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Randomized Controlled Trial

# Topical vitamin D3: A randomized controlled trial (RCT)

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SUMMARY

*Objective:* The intent of this study was to test the effect of Top-D, a topical Vitamin D preparation, in delivering vitamin D.

*Methods:* Five hundred and fifty healthy patients, with vitamin D insufficiency and deficiency were recruited after written informed consent. Demographic data was recorded, adequate history and clinical examination was done to rule out any metabolic diseases. Complete blood picture, serum calcium, phosphorous, Parathormone and 25 Hydroxy-vitamin D3 (25OHD) was carried out before enrollment of the patients. Patients were divided randomly into two groups 350 in study group and 200 in the control group. Patients in the study group were given Top-D (Vitamin D3 gel made from proniosomal technology) to apply daily on the skin. Top-D 1 g contained 5000 IU of vitamin D3. The control group was given 1 g of Aloe vera gel to be applied every day. The two groups had no knowledge to which group they belong. After 4 months serum 25OHD was tested again.

*Results:* Three hundred and forty five patients in study group and 192 in control group completed the study. The mean age of the patients in the both the groups was 42 years (18–80 years). The pretreatment 25OHD level in the study group was 11.03 ± 4.57 (2–12) ng/l compared to the control group 10.36 ± 4.09 (2–21) and post treatment the levels were 37.17 ± 6.04 (12–54) ng/ml and 10.51 ± 3.5 (2–19) ng/ml ($p < 0.001$).

*Conclusion:* The results of this study indicate that transdermal route of vitamin D is potentially, safe and can give desired results to raise the vitamin D levels. This route is an alternate route for supplementation of vitamin D which should be utilized.



## 1. Introduction

Vitamin D (VD) is one of the fat soluble vitamin which is important to maintain bone health and in prevention of rickets or osteomalacia in the adults. In majority of patients the Vitamin D deficiency or insufficiency occurs due to lack of sun exposure or due nutritional causes. Initial studies in 1980 showed that low level of vitamin D was common among Saudi Arabian population. Sedrani et al. (1983, 1984) [1,2] has shown that vitamin d deficiency existed irrespective of the season due to low exposure to the sunlight. Recent studies of Al-Turki et al. [3], Sadat-Ali et al. [4] found that about 60 percent of men and women in over 50 years of age had vitamin D deficiency but some studies put the deficiency of vitamin D to be 95–100% [5,6]. Added to this vitamin D Deficiency persisted even after prescription of vitamin D. One of the reasons that patients did not take medications as they were taking large number of oral medications daily [7–9]. It was reported that many of the oral medications prescribed are taken [10] and it was estimated for noncompliance of oral medications range between 62 and 84 percent [11,12]. hence we believe that in the young and elderly oral route can be avoided if topical route is available. The approval by the US FDA scopolamine as transdermal patch 40 years ago, the number of topical drug delivery increased [13–19].

Vitamin D is available in the form of tablets, drops and injection form and the compliance for oral VD and calcium was less than 60% [20–23]. Segal et al. (2009) [20] found that by end of 3 months, 23.8% of patients were taking properly and 26.2% more were partially compliant. It is our belief that if topical Vitamin D is available, the compliance might increase. This prospective RCT study was done to assess the outcome of topical delivery of VD.

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**Table 1**
Patients data.

| Parameter | Study Group | Control Group |
|---|---|---|
| Age (Years) | 42.59 ± 15.74 (18–80) | 41.6 ± 16.6 (18–80) |
| Males | 65 | 55 |
| Females | 280 | 137 |
| Vitamin D level Pre Treatment (ng/mL) | 12.03 ± 4.57 (2–12) | 10.36 ± 4.09 (2–21) |
| Vitamin D level Post Treatment (ng/mL) | 37.17 ± 6.04 (12–54) | 10.51 ± 3.5 (2–19) |

