International Journal of Current Pharmaceutical Research

ISSN- 0975-7066 Vol 16, Issue 2, 2024

Original Article

A PROSPECTIVE COMPARATIVE STUDY ON EFFICACY OF ORAL VITAMIN D FORMULATIONS IN PATIENTS WITH CHRONIC LOW BACK PAIN WITH VITAMIN D DEFICIENCY AT A TERTIARY CARE HOSPITAL

K. SANTHA BAI[1], D. JAYASREE[2], BHARATHI UPPU[3], SOWMYA DEEPTHI C.*[4]

[1,2,4]Department of Pharmacology, Government Medical College Nandyal, Andhra Pradesh, India. [3]Department of Pharmacology, Sri Venkateswara Medical College, Tirupati, Andhra Pradesh, India

*Corresponding author: Sowmya Deepthi C.; *Email: drsowmyadeepthi@gmail.com

Received: 21 Dec 2023, Revised and Accepted: 24 Jan 2024

ABSTRACT

Objective: Chronic low back pain is a global health problem with significant medical and economic burden. Vitamin D deficiency and obesity are its risk factors. The objective was to determine efficacy of oral vitamin D formulations in patients with chronic low back pain with vitamin D deficiency.

Methods: A prospective analytical cohort study was conducted. Patients with self-reported chronic low back pain and with vitamin D concentrations ≤30 ng/dl were identified and randomized into 3 groups namely Granule, Nano syrup and soft gel capsule group. Vitamin D supplementation of 60,000 IUs per dose for ten consecutive days was given in the form of granule (1 g sachet), Nano syrup (5 ml bottle) and soft gel capsule. We measured (25-hydroxyvitamin D [25(OH)D]) concentrations and to assess pain, Visual analogue scale and Modified Oswestry low back pain disability questionnaire (MODQ) were used before and 12 w after the intervention.

Results: After 12 w 25(OH)D levels increased significantly with vitamin D supplementation in all the groups but more in the Nano syrup group. There was also significant reduction in back pain intensity in all the groups after vitamin D supplementation. However in Nano syrup group, there was a significantly greater reduction in back pain compared with other groups.

Conclusion: Our findings suggest that vitamin D supplementation in vitamin D deficient adults may improve chronic low back pain. Hence, testing for vitamin D deficiency in those with chronic low back pain may be warranted.

Keywords: Chronic low back pain, Vitamin D, Granules, Nano syrup, Soft gel

DOI: https://dx.doi.org/10.22159/ijcpr.2024v16i2.4031 Journal homepage: https://innovareacademics.in/journals/index.php/ijcpr

INTRODUCTION

Chronic low back pain (CLBP), defined as low back pain of more than 3 mo, is one of the most common problem that warrant patients to see a doctor. In India, back and neck pain is ranked as one of the leading cause of years lived with disability [1, 2]. Unhealthy food habits, sedentary work style and less exposure to sun light [3, 4] inclined towards CLBP in urban population. Under nutrition, heavy physical activity and unawareness leads to CLBP in rural population. Over time, the constant pain and lack of improvement in the condition causes serious emotional issues. Depression, anger, anxiety and mood swings are some of the emotional side effects of chronic pain. CLBP is often associated with loss of work productivity and thus produces huge economic burden on individuals as well as on the nation [3].

The estimated worldwide lifetime prevalence of low back pain varies from 50% to 84% [5]. Similarly, some studies in developing countries have revealed much higher incidence of 72.4% in Nigeria, 64% in China, and 56.2% in Thailand [6]. The occurrence of low back pain in India is also alarming with nearly 60% of the people in India have suffered from low back pain at some time during their lifespan[7]. Two studies found that individuals of lower economic status had higher prevalence of CLBP than those of higher economic status [8, 9].

Vitamin D is a proven anabolic hormone that promotes skeletal muscle and bone health as well as maintains immune function [10-13]. Hypovitaminosis D is an overtly underestimated, preventable and correctable etiological factor for CLBP. Vit. D<30 ng/ml was considered as hypovitaminosis D, 20-29.9 ng/ml as insufficiency, <20 ng/ml as deficiency. Vitamin D supplementation has been shown to provide "anti-inflammatory benefits" [14-16]. This study was designed to evaluate the differences in outcomes with various oral formulations of vitamin D available in market.

