% stronger than the non-dominant hand (17). The grip strength and pinch power was measured pre-operatively in uninjured contralateral hand, and then post-operatively, grip strength was evaluated in the injured hand after three and six months. The pain VAS is a self-reported questionnaire that represents patient's pain intensity from one (no pain) to ten (worst pain) (18). The VAS questionnaire was used to assess the severity of pain in patients, which was evaluated before and after the surgery. Dash score was devalued in both groups after six months. The DASH questionnaire

is a patient-rated tool and is the most validated measure of upper extremity functional status. Questions are based on daily activities, symptoms, including pain, an optional work and sports/performing arts module. A final score is calculated, ranging from 0 (no disability) to 100 (the most severe disability). Thus, a higher score indicates greater disability (19).

Parametric variables are presented as means \pm standard deviations (SD) and dichotomous variables are reported as frequencies and percentages. The mean grip strength, pinch power, VAS, and DASH scores were compared between groups using an independent samples t test preoperatively and at the third and sixth month. The change from baseline values in grip strength, pinch power, VAS, and DASH scores within the study groups was compared by the paired t test. Proportions were compared using Fisher's exact test. The IBM SPSS Statistics software version 16 was used for statistical analyses. P values less than 0.05 were considered statistically significant.

4. Results

The mean age of subjects in vitamin D supplemented and placebo group was 57.98 \pm 7.15 and 59.15 \pm 8.03, respectively. There was no statistically significant difference in mean age between the two groups (P = 0.577). Right hand involvement was seen in 92% and 88.9% of patients in intervention and placebo groups, respectively. Altogether, 44% of patients from both groups were righthanded. There was no statistically significant difference between the dominant hand and injured hand in the two groups of study (P = 0.975 and P = 0.710, respectively). The mean serum level of vitamin D pre-operatively in patients with supplemented vitamin D and placebo group was 42.36 \pm 6.61 ng/mL and 40.46 \pm 6.64 ng/mL, respectively. There was no statistically significant difference in mean serum vitamin D level between the two groups before the study (P = 0.315).

In patients that received vitamin D supplementation, the grip strength in the third and sixth month after the surgery was 18.68 ± 3.00 and 29.36 ± 2.41 , respectively. The observed grip strength changes at the end of the study were significantly different from that of the third month (P = 0.0001). The mean grip strength of the patients in vitamin D supplemented group was significantly higher than the placebo group in both third and sixth month (P = 0.011 and P = 0.003, respectively). The pinch power was significantly increased at the sixth month compared to the third month in patients that received vitamin D supplementation (1.32 \pm 2.14 and 0.67 \pm 0.96, respectively, P =

0.0001). There was no statistically significant difference between the mean pinch strength changes at the beginning, the third month, and the end of the study between the two groups (P = 0.145). The mean DASH score of subjects in intervention and placebo group was 16.72 \pm 5.67 and 17.37 \pm 5.09, respectively. There was no statistically significant difference between the two groups in terms of mean DASH score (P = 0.665) (Table 1).

5. Discussion

Osteoporosis and decreased bone density after menopause are exacerbated and are a major cause of disability, reduced life expectancy and mortality in the elderly, which leads to an increased risk of fracture. Important complications of osteoporosis are the increased risk of pathologic fractures, especially the distal radius fracture, which is one of the most common fractures in postmenopausal females. The purpose of therapeutic options for the above problems is to maintain the density of the bone structure in order to prevent the occurrence of pathologic fractures. Today, various prevention and therapeutic strategies, including hormone therapy, vitamin D supplementations, etidronate, calcium compounds, and estrogen-containing combination therapies are available; thus, it seems that the provision of new drugs or new therapies will be helpful (20-22).

Many cells have vitamin D receptors. This vitamin plays an important role in preventing fractures, improving bone density, and muscle strength. It is well known that vitamin D deficiency can cause osteoporosis and increase the susceptibility to fractures (23-25). The purpose of this study was to evaluate the effect of vitamin D supplementation on grip strength, pinch power, and pain intensity in menopausal females with distal radius fracture after surgery.

In this study, 25 patients in the group treated with vitamin D supplements and 27 patients were also evaluated as the placebo. The mean age of the patients in the group that received the supplementation of vitamin D and in the placebo group, was about 50 to 60 years old. The mean age in both studied groups were approximately the same, which revealed probability of having distal radius fracture (50 to 60 years old in post-menopausal women, which was due to osteoporosis and frequency of falls at this age). In 44% of right-handed patients, right hand fractures were seen in approximately 90% of cases. The mean serum level of vitamin D pre-operatively in patients with supplemented vitamin D and placebo group was 42.36 \pm 6.61 ng/mL and 40.46 \pm 6.64 ng/mL, respectively.

