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A Prospective Study to Evaluate the Efficacy of Vitamin D3 Granules 60,000 IU Supplementation in Vitamin D Deficient Apparently Healthy Adults

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Abstract: ***Background: To evaluate the efficacy of vitamin D3 granules 60,000 IU supplementation in increasing serum 25 hydroxyvitamin D [25(OH)D] levels in Vit D deficient apparently healthy adults. Methods: Healthy adults in an urban area were screened for 25(OH)D (radioimmunoassay method). Those found to be deficient or insufficient in vitamin D (defined as 25(OH) D <30 ng/ml) were supplemented with oral cholecalciferol granules 60,000 IU/week for eight weeks. Serum 25(OH) D level was estimated at the end of 8 weeks. Results: A total of 125 subjects (age above 25 years) were enrolled for the study. Baseline data was available for 103 subjects as per the study protocol. Of these 103 subjects, 69.9 % subjects were found to be vitamin D deficient (<20 ng/ml) and the mean plasma vitamin D3 25(OH)D level was 9.8 ng/ml at baseline. At the end of the study, the mean 25(OH) D plasma level was noted to be 27.4 ng/ml. The mean change from baseline was 17.6 ng/ml. Among these 103 participants only 30.1% had 25(OH) D >20 ng/ml <30 ng/ml at baseline, which increased to at the end of the study following vitamin D3 supplementation for eight weeks. Conclusion: This study showed that vitamin D deficiency is highly prevalent in the urban healthy adult population. Eight weeks of vitamin D3 60,000 IU/week oral granules supplementation increased serum 25(OH)D to optimal levels.***

Keywords: Vitamin D deficiency, adults, 25(OH)D

1. Introduction

Vitamin D has been traditionally known as the antiricketic factor or the sunshine vitamin. It is considered unique due to its ability to be synthesized in the body and functioning as a hormone. Additionally, it plays a crucial role in calcium homeostasis and bone mineral metabolism. Vitamin D endocrine system is also known to support a wide range of fundamental biological functions in cell differentiation, inhibition of cell growth as well as innate and adaptive immunity.[1-3] In adults, chronic vitamin D deficiency leads to osteoporosis, osteomalacia, muscle weakness and increased risk of falls and fractures. Inadequate vitamin D intake and low blood levels of vitamin D metabolites are related to increased incidence of several autoimmune diseases involving the T helper type 1 lymphocyte, including multiple sclerosis, rheumatoid arthritis, type 1 diabetes, systemic lupus erythematosus and psoriasis. Lower levels of vitamin D, adjusted for body mass index, are also associated with increased risk of hypertension, myocardial infarction and may lead to death as a result of cardiovascular disease.2 The active metabolite of vitamin D, 1,25-dihydroxyvitamin D [1,25(OH)2D], acts in a wide range of tissues. The vitamin D receptors (VDRs) are present in many cells, including those of the liver, pancreas, brain, lung, breast, skin, muscle and adipose tissue.[4] Accumulating research suggests that low serum 25-hydroxyvitamin D3 [25(OH)D] concentrations may be inversely associated with type 2 diabetes, metabolic syndrome, insulin resistance and cardiovascular disease.[5] Vitamin D deficiency does indeed constitute an epidemic in many populations across the world and has been reported in healthy population. In India also, more than 90% of apparently healthy Indians have subnormal 25(OH)D levels. Low dietary vitamin D intake and poor exposure to sunlight are common causes of vitamin D deficiency in the general population.12 Sunlight is known to be the primary source of vitamin D and its production in the skin depends on exposure to sunshine, latitude, skin-covering clothes, the use of sunscreen lotions and skin pigmentation in healthy individuals. The vitamin D status depends on the production of vitamin D3 and vitamin D intake through the diet or vitamin D supplements. Usually, upto 90% of vitamin D in the body comes from the production in the skin under the influence of ultraviolet radiation. The preferred and most commonly used parameter for assessment of vitamin D status is serum 25(OH)D concentration. 25(OH)D is the major circulating metabolite of vitamin D and reflects the vitamin D inputs from cutaneous synthesis and dietary intake.5 Usually, serum 25(OH)D is lower at higher latitudes and with darker skin types. Several studies have shown a high prevalence (50-97%) of vitamin D deficiency in tropical and subtropical regions of India and other South Asian countries, despite abundant sunlight.[5-7]

2. Review of Literature

The optimal dose of vitamin D intake for the general population remains a subject of controversy. Experts now feel that 25-hydroxyvitamin D (25(OH)D) level of 30ng/ml is required for maintaining optimal skeletal health [8].

Vitamin D is metabolised in the liver to 25(OH) D and then in the kidneys to its active form 1, 25(OH)2 D. 8-9 It is also recognised that many other tissues in the body, including macrophages, brain, colon, prostate, breast and other, have the enzymatic machinery to locally produce 1,25(OH)2D.[9] A published literature suggests that vitamin D3 granules eight weeks of vitamin D3 60,000 IU/week oral granules supplementation increased serum 25 (OH) D to optimal levels in most of the subjects with Vitamin D deficiency.[10]

3. Objectives

To evaluate the efficacy of vitamin D3 granules 60,000 IU supplementation in vitamin D deficient apparently healthy adults.