MATERIALS AND METHODS

This is a randomized, prospective, open labeled, analytical cohort study. Ethics committee approval was taken. Participants of both the genders between 18 and 45 y of age with low back pain for more than 3 mo were included. Pregnant and lactating women, patients on vitamin D supplements for the past three months, patients on drugs altering vitamin D metabolism, medical or surgical disorders affecting vitamin D metabolism, pre-existing co morbidities, neurological back pain, congenital or developmental malformations of spine and patients with history of trauma were excluded. Informed consent was taken and a total of 127 patients were screened for serumVitamin D levels. 89 participants with vitamin D<20 ng/ml were selected and were sub grouped as per the randomization chart. The three treating groups named were Granule group, Nano syrup group and soft gel capsule group according to the vitamin D formulations used respectively.

Vitamin D supplementation of 60,000 IUs per dose for ten consecutive days was given in the form of granules (Cipcal D3, 1 g sachet), nano syrup using aqueous nano technology (Calvis D3, 5 ml bottle), soft gel capsule (Callexa-60K). All the patients were treated with an analgesic (aceclofenac) and an antacid (ranitidine) uniformly for five days.

Review analysis was done at every three weeks. Blood sample was collected after 12 w after treatment with vitamin D. To analyse low back pain and functional disability, Visual analogue scale (VAS) and Modified Oswestry low back pain disability questionnaire (MODQ) were used. During the study period participants were monitored and noted for any adverse drug reactions. Out of 89, only 71 patients completed the study.

RESULTS

Out of the 71 participants, 41 were female and 30 were male and the demographic details of the participants are as shown. The mean age of participants among the three groups was 39 y. there was no significant difference in the age and gender distribution among the study participants. Average BMI of the participants was 28.

Table 1: Shows basic characters of all study participants

Basic characters	Granule group (n=24) mean±SD	Nano syrup group (n=24) mean±SD	Soft gel capsule group (n=23) mean±SD
Age (years)	35±5.7	40±4.08	38±7.08
Male (n)	11	9	10
Female (n)	13	15	13
Body mass index (kg/m^2)	28.6±4.3	29.2±3.9	28.1±3.9

Table 2: Shows mean±SD of BMI (kg/m^2), vitamin D, VAS and MODQ before and after the study

BMI	Granule group mean±SD	Nano syrup group mean±SD	Soft gel capsule group mean±SD
Pre BMI (kg/m^2)	28.6±4.3	29.2±3.9	28.01±3.7
Post BMI (kg/m^2)	28.1±4.2	28.7±4	27.4±3.7
Pre vitamin D (ng/ml)	14.8±2.8	14.5±3.2	14.41±2.9
Post vitamin D (ng/ml)	49.4±5.6	80.8±8.1	46.33±6
Pre VAS	3.7±1	4±1.1	3.6±1
Post VAS	3±1.11	3.3±1	3.2±1
Pre MODQ%	32.2±4.3	35.5±11.5	33.5±3.9
Post MODQ%	14.04±2.5	8.9±1.3	18.1±3.3

There was a significant difference in the Mean values of BMI (kg/m^2) at baseline and after 12 w in all the 3 groups but a higher difference is seen in the Nano syrup group as shown in table 2. Also there was significant difference in pre and post mean±SD of vitamin D (ng/ml) in all three groups but highest increase of mean in vitamin D (ng/ml) was noted in Nano syrup group. mean±SD of Pre and post VAS and MODQ% was significant in all groups and highest improvement in the Nano syrup group.