Vitamin D has a key role in muscle functions. Human muscle tissues have vitamin D receptors, which influences muscle functions. It has been shown that vitamin D supplementation can increase the frequency of muscle fibers. Thus, vitamin D supplementation may change the composition of muscle fibers and contribute to activities of gripping muscles of hands (7, 26).

In the current study, supplementation of vitamin D was associated with better grip strength recovery at the third and sixth month after the surgery. Vitamin D supplementation was not significantly associated with pinch power recovery between the two groups, however, pinch power was significantly increased at the sixth month compared to third month in patients of both groups with or without vitamin D supplementation.

Reports regarding the relation between vitamin D level and muscle strength are contradictory. In ambulatory persons aged ≥ 60 years, serum vitamin D levels between 40 nmol/L to 94 nmol/L were associated with better musculoskeletal function in lower extremities than concentrations of less than 40 nmol/L (23). In addition, in another study, there was a positive relationship between vitamin D concentration and muscle strength in adolescent females (27).

A meta-analysis study found that daily vitamin D supplementation consistently showed better effects on muscle strength (28), which was in concordance with the current study. In a study conducted with Janssen indicated that vitamin D supplementation improved muscle strength and daily functional ability in elderly people (29). In another study by Lee et al. vitamin D supplementation helped in grip strength recovery (30), which approves the current study. In another study, vitamin D supplementation did not have a significant effect on muscle strength in adults with a baseline serum vitamin D level of < 25 nmol/L (15). On the other hand, in a study performed by Marantes et al. no consistent association between low vitamin D level and low muscle mass or strength, particularly in older males and females was reported (10).

5.1. Conclusions

Vitamin D supplementation was significantly helpful in improving grip strength recovery in post-menopausal women after distal radius fracture, however, no significant differences was observed in supplementation of vitamin D on pinch power and pain intensity after distal radius fractures.

Kazemi A et al.

Table 1. Mean and Changes of Grip Strength, Pinch Power, VAS and DASH Score Between Two Groups at Base Line, Third and Sixth Month After the Surgery Intervention Group Placebo Group Supplementary Vitamin D P Value Between Groups Grip strength Base (initial assessment) 37.88 ± 3.33 36.33 ± 2.94 0.919 -19.20 ± 3.84 0.0001*, (month 3/base) Month 3 18.68 ± 3.00 16.62 ± 2.58 0.011 0.0001*, (month 3/base) -19.70 ± 3.83 29.36 ± 2.41 24.30 ± 2.19 +10.68 ± 3.32 0.0001*, (month 6/month 3) +7.66 ± 3.13 0.0001*, (month 6/month 3) 0.003 Pinch power Base 4.12 ± 1.16 4.26 ± 1.40 0.755 0.96 ± 0.67 1.07 ± 0.54 0.507 -3.16 ± 1.24 0.0001*, (month 3/base) -3.18 ± 1.61 0.0001*, (month 3/base) Month 6 2.32 ± 1.14 2.00 ± 1.03 0.347 +1.36 + 1.03 0.0001*. (month 6/month 3) $+0.92 \pm 0.95$ 0.0001*. (month 6/month 3) VAS score -2.92 ± 2.25 0.0001*, (month 6/base) 0.0001*, (month 6/base) -1.74 ± 1.55 4.80 ± 2.70 4.04 ± 2.32 0.804 Month 6 1.88 ± 1.48 2.30 ± 1.56 0.241 DASH score

0.665

Acknowledgments

Month 6

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16.72 ± 5.67

17.37 ± 5.09

Footnotes

Authors' Contribution: Study concept and design: Abolfazl Kazemi, Masoud Shayesteh Azar, and Mehran Razavipour. Data collection and study management: Abolfazl Kazem. Drafting of the manuscript: Abolfazl Kazemi and Mehran Razavipour. Statistical analysis: Mohammad Khademloo, Hosein Azade. Revision of the manuscript: Mehran Razavipour and Salman Ghaffari.

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References

- Wright S, Beringer T, Taggart H, Keegan D, Kelly J, Whithead E, et al. A study of male patients with forearm fracture in Northern Ireland. Clin Rheumatol. 2007;26(2):191-5. doi: 10.1007/s10067-006-0261-y. [PubMed: 16552462].
- 2. Canale ST, Beaty JH. Campbell's operative orthopaedics e-book. Elsevier Health Sciences; 2012.
- Bohannon RW. Dynamometer measurements of hand-grip strength predict multiple outcomes. *Percept Mot Skills*. 2001;93(2):323–8. doi: 10.2466/pms.2001.93.2.323. [PubMed: 11769883].