4. Materials and Methods

The study was planned to include 125 apparently healthy urban adults who came to Yenepoya Medical college hospital. Subjects were enrolled in the study according to the inclusion and exclusion criteria mentioned below.

4.1 Inclusion Criteria

- >25 years of age, upper limit at the discretion of investigator.
- Subjects with 25(OH)D levels <30 ng/ml.
- Ability to understand and the willingness to sign and date a written informed consent at the screening visit before performing any protocol specific procedures.

4.2 Exclusion Criteria

- Age <25 years.
- Children, pregnant and lactating mothers.
- Any form of acute illness or terminal illness.
- Uncontrolled hypertension or uncontrolled diabetes.
- Any form of endocrine disorder, which could alter the plasma levels of vitamin D.
- Those receiving any form of therapy in the preceding one week, which would affect the plasma levels of vitamin D like vitamin D preparations,calcium, corticosteroids, etc.

4.3 Study Procedures

The patients were selected randomly in the Out Patient Department (OPD) and were screened for vitamin D deficiency. The serum 25(OH)D estimation was done using radioimmunoassay (RIA) method. Subjects who had 25(OH)D levels <30 ng/ml were enrolled in the study and were supplemented with vitamin D3 60,000 IU/week for eight weeks as rapid restoration phase. Subjects were instructed to consume the whole sachet with water as per the recommended schedule. Serum vitamin D (25(OH)D) estimation was repeated at follow-up after eight weeks. The study schedule is depicted in Figure 1. The primary endpoint of this study was to assess the prevalence of vitamin D deficiency in urban healthy adult population and the secondary endpoint was to evaluate the efficacy of oral cholecalciferol 60,000 IU granules in increasing 25(OH)D levels from baseline to that at 8 weeks.

The statistical analysis was performed in subjects for whom the baseline and follow-up vitamin D levels were available. The measurement data were expressed as means with one standard deviation (SD). The 95% confidence intervals (CI) were computed for differences between the data wherever applicable. Discrete data were expressed as numbers (counts) with percentages (proportions). Vitamin D3 status (ranking data) was compared between baseline and the follow-up period was analyzed for differences using Wilcoxon sign rank test. Vitamin D3 levels and change from baseline in vitamin D3 levels were analyzed for differences in different subgroups gender, age groups using one way ANOVA. Correlation (Pearson's) was done between changes in plasma vitamin D3 and the number of sachets used. All testing was performed using 2-sided tests at alpha 0.05.

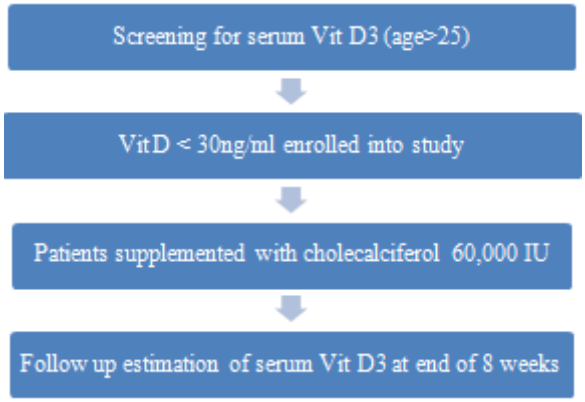

Figure 1: Study methodology

5. Results

A total of 125 subjects (age above 25 years) were enrolled as per the inclusion and exclusion criteria in this single center study. In this article, we present and discuss the data for 103 subjects who consumed all eight sachets of the study drug and completed the study. In spite of the strict follow-up, the number of subjects completing the study was low, probably due to their busy schedule and thereby inability to follow the procedures and make it for second blood collection or it may be ignorance about vitamin D deficient status and its importance.

Baseline data was available for 103 subjects as per the study protocol. Of these 103 subjects, 69.9 % subjects were found to be vitamin D deficient (<20 ng/ml) and the mean plasma vitamin D3 25(OH)D level was 9.8 ng/ml at baseline. At the end of the study, the mean 25(OH) D plasma level was noted to be 27.4 ng/ml. The mean change from baseline was 17.6 ng/ml. Among these 103 participants only 30.1% had 25(OH) D >20 ng/ml <30 ng/ml at baseline, which increased to at the end of the study following vitamin D3 supplementation for eight weeks.