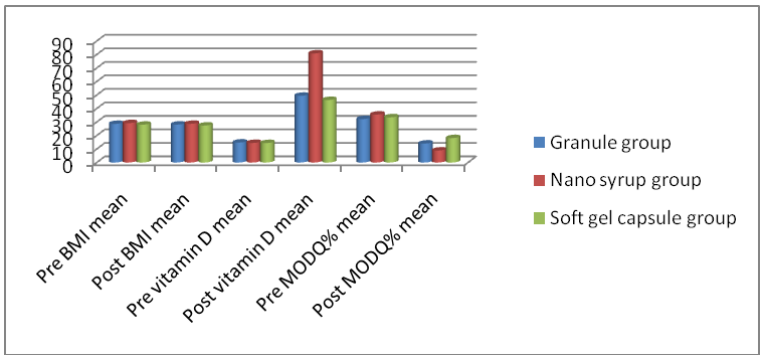

Fig. 1: Shows mean values of BMI (kg/m^2), vitamin D, VAS and MODQ before and after the study in all the 3 groups

Table 3: Shows paired T test value and P value of vit D (ng/ml) and MODQ% of all three groups

Study groups	Paired T test vitamin D		Paired T test VAS		Paired T test MODQ	
	T value	P value	T value	P value	T value	P value
Granule group	27.682	<0.001	-5.6	<0.001	-18.348	<0.001
Nano syrup group	37.94	<0.001	-7.2	<0.001	-11.03	<0.001
Soft gel capsule group	28.84	<0.001	-3.1	0.005	-15.61	<0.001

The increase in vitamin D levels at the end of the study was significant in all the 3 study groups. The pain intensity reduced significantly along with improvement in the functional disability in all the three groups.

Table 4: Shows gender statistics of BMI, Vitamin D and MODQ before and after the study

n=71	Male (30)	Female (41)
PRE BMI (kg/m^2) mean±SD	29.6±4.5	27.9±3.3
POST BMI (kg/m^2) mean±SD	29±4.7	27.4±3.3
PRE vitamin D (ng/ml) mean±SD	12.8±2.2	15.8±2.8
POST vitamin D (ng/ml) mean±SD	56.8±17.6	60.3±16,6
Pre VAS	4.1±1.1	3.6±1.05
Post VAS	3.4±0.95	2.9±1.05
PRE MODQ% mean±SD	33.1±4.2	34.2±9.3
POST MODQ% mean±SD	13.2±4.6	14±4.5

There was no significant difference in pre and post mean±SD of BMI (kg/m^2) and vitamin D levels in male and female. There is not much difference in mean±SD of VAS and MODQ% of male and female.

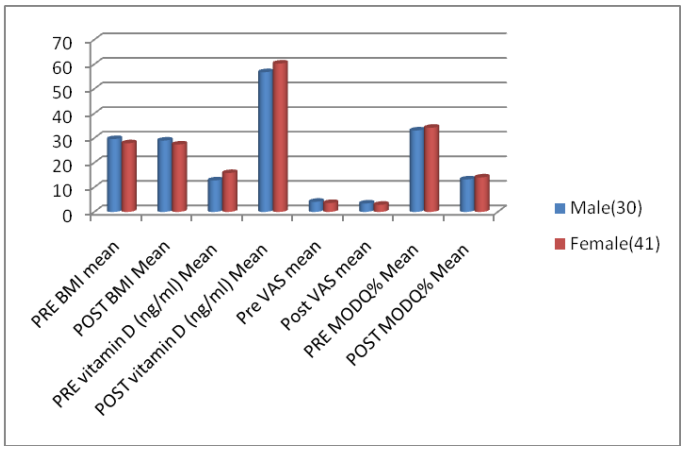

Fig. 2: Gender statistics of mean values of BMI, Vitamin D and MODQ before and after the study

DISCUSSION

Vitamin D deficiency (serum level<20 ng/ml) has been linked with impaired skeletal health and disorders such as osteoporosis, osteomalacia, or rickets [17, 18]. Without vitamin D, human body cannot process calcium effectively from our diet. When bones are unable to absorb enough calcium, [19, 20] patients might develop musculoskeletal pain, osteoporosis, a condition where bone becomes porous and loses density increasing the risk of fractures even in minor falls or accidents [21]. Vitamin D deficiency has been associated with headache, abdominal, knee, and back pain, persistent musculoskeletal pain, coastochondritic chest pain, and failed back syndrome and with fibromyalgia [22, 23]. Persistent pain is associated with Vitamin D-related bone demineralization, myopathy, and musculoskeletal pain. Strict vegan diet, may led to suffering from low Vitamin D levels and vitamin D supplementation is essential as most of the natural food sources of vitamin D are non-vegetarian such as fish oil, beef liver, and milk [24]. Melanin in skin reduces its ability to make vitamin D in response to sunlight. Hence it is recommended for people with dark skin and have relocated to a country with less sunlight may need to take Vit D supplements. It is recommended to spend at least 10–15 min in the sun every day.