- 4. Dua M, Sharma J, Neema PP. Evaluation of role of vitamin D in grip strength in post-menopausal women with fracture of distal end radius treated with closed reduction and percutaneous K-wire fixation. *Indian J Orthop Surg.* 2016;2(1):110–4. doi: 10.5958/2395-1362.2016.00021.9.
- Capiati D, Benassati S, Boland RL. 1,25(OH)2-vitamin D3 induces translocation of the vitamin D receptor (VDR) to the plasma membrane in skeletal muscle cells. J Cell Biochem. 2002;86(1):128–35. doi: 10.1002/jcb.10191. [PubMed: 12112023].
- Liu S, Song Y, Ford ES, Manson JE, Buring JE, Ridker PM. Dietary calcium, vitamin D, and the prevalence of metabolic syndrome in middle-aged and older U.S. women. *Diabetes Care*. 2005;28(12):2926– 32. doi: 10.2337/diacare.28.12.2926. [PubMed: 16306556].
- Endo I, Inoue D, Mitsui T, Umaki Y, Akaike M, Yoshizawa T, et al. Deletion of vitamin D receptor gene in mice results in abnormal skeletal muscle development with deregulated expression of myoregulatory transcription factors. *Endocrinology*. 2003;144(12):5138–44. doi: 10.1210/en.2003-0502. [PubMed: 12959989].
- Santillan G, Katz S, Vazquez G, Boland RL. TRPC3-like protein and vitamin D receptor mediate 1alpha,25(OH)2D3-induced SOC influx in muscle cells. Int J Biochem Cell Biol. 2004;36(10):1910–8. doi: 10.1016/j.biocel.2004.01.027. [PubMed: 15203106].
- Annweiler C, Beauchet O, Berrut G, Fantino B, Bonnefoy M, Herrmann FR, et al. Is there an association between serum 25-hydroxyvitamin D concentration and muscle strength among older women? Results from baseline assessment of the EPIDOS study. J Nutr Health Aging. 2009;13(2):90-5. doi: 10.1007/s12603-009-0013-1. [PubMed: 19214335].
- Marantes I, Achenbach SJ, Atkinson EJ, Khosla S, Melton LJ 3rd, Amin S. Is vitamin D a determinant of muscle mass and strength? J Bone Miner Res. 2011;26(12):2860–71. doi: 10.1002/jbmr.510. [PubMed: 21915904]. [PubMed Central: PMC3248226].
- Ganji V, Zhang X, Tangpricha V. Serum 25-hydroxyvitamin D concentrations and prevalence estimates of hypovitaminosis D in the U.S. population based on assay-adjusted data. *J Nutr.* 2012;**142**(3):498–507. doi:10.3945/jn.111.151977. [PubMed: 22323766].
- Moradzadeh K, Keshtkar A, Hossein Nezhad A, Rajabian R, Nabipour I, Omrani G. [Normal values of vitamin D and prevalence of vitamin D deficiency among Iranian population]. Sci J Kurdistan Univ Med Sci. 2006;10(4):33-43. Persian.

