

ORIGINAL ARTICLE

COMPARISON OF DIFFERENT FORMULATIONS OF VITAMIN D

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Background: Vitamin D Deficiency (VDD) is responsible for a wide spectrum of clinical diseases and vitamin D deficiency prevalence is frightening in most parts of the world including Pakistan. Therefore, supplementations of vitamin D are used in the population at high risk for the prevention and the treatment of vitamin D deficiency. Vitamin D supplementation comes in various formulations both oral and intramuscular. Cholecalciferol is the most commonly used preparation which is given through these routes of administration. There is need to study the fact that how much vitamin D levels are raised after administration of these different formulations as this can be a pivotal factor in determining dosage and route of vitamin D3. **Methods:** This cross-sectional study conducted on 320 cases and compared the efficacy of various Vitamin D3 preparations in raising Vitamin D levels conducted in Department of Endocrinology and Metabolism, Services Hospital, Lahore from February to July, 2016. Blood serum was drawn for vitamin D level in the cases at the time of presentation and after treatment. **Results:** Three hundred & twenty patients were enrolled in study and divided into four groups (A, B, C, D). There was no significant difference between groups (A, B, C, D) in change in vitamin D levels after 3 months of treatment (*p*-Value 0.446). **Conclusion:** Different preparations of vitamin D are equally effective in raising vitamin D levels at 12 weeks. However, there is a need to conduct large scale studies to further validate these results.

Keywords: Deficiency; Vitamin D; Administration; Dosage; Efficacy

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INTRODUCTION

Vitamin D Deficiency (VDD) is a worldwide pandemic which has recently come in limelight.¹ It is responsible for a wide spectrum of clinical diseases² and vitamin D deficiency prevalence is frightening in most parts of the world including Pakistan. Vitamin D deficiency occurs in 20–80% the males as well as the females in Europe, Canada & United States of America.^{1,3,4} It has been estimated that 53.5% of Pakistani population had vitamin D deficiency, 31.2% had insufficient vitamin D, and only 15.3% normal vitamin D.⁵ Vitamin D Deficiency occurs in all ages, both genders, various professions, whether the population lives in the big cities or the small towns or the villages.^{6,7}

Sunlight exposure is the biggest source for making of vitamin D in the body. Though subcontinent is enriched with sunlight throughout year but still decreased synthesis of vitamin D through the skin may be due to decreased exposure to the UV light which may be attributed to the raised pigmentation of the skin, use of the sunscreens, some cultural and social norms, wearing of extra clothes and the more modern life style.⁸ The inadequate exposure to sunlight, decreased intake and the fortification of food leads to deficiency/insufficiency of vitamin D in Asian population. Therefore, supplementations of

vitamin D are used in the population at high risk for the prevention and the treatment of vitamin D deficiency.⁹

Vitamin D supplementation comes in various formulations both oral and intramuscular. Oral formulations are preferred where just dietary deficiency is the cause and intramuscular preparations are needed where malabsorption is the main cause of deficiency.¹⁰ Cholecalciferol is the most commonly used preparation which is given through these routes of administration. The daily requirement of Vitamin D supplementation ranges from 800IU/Day to 4000 IU/day from different authorities.^{11,12} The requirement increases with age.

It has been reported that different preparations of Vitamin D3 have been used. There is need to study the fact that how much vitamin D levels are raised after administration of these different formulations as this can be a pivotal factor in determining dosage and route of vitamin D3. It can also explain the extremely diverse recommendations of daily requirement of vitamin D3.

Hence, we performed a study to solve the dilemma about various preparations of vitamin D that is oral, intramuscular, weekly or monthly regimens to compare the efficacy of various preparations of vitamin D available in the market. In this study, we compared the efficacy of various Vitamin D3 preparations in raising Vitamin D levels.

MATERIAL AND METHODS

It was cross sectional study conducted in Department of Endocrinology and Metabolism, Services Hospital, Lahore from February to July, 2016. A sample size of 320 patients was calculated using % level of significance, 4% margin of error with expected normal vitamin D level in 38% of cases. 320 patients were enrolled in study using non-Probability Consecutive Sampling. Vitamin D deficiency was defined as Mild deficiency if Vitamin D levels were between 20–30 ng/ml, moderate deficiency if Vitamin D levels between 10–20 ng/ml and severe deficiency if Vitamin D level below 10 ng/ml. Patients of both genders with Vitamin D levels less than 30 ng/ml were included in the study. Patients with renal dysfunction (Creatinine >1.2 mg/dl), Patients with Liver disorders (SGPT, SGOT two times upper limit of normal, reversed albumin to globulin ratio and prolonged PT), patients with a diagnosis of malabsorption due to any cause, pregnant and lactating females were excluded from study.

Three hundred & twenty patients fulfilling the inclusion criteria were enrolled in the study. Informed consent was taken from each participant of the study. Patients were randomly divided into 4 groups (A, B, C, D) using web based computer generated random number table (<http://stattrek.com/statistics/random-number-generator.aspx>). Group A was given 600,000 IU Vitamin D3 once only. Group B was given 200,000IU per oral monthly for 3 months. Group C was given 200,000 IU Vitamin D3 intramuscular monthly for 3 months. Group D was given 50,000 IU Vitamin D3 per oral every week for 3 months. Vitamin D levels were obtained before treatment and after completion of treatment to see rise in Vitamin D levels.

All the collected information was transferred to SPSS version 20 and analysed. Mean and standard deviations were calculated for all quantitative variables like age, sex, S. Calcium, Phosphorous Alkaline phosphatase & Vitamin D levels at baseline & after 3 months, that is, on completion of treatment. Frequency and percentages were calculated for all qualitative variables like gender. Efficacy was compared in all four groups using chi square test. Independent sample t test was applied to see efficacy of treatment in groups A, B, C & and D. Post stratification chi square test was applied for age, gender, S. Calcium, Phosphorous & Vitamin D at baseline & at 3 months on completion of treatment.