Majority of vitamin D formulations available in the market in the form of tablets, capsules or sachets are conventional fat-soluble preparations. Vitamin D being a non-polar lipid with poor bioavailability due to its low solubility in aqueous fluids of gastrointestinal tract, a robust drug delivery system in the form of Nano syrup formulations of vitamin D3 has been recently introduced in the market for supplementation [25, 26]. In this study we compare the efficacy and safety of three different formulations which are Granules, Nano syrup and soft gel capsules. Presently 60000IU vitamin D given in the forms of Granules available as 1 gm sachets, Nano syrup 5 ml single dose syrup and one soft gel capsule for 10 d daily. Al Faraj S *et al.* reported high prevalence (83%) of hypovitaminosis D in patients with chronic low back pain (CLBP) and all of them had normal vitamin D by three months of oral 5000 to 10,000 IUs of vitamin D/day with 95% LBA recovery [27].

Average age of our study population was 39 y and average BMI (kg/m^2) is 28. There was a significant difference in pre and post BMI change in all groups but highest for Nano syrup group. In our study after treatment with vitamin D in the form of granules, Nano syrup, soft gel capsules vitamin D levels improved in all the participants but highest increase was seen in the Nano syrup group. Nanoparticles, as drug delivery systems, impart several advantages concerning improved efficacy as well as reduced adverse drug reactions. Throughout the study none of the study participants reported any serious adverse drug reactions. Mild abdominal discomfort was encountered in few subjects which subsided after few hours.

Most of vitamin D preparations are prescribed as 1000-2000 IU once a day for 3 mo or high dose of 60000 IU weekly once for 4-6 w regimens. In a study, daily supplementation with 5500 and 11000 IU of vitamin D for twenty weeks lead to a peak increase of vitamin D to 64 and 88 ng/ml respectively [28]. Similarly, 43.48% of study patients remained with hypovitaminosis D after eight weeks of weekly 60,000 IUs of vitamin D supplementation [29]. Long term prescribing regimens will reduce the patient compliance ultimately affecting the improvement in vitamin D levels. This high dose vitamin D therapy of 60000IU per day for ten days is very effective in improving vitamin D levels along with analgesics and muscle relaxants in CLBP.

Back pain is a common and disabling condition with an evaluated lifetime prevalence rate of 80% and, of those with chronic low back pain, at least 50% are overweight or obese and more than 60% are considered vitamin D deficient [30]. Hence, those with chronic low back pain who are overweight or obese represent a large and potentially important group, in whom vitamin D testing may be warranted. Given the heavy burden of back pain worldwide and limited treatment options available, vitamin D Nano syrup formulation may represent a novel and easily accessible therapy that may not only improve bone health parameters for vitamin D deficient individuals but may also reduce the burden of low back pain. Cost of nano syrup formulation is expensive and almost double when compared to the other 2 formulations. There was not much difference in the cost of Granules and soft gel formulation.

CONCLUSION

Vitamin D plays important role in the pathology of chronic low back pain. In this study in all groups vitamin D levels were increased effectively but highest increased in Nano syrup group. There is also significant change in BMI of participants. There was a significant change in MODQ% in all 3 groups with highest change in Nano syrup group. These results with different formulations show that correction of vitamin D deficiency is significant and effective in the management of chronic low back pain. Future studies should include to evaluate different dosage regimens, different formulations and in different age groups.

FUNDING

Nil

AUTHORS CONTRIBUTIONS

All authors have contributed equally.

