

The role of oral vitamin D3 supplementation in the treatment of Chronic Rhinosinusitis in adults with Vitamin D deficiency

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ABSTRACT

Background: Chronic Rhinosinusitis (CRS) is a chronic inflammatory disorder of the mucosal lining of the nose and paranasal sinuses. The ability of Vitamin D (VD3) to augment innate and adaptive immune responses has sparked interest in its immunologic role in the treatment of CRS. In this study, the incidence of vitamin D deficiency in CRS patients was compared to normal population and the beneficial role of Vitamin D supplementation in its treatment was also evaluated. **Materials and Methods:** It is a retrospective 1-year study of 200 CRS patients with Vitamin D deficiency. The patients were divided into two groups, i.e. 100 patients were given oral Vitamin D supplements and the other group of 100 patients were treated as placebo. Both Vitamin D levels and the Total Nasal Symptom Score (TNSS) were assessed at the start and end of the study period. **Results:** Of the 200 subjects with CRS, 100 were given oral vitamin D supplementation in the form of Cholecalciferol 60000IU weekly once for 3 months and the other group were treated with placebo. Before the treatment, the average level of serum Vitamin D was 12.31 ng/ml. After 3 months, it increased significantly to 29.71 ng/ml. Similarly, the pretreatment TNSS score was on average 11.92. After 3 months, the scores fell by an average of 10.65 points, a significant statistical difference ($P < 0.05$). **Conclusion:** There is a higher prevalence of vitamin D deficiency in CRS patients and that vitamin D supplementation in these patients went a long way in alleviating their symptoms.

Keywords: Chronic rhinosinusitis, immunomodulation, vitamin D supplementation

Introduction

Chronic rhinosinusitis (CRS) is a disease of the upper respiratory tract characterized by diffuse inflammation of the sinonasal mucosa.^[1] It is a significant health problem whose incidence and prevalence are rising. CRS remains difficult to treat in many cases and causes a large socioeconomic burden. It is one of the most prevalent chronic diseases worldwide.^[2] CRS is a multifactorial disease. The proposed etiologies include anatomic factors, infectious causes, fungi, immunological disorders, biofilms, and

genetic causes.^[3] The final result of all these pathophysiological factors is a chronic inflammation in the sinonasal mucosa.^[4]

The role of Vitamin D, which has a structure similar to that of steroids, has been suggested as an immunomodulatory agent besides its famed pro-skeletal effects. Accordingly, the deficiency of this vitamin has been identified as an etiologic factor in many chronic inflammatory diseases, including inflammatory bowel disease, multiple sclerosis, allergic rhinitis, and asthma.^[5] Low serum 25-OH-VitD levels also have been related to airway hyperresponsiveness, impaired pulmonary function, increased frequency of asthma exacerbation, and decreased responsiveness to corticosteroids.^[6]

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The present study is aimed at not only to see the incidence of vitamin D deficiency in CRS patients but also to determine the role of vitamin D supplementation in its treatment considering CRS as a chronic inflammatory disease with immunological aspects. Although several studies in the past have been designed, still the results are controversial and varied.

Materials and Methods

The present study was conducted from January 2019 to December 2019 at our ENT OPD on 200 patients with CRS. They were divided into two groups, i.e. 100 patients received oral vitamin D supplements (Cholecalciferol 60000IU granules in 1 g sachet, weekly once for 3 months) and 100 received placebo. The inclusion criteria included patients of both sexes with age ranged from 18 to 60 years. Informed written consent was taken from every patient to participate in study. Exclusion criteria included pregnancy and lactation, patients taking multivitamins containing vitamin D for at least 6 months or who are sensitive to it, patients on systemic steroids or nonsteroidal antiinflammatory agents for at least 3 months, and patients with a history of nephrolithiasis, chronic renal disease, and severe liver disease.

Clinical diagnosis of CRS was based on the presence of two major criteria or one major and two minor criteria, and persistence of the signs and symptoms for more than 12 weeks. The major criteria were facial pressure or pain, facial fullness, nasal obstruction, nasal discharge or postnasal drip, anosmia or hyposmia, and purulent discharge in rhinoscopy examination. On the other hand, the minor criteria entailed headache, fever, bad breath, fatigue, and pain or fullness in the jaw and ear. For this, a thorough clinical and radiological evaluation of the patients was done, which included CT scan of nose and paranasal sinuses along with Diagnostic Nasal Endoscopy. Levels of VD3 were measured by enzyme-linked immunosorbent assay (ELISA). VD3 deficiency was defined as <20 ng/ml. The Total Nasal Symptom Score (TNSS) was recorded in the form of questionnaire before the intervention and at the end of the first and then at the end of third month [Table 1].