RESULTS

Three hundred & twenty patients were enrolled in study and divided into four groups (A, B, C, D). Mean age of study population in each group and gender distribution is given in table-1. Vitamin D levels in Groups at baseline, Vitamin D levels after 12 weeks of treatment and Change in Vitamin levels after 3 months of treatment are given in table-2. There was no significant difference between groups (A, B, C, D) in change in vitamin D levels after 3 months of treatment (*p*-Value 0.446) table-2.

Table-1: Demographic characteristics of study population

Vitamin D Preparation	Mean±SD	Males	Females
Group A	40.12±2.165	43	37
Group B	41.61±3.936	39	41
Group C	45.12±2.037	35	45
Group D	41.32±5.367	33	47

Table-2: Change in Vitamin D levels with different preparation of Vitamin D at 3 months

Vitamin D preparation	Vitamin D Levels at baseline	Vitamin D Levels at 12 weeks	Change in Vitamin D level after 3 months
Inj Vitamin D3 600,000IU PO	13.30±6.546	56.65±9.398	43.34±10.357
Inj Vitamin D3 200,000IU PO	12.20±4.758	53.90±8.316	41.88±9.195
Inj Vitamin D3 200,000IU IM	14.05±6.769	55.15±7.188	41.10±8.482
Cap Vitamin D3 50,000IU PO	12.65±5.261	54.45±6.486	41.73±7.770
Total	13.05±5.908	55.04±7.955	42.01±8.997
<i>p</i> -Value	0.216	0.146	0.446

DISCUSSION

Vitamin D deficiency is the new pandemic of the current era. Though, Vitamin D has been known for more than a century, but now, in the recent past, multiple different functions of vitamin D have been studied.¹⁴ It has been proposed to be recommended in Rickets, osteomalacia, osteoporosis, pregnancy, renal failure, fibromyalgia, obstructive pulmonary diseases and many others.^{15–18} Across the globe, Deficiency of vitamin D is a disease which is the least diagnosed one & its prevalence is very high among the population.¹⁹ Some data suggest that inadequate exposure to sunlight is the topmost factor which is responsible for the vitamin D deficiency to become a pandemic all over the world because there are some foods which have vitamin D content (e.g. mushrooms exposed to sunlight and salmon caught from the jungles).² The Recommend Dietary Allowances (RDA) for vitamin D cannot be achieved by the food content of vitamin D as shown by the data on the adults as well as on the children. In the subcontinent, vitamin D produced by skin, is less in amount, due to raised levels of melanin in the skin or due to the

excessive usage of clothes and the sunscreens or due to stay at the homes for almost the whole day.⁸ Treatment of Deficiency of vitamin D includes (a) fortification of vitamin D (food processing is done and the micronutrients are added to the food contents) (b) Vitamin D supplements (larger doses of micronutrients are added, either in capsule form or the syrup). In the general public and those persons who are vulnerable to vitamin D deficiency, food can be fortified to raise the Vitamin D levels and this becomes a very effective solution to this problem.^{20–22} But, it is necessary to involve politically motivated persons and some ministries (like health, social welfare etc. etc.) to work together & make some policies to enhance the vitamin D levels of the population of the country. In the subcontinent, fortified food is used on small scales; therefore, vitamin D supplements remain the most effective choice.²³

There are multiple supplements of vitamin D are available. Physicians are prescribing vitamin D in multiple preparations such as Vitamin D 600,000 IU per oral, Vitamin D 200,000IU per oral, Vitamin D 200,000 IU intramuscular, Vitamin D 50,000IU per oral. However, no study is available to throw light on comparison of efficacy of different vitamin D preparations to raise vitamin d level after administration. This makes it difficult to recommend a definite dose of vitamin D for these preparations for a given vitamin D levels

The study was done with a view to determine the fact that how much, a vitamin d preparation dose can increase vitamin D level in patients of vitamin d deficiency. It was concluded that vitamin D change after treatment for 3 months with different preparation of vitamin D is not significantly different and all these preparations raise vitamin D level almost equally.

Our result is similar to other studies looking at that outcome of different preparations of vitamin D oral as well as intramuscular as demonstrated by Mustafa MA *et al.*, who showed in their study among the various preparations of vitamin D 3, non-significant statistical difference was seen, in increasing the levels of vitamin D. It is in accordance with the results of our study which also demonstrate the same facts.²⁴

In another study, Cipriani C *et al.*, comparison was done between the single dose of 600,000IU intramuscularly versus the oral dose. It showed the better initial results with the oral dose, in respect to the bioavailability as well as the efficacy and hence the equivalent oral dose is considered more effective in raising the levels of vitamin D as compared to the intramuscular counterpart, however the intramuscular dose had produced the gradually

increasing sustained levels when further observed for the next 4 months. This also supports the results of our study in which all preparations show equal efficacy though no effort was made to see immediate effect of these preparations on Vitamin D levels. Further studies will be needed to clarify this fact further.²⁵

Zabihyeganeh M *et al.* Conducted a trial which also showed similar results, i.e., the two regimens proved equally safe & effective in the treatment of vitamin D deficiency. However, it proved that the oral route was superior for the initial short duration.²⁶

CONCLUSION

Different preparations of vitamin D are equally effective in raising vitamin D levels at 12 weeks. However, there is a need to conduct large scale studies to further validate these results.

AUTHORS' CONTRIBUTION

HMFR: Principal investigator. U, UM & SK: Data collection. Z & KKC: Contributed in compiling the collected data & formulating the statistics & final results.

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