CONFLICT OF INTERESTS

Declared none

REFERENCES

1. Bansal D, Asrar Mir Mahmood, Ghai Babita, Pushpendra D. Prevalence and impact of low back pain in a community-based population in Northern India. Pain Phys. 2020;23(4):E389-98. PMID 32709185.

2. Ganesan S, Shankar Acharya A, Chauhan R, Acharya S. Prevalence and risk factors for low back pain in 1,355 young adults: a cross-sectional Study Asian Spine J. 2017 Aug;11(4):610-7. doi: 10.4184/asj.2017.11.4.610, PMID: 28874980.
3. Ekman M, Jonhagen S, Hunsche E, Jonsson L. Burden of illness of chronic low back pain in sweden: a cross-sectional, retrospective study in primary care setting. Spine. 2005;30(15):1777-85. doi: 10.1097/01.brs.0000171911.99348.90, PMID 16094281.
4. Wacker M, Holick MF. Sunlight and vitamin D: a global perspective for health. Dermatoendocrinol. 2013;5(1):51-108. doi: 10.4161/derm.24494, PMID 24494042.
5. Badley EM, Rasooly I, Webster GK. Relative importance of musculoskeletal disorders as a cause of chronic health problems, disability, and health care utilization: findings from the 1990 Ontario Health Survey. J Rheumatol. 1994;21(3):505-14. PMID 8006895.
6. Loney PL, Stratford PW. The prevalence of low back pain in adults: A methodological review of the literature. Phys Ther. 1999;79(4):384-96. doi: 10.1093/ptj/79.4.384, PMID 10201544.
7. Koley S, Sandhu NK. An association of body composition components with the menopausal status of patients with low back pain in tarn Taran, Punjab, India. Journal of Life Sciences. 2009;1(2):129-32. doi: 10.1080/09751270.2009.11885144.
8. Meucci RD AG, Paniz VM, Silva MC, Wegman DH. Increase of chronic low back pain prevalence in a medium-sized city of southern Brazil. BMC Musculoskelet Disord. 2013;14:155. doi: 10.1186/1471-2474-14-155.
9. Silva MC, Fassa AG, Valle NC. Chronic low back pain in a Southern Brazilian adult population: prevalence and associated factors. Cad Saude Publica. 2004;20(2):377-85. doi: 10.1590/s0102-311x2004000200005, PMID 15073617.
10. Badsha H, Daher M, Ooi Kong K. Myalgias or non-specific muscle pain in Arab or Indo-Pakistani patients may indicate vitamin D deficiency. Clin Rheumatol. 2009;28(8):971-3. doi: 10.1007/s10067-009-1146-7, PMID 19277814.
11. Rosen CJ, Adams JS, Bikle DD, Black DM, DeMay MB, Manson JE. The nonskeletal effects of vitamin D: an endocrine society scientific statement. Endocr Rev. 2012;33(3):456-92. doi: 10.1210/er.2012-1000, PMID 22596255.
12. Charoenngam N, Holick MF. Immunologic effects of vitamin D on human health and disease. Nutrients. 2020;12(7):2097. doi: 10.3390/nu12072097, PMID 32679784.
13. Mora JR, Iwata M, Von Andrian UH. Vitamin effects on the immune system: vitamins A and D take centre stage. Nat Rev Immunol. 2008;8(9):685-98. doi: 10.1038/nri2378, PMID 19172691.
14. van Etten E, Stoffels K, Gysemans C, Mathieu C, Overbergh L. Regulation of vitamin D homeostasis: implications for the immune system. Nutr Rev. 2008;66(10) Suppl 2:S125-34. doi: 10.1111/j.1753-4887.2008.00096.x, PMID 18844839.
15. Buell JS, Dawson Hughes B. Vitamin D and neurocognitive dysfunction: preventing "D"ecline? Mol Aspects Med. 2008;29(6):415-22. doi: 10.1016/j.mam.2008.05.001, PMID 18579197.