## 2. Patients and methods

The study was approved by the IRB of Imam AbdulRahman Bin Faisal University and funded by the Deanship of Scientific Research, Imam AbdulRahman Bin Faisal University, Dammam Saudi Arabia. An informed written consent was obtained from 550 healthy patients, with vitamin D deficiency and vitamin D insufficiency. Patients demographic data was collected. Complete history, thorough clinical examination was done to rule out any metabolic diseases. Blood was collected for complete blood picture, serum calcium, phosphorous, alkaline phosphatase, Parathormone and 25 Hydroxy-vitamin 3 (25OHD) levels. 25OHD3 was measured in King Fahd Hospital of the University, Alkhobar by chemiluminescence immunoassay (CLIA). A vitamin D3 level of ≥30 ng/mL was accepted as normal, 21–29 ng/mL as insufficiency and ≤20 ng/mL as deficiency. The patients were randomized into two groups of 350 in study arm and 200 in control arm. Participants were instructed not to change their dietary habits and increase sunlight exposure. Patients in the study group were given Top-D (Vitamin D3 gel made from proniosomal technology) to apply daily on the skin. Top-D 1 g contained 5000 IU of vitamin D3. The control group was given 1 g of Aloe vera gel to be applied every day. The two groups had no knowledge to which group they belong. After 4 months serum 25OHD was tested again. The data was analyzed using SPSS Inc version 19.

The Study was monitored by the Monitoring Office for Research and Research Ethics (MORRE) of the Imam AbdulRahman Bin Faisal University, Dammam, Saudi Arabia.

The study was registered with www.clinicaltrials.gov. (ClinicalTrials.gov Identifier: NCT02735200).

## 3. Results

Three hundred and forty five patients in study group and 192 in control group completed the study. The mean age of the patients in the study group was 42.59 ± 15.74 (18–80) years and 41.6 ± 16.6 (18–80) years in control group. In the study group there were 65 males and 280 females, whereas in control group males were 55 and 137 females (Table 1). The pretreatment 25OH D3 level in the study group was 11.03 ± 4.57 (2–12) ng/mL compared to control group patients 10.36 ± 4.09 (2–21) ($p < 0.9$) and post treatment levels were 37.17 ± 6.04 (12–54) ng/mL and 10.51 ± 3.5 (2–19) ng/mL ($p < 0.001$) (Fig. 1 and Fig. 2). In the study group 36 (10.28%) patients there was failure of vitaminD3 levels to reach above normal level. The level improved from 11.8 ± 4.86 to 20.78 ± 6.15 ng/mL ($p < 0.001$) (Fig. 3).

In the study group 11 patients complained of initial irritation but decided to continue to be in the study. In the control group 7 patients had itching which subsided with time (Aloe-Vera).

## 4. Discussion

The regular use of topical vitamin D3 (TOP-D) was effective in raising vitaminD3 levels within four months above the threshold of ≥30 ng/mL which was considered as normal levels in this study. The findings of this study is in line with results of the initial reported study [23]. Our study is the first clinical study of level II evidence which involved 345 patients. The justifications of developing a topical delivery of vitamin D are three-fold. The vitamin D deficiency and insufficiency is World wide, even in areas where sunlight is available all the year around and the benefits of vitamin

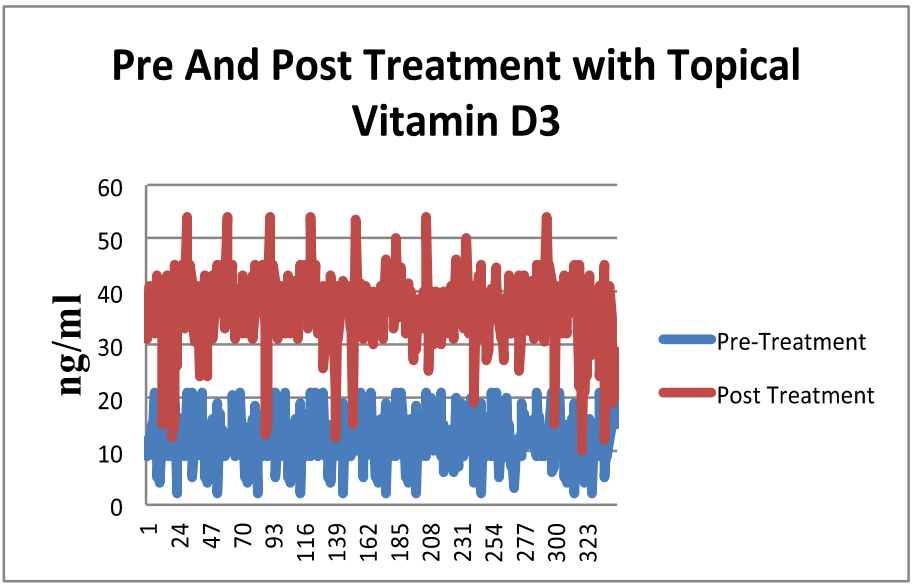


**Fig. 1.** Test group.