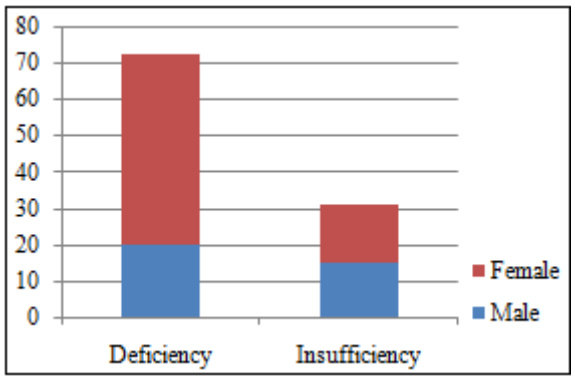

Table 1: Demographic Characters

Vit D3 Value	Number	%
Deficiency (20ng/ml)	72	69.9
Insufficiency (20-30ng/ml)	31	30.1

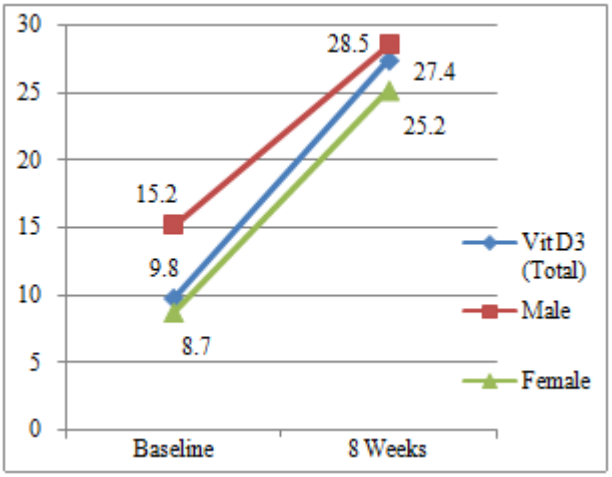

Table 2: Vitamin D3 25(OH)D Status at Baseline

Vit D3 Value	Male	Female
Deficiency (20ng/ml)	20	52
Insufficiency (20-30ng/ml)	15	16
Total	35	68

Table 3: Change in 25(OH)D levels at the end of eight weeks with 60,000 IU vitamin D

	Baseline (mean)	8 weeks (mean)	change
Plasma Vit D3	9.8	27.4	17.6
Male	15.2	28.5	13.3
Female	8.7	25.2	16.5

6. Discussion

The understanding of various facets of vitamin D3 has come a long way from being regarded as just a vitamin to now being labeled as a hormone or a metabolic modulator. The awareness about vitamin D sufficiency and its importance in optimal health is increasing.

The role of vitamin D in calcium absorption and metabolism for bone health is well-established. Furthermore, since the past two decades, the importance of vitamin D in reducing the risk of cancer, multiple sclerosis and type 1 diabetes mellitus is being explored. There have been many reviews and discussions on the role of vitamin D and prevention of disease and maintenance of optimal health in the past decade.[11]

In the present study, among 178 subjects, 94.94% had vitamin D deficiency and 5.06% had insufficiency, which is similar to other studies in the past. All the subjects having vitamin D deficiency or insufficiency were supplemented with vitamin D3 granules per week for eight weeks. According to the results established by previous studies,3 the supplementation of vitamin D3 60,000 IU in the present study was justified. In the study by Goswami et al,12 weekly supplementation of vitamin D granules 60,000 IU resulted in correction of vitamin D level to optimal level after eight weeks of administration. However, to maintain the 25(OH)D levels, vitamin D supplementation has to be ongoing after the eight weeks of vitamin D-loading schedule. Marwaha et al3 mentioned that based on the results of studies, a regular supplementation of at least 2,000 IU/day vitamin D is required to maintain normal vitamin D levels. This study (Marwaha et al) also highlighted the inadequacy of a daily vitamin D intake of 200-400 IU in normalizing serum 25(OH)D.3

In our study, the Baseline data was available for 103 subjects as per the study protocol. Of these 103 subjects, 69.9 % subjects were found to be vitamin D deficient (<20 ng/ml) and the mean plasma vitamin D3 25(OH)D level was 9.8 ng/ml at baseline. At the end of the study, the mean 25(OH) D plasma level was noted to be 27.4 ng/ml. The mean change from baseline was 17.6 ng/ml. Among these 103 participants only 30.1% had 25(OH) D >20 ng/ml <30 ng/ml at baseline, which increased to at the end of the study following vitamin D3 supplementation for eight weeks. Many studies show vitamin D deficiency in Indians despite the sunny climate throughout the year, irrespective of their age group and gender.

Goswami et al weekly supplementation of vitamin D granules 60,000 IU resulted in correction of vitamin D level to optimal level after eight weeks of administration.

Recent clinical practice guidelines also recommend vitamin D oral supplementation 50,000-70,000 IU/week for eight weeks in vitamin D deficiency to normalize 25(OH)D levels to above 30 ng/ml. While analyzing the results, it was observed that the subjects had consumed the study drug either with water or with milk. The subanalysis was conducted for further investigation, which showed that the increase in 25(OH)D levels was statistically significant both when consumed with water or milk. Though the 25(OH)D levels increased better when consumed with milk, no statistically significant difference was observed. Further follow-up and evaluation of regular supplementation for sustained improvement in 25(OH)D levels is required. Other limitations of the present study are that the subjects were not on controlled diet, lifestyle, sun exposure, etc.

7. Conclusion

The deficiency of vitamin D is highly prevalent (>95%)in urban healthy adult population. The administration of vitamin D3 granules in the initial rapid restoration phase of 60,000 IU/week for eight weeks led to optimizing of the 25(OH)D levels. There is a need for trials of longer duration of treatment, to evaluate the effect of different lifestyle factors in this population.

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