16. Calton EK, Keane KN, Newsholme P, Soares MJ. The impact of vitamin D levels on inflammatory status: a systematic review of immune cell studies. Plos One. 2015;10(11):e0141770. doi: 10.1371/journal.pone.0141770, PMID 26528817.
17. Holick MF. Vitamin D deficiency. N Engl J Med. 2007;357(3):266-81. doi: 10.1056/NEJMra070553, PMID 17634462.
18. Wacker M, Holick MF. Vitamin D-effects on skeletal and extraskeletal health and the need for supplementation. Nutrients. 2013;5(1):111-48. doi: 10.3390/nu5010111, PMID 23306192.
19. Haussler MR, Whitfield GK, Kaneko Ichiro, Forster Ryan, Saini Rimpi, Hsieh Jui-Cheng. The role of vitamin D in the FGF23, klotho, and phosphate bone-kidney endocrine axis. Rev Endocr Metab Disord. 2012 Mar;13(1):57-69. doi: 10.1007/s11154-011-9199-8, PMID 21932165.
20. Bikle DD, Zolock DT, Morrissey RL, Herman RH. Independence of 1,25-dihydroxyvitamin D3-mediated calcium transport from de novo RNA and protein synthesis. J Biol Chem. 1978 Jan;253(2):484-8. doi: 10.1016/S0021-9258(17)38235-2, PMID 618881.
21. Cauley JA, Parimi N, Ensrud Kristine Kristine E, Bauer Douglas Douglas C, Cawthon Peggy Peggy M, Cummings Steven Steven R. Serum 25-hydroxyvitamin D and the risk of hip and nonspine fractures in older men. J Bone Miner Res. 2010;25(3):545-53. doi: 10.1359/jbmr.090826, PMID 19775201.
22. Holick MF, Binkley NC, Bischoff Ferrari Heike Heike A, Gordon Catherine Catherine M, Hanley David David A, Heaney Robert Robert P, Connie M. Weaver Endocrine society. Evaluation, treatment, and prevention of vitamin D deficiency: an endocrine society clinical practice guideline. J Clin Endocrinol Metab. 2011;96(7):1911e1930.
23. Shipton EE. Vitamin D and pain: vitamin d and its role in the aetiology and maintenance of chronic pain states and associated comorbidities. Pain Res Treat. 2015. doi: 10.1155/2015/904967, PMID: 26090221.
24. Institute of Medicine, Food and Nutrition Board. Dietary reference intakes for calcium and vitamin D. Washington, DC: National Academy Press; 2010.
25. Walia N, Dasgupta N, Ranjan S, Chen L, Ramalingam C. Fish oil based vitamin D nanocapsulation by ultrasonication and bioaccessibility analysis in simulated gastrointestinal tract. Ultrason Sonochem. 2017;171:623-35.
26. Gupta R, Behera C, Paudwal G, Rawat N, Baldi A, Gupta PN. Recent advances in formulation strategies for efficient delivery of vitamin D. AAPS PharmSciTech. 2018;20(1):11. doi: 10.1208/s12249-018-1231-9, PMID 30560516.
27. Al Faraj S, Al Mutairi K. Vitamin D deficiency and chronic low back pain in Saudi Arabia. Spine. 2003;28(2):177-9. doi: 10.1097/00007632-200301150-00015, PMID 12544936.
28. Berridge MJ. Vitamin D and depression: cellular and regulatory mechanisms. Pharmacol Rev. 2017;69(2):80-92. doi: 10.1124/pr.116.013227, PMID 28202503.
29. Goswami R, Gupta N, Ray D, Singh N, Tomar N. Pattern of 25-hydroxy vitamin D response at short (2 mo) and long (1 y) interval after 8 w of oral supplementation with cholecalciferol in Asian Indians with chronic hypovitaminosis D. Br J Nutr. 2008;100(3):526-9. doi: 10.1017/S0007114508921711.
30. Rkain H, Bouaddi I, Ibrahimi A, Lakhdar T, Abouqal R, Allali F. Relationship between vitamin D deficiency and chronic low back pain in postmenopausal women. Curr Rheumatol Rev. 2013;9(1):63-7. doi: 10.2174/1573397111309010011, PMID 25198368.