- Ward KA, Das G, Roberts SA, Berry JL, Adams JE, Rawer R, et al. A randomized, controlled trial of vitamin D supplementation upon musculoskeletal health in postmenarchal females. *J Clin Endocrinol Metab*. 2010;95(10):4643–51. doi: 10.1210/jc.2009-2725. [PubMed: 20631020].
- El-Hajj Fuleihan G, Nabulsi M, Tamim H, Maalouf J, Salamoun M, Khalife H, et al. Effect of vitamin D replacement on musculoskeletal parameters in school children: A randomized controlled trial. J Clin Endocrinol Metab. 2006;91(2):405-12. doi: 10.1210/jc.2005-1436. [PubMed: 16278262].
- Stockton KA, Mengersen K, Paratz JD, Kandiah D, Bennell KL. Effect of vitamin D supplementation on muscle strength: A systematic review and meta-analysis. Osteoporos Int. 2011;22(3):859–71. doi: 10.1007/s00198-010-1407-y. [PubMed: 20924748].
- Close GL, Leckey J, Patterson M, Bradley W, Owens DJ, Fraser WD, et al.
 The effects of vitamin D(3) supplementation on serum total 25[OH]D concentration and physical performance: A randomised doseresponse study. Br J Sports Med. 2013;47(11):692–6. doi: 10.1136/bjsports-2012-091735. [PubMed: 23410885].
- Crosby CA, Wehbe MA, Mawr B. Hand strength: normative values. *J Hand Surg Am*. 1994;19(4):665-70. doi: 10.1016/0363-5023(94)90280-1. [PubMed: 7963331].
- 18. Hawker GA, Mian S, Kendzerska T, French M. Measures of adult pain: Visual analog scale for pain (VAS Pain), numeric rating scale for pain (NRS Pain), McGill pain questionnaire (MPQ), short-form McGill pain questionnaire (SF-MPQ), chronic pain grade scale (CPGS), short form-36 bodily pain scale (SF-36 BPS), and measure of intermittent and constant osteoarthritis pain (ICOAP). Arthritis Care Res (Hoboken). 2011;63 Suppl 11:S240-52. doi: 10.1002/acr.20543. [PubMed: 22588748].
- Dowrick AS, Gabbe BJ, Williamson OD, Cameron PA. Outcome instruments for the assessment of the upper extremity following trauma: A review. *Injury.* 2005;36(4):468–76. doi: 10.1016/j.injury.2004.06.014. [PubMed: 15755426].
- Lips P, van Schoor NM. The effect of vitamin D on bone and osteoporosis. Best Pract Res Clin Endocrinol Metab. 2011;25(4):585-91. doi: 10.1016/j.beem.2011.05.002. [PubMed: 21872800].
- Rachner TD, Khosla S, Hofbauer LC. Osteoporosis: Now and the future. *Lancet*. 2011;377(9773):1276–87. doi: 10.1016/S0140-6736(10)62349-5. [PubMed: 21450337]. [PubMed Central: PMC3555696].

- Diaz-Garcia RJ, Oda T, Shauver MJ, Chung KC. A systematic review of outcomes and complications of treating unstable distal radius fractures in the elderly. *J Hand Surg Am.* 2011;36(5):824-35 e2. doi: 10.1016/j.jhsa.2011.02.005. [PubMed: 21527140]. [PubMed Central: PMC3093102].
- 23. Bischoff-Ferrari HA, Dietrich T, Orav EJ, Hu FB, Zhang Y, Karlson EW, et al. Higher 25-hydroxyvitamin D concentrations are associated with better lower-extremity function in both active and inactive persons aged > or =60 y. *Am J Clin Nutr.* 2004;**80**(3):752–8. doi: 10.1093/ajcn/80.3.752. [PubMed: 15321818].
- Alagol F, Shihadeh Y, Boztepe H, Tanakol R, Yarman S, Azizlerli H, et al. Sunlight exposure and vitamin D deficiency in Turkish women. *J Endocrinol Invest*. 2000;23(3):173–7. doi: 10.1007/BF03343702. [PubMed: 10803475].
- Bakhtiyarova S, Lesnyak O, Kyznesova N, Blankenstein MA, Lips P. Vitamin D status among patients with hip fracture and elderly control subjects in Yekaterinburg, Russia. Osteoporos Int. 2006;17(3):441-6. doi: 10.1007/s00198-005-0006-9. [PubMed: 16328605].
- Sato Y, Iwamoto J, Kanoko T, Satoh K. Low-dose vitamin D prevents muscular atrophy and reduces falls and hip fractures in women after stroke: A randomized controlled trial. *Cerebrovasc Dis.* 2005;20(3):187– 92. doi: 10.1159/000087203. [PubMed: 16088114].
- Ward KA, Das G, Berry JL, Roberts SA, Rawer R, Adams JE, et al. Vitamin D status and muscle function in post-menarchal adolescent girls.
 J Clin Endocrinol Metab. 2009;94(2):559-63. doi: 10.1210/jc.2008-1284.
 [PubMed: 19033372].
- 28. Muir SW, Montero-Odasso M. Effect of vitamin D supplementation on muscle strength, gait and balance in older adults: A systematic review and meta-analysis. *J Am Geriatr Soc.* 2011;**59**(12):2291–300. doi: 10.1111/j.1532-5415.2011.03733.x. [PubMed: 22188076].
- Janssen HC, Samson MM, Verhaar HJ. Vitamin D deficiency, muscle function, and falls in elderly people. Am J Clin Nutr. 2002;75(4):611–5. doi: 10.1093/ajcn/75.4.611. [PubMed: 11916748].
- 30. Lee HJ, Gong HS, Song CH, Lee JE, Lee YH, Baek GH. Evaluation of vitamin D level and grip strength recovery in women with a distal radius fracture. *J Hand Surg Am.* 2013;38(3):519-25. doi: 10.1016/j.jhsa.2012.12.002. [PubMed: 23391356].