The results were analyzed by GraphPad In Stat using student's unpaired *t*-test for comparison of TNSS between two groups. A *P* value of < 0.05 was considered as statistically significant.

Results

All 100 patients in the test group were given oral vitamin D supplementation in the form of Cholecalciferol 60000IU granules in sachet form to be taken weekly once for 3 months. At baseline, before the treatment, the average level of serum Vitamin D was about 12.31 ng/ml. By the end of the study, i.e. after 3 months, the average Vitamin D level of the patients had increased significantly to 29.71 ng/ml [Table 2]. Similarly, the pretreatment TNSS score was on average 11.94. After 3 months, the scores fell by an average of 10.65 points, a significant statistical difference. The TNSS fell dramatically lower in the active group during the first month of the study. In contrast,

scores fell more gradually for the placebo group and by the third month of the study, there was a statistical difference in the TNSS between the 2 groups [Table 3]. The student's unpaired "t" test was used for comparison between two groups which showed no difference in pretreatment TNSS but significant difference in posttreatment TNSS both after 1 month (*P*-value < 0.0001) and again after the third month (*P*-value < 0.0001).

Discussion

Our study assumes significance specially to primary care physicians working across the country as they are usually the first line of contact with these CRS patients. If they are well aware of the role of vitamin D deficiency in CRS, they will be in a better position to treat them according to the established protocol and, thus, avoid indiscriminate use of antimicrobials.

In our study, there is a significant vitamin D deficiency among patients with CRS. In the present study, the mean serum level of VitD was 12.31 ng/ml. In a study conducted in Tehran, Iran, (2004), the mean serum level of VitD was reported as 20.65 ng/ml.^[7] Another study in Isfahan, Iran, 2007, the mean levels of this vitamin were

Table 1: Total nasal symptom score (TNSS) (for each of sneezing, rhinorrhea, itching, and congestion)

0=None	No signs or symptoms present
1=Mild	Signs/symptoms clearly present but minimal awareness of them; tolerable
2=Moderate	Clear awareness of signs/symptoms; bothersome but tolerable
3=Severe	Signs/symptoms difficult to tolerate; might cause interference with activities of daily living, sleeping, or both

Table 2: Baseline demographics

	Oral vitamin D (n=100)	Placebo (n=100)
Sex, n (%)		
Women	66 (66%)	58 (58%)
Men	34 (34%)	42 (42%)
Mean age, years (range)	33.21 (15-59)	34.26 (15-60)
Mean Vitamin D Level in ng/mL (pretreatment)	12.31	25.75
Mean Vitamin D Level (posttreatment)	29.71	26.23

Table 3: Comparison of total nasal symptom score in the vitamin D and placebo groups

	Test Mean±SD (Range)	Placebo Mean±SD (Range)
Pretreatment TNSS	11.94±0.28 (11.00-12.00)	11.96±0.24 (11.00-12.00)
1 month posttreatment TNSS	6.23±1.33 (4.00-8.00)	8.74±0.7504 (5.00-10.00)
3 rd month posttreatment TNSS	0.33±0.61 (0.00-3.00)	2.29±1.581 (0.00-6.00)

estimated as 18 and 21 ng/ml in females and males, respectively.^[8] There are also inconsistent results; for example, in a study performed in Turkey in 2014, Bozkurt *et al.* studied Vitamin D serum level was 14.7 ng/ml.^[9] Alagol *et al.* in Turkey (2000) observed the mean Vitamin D serum level was estimated in 48 females to be 9 ng/ml in the individuals dressing in the European, Islamic (the areas exposed to the sun are hands and face), and traditional Islamic (the face is also covered) styles.^[10] Different styles of wearing, from western to traditional Islamic, in Turkey can significantly affect the results of the mentioned study, such as the measurement of Vitamin D serum levels. Our study also demonstrated that vitamin D supplementation had a favorable impact on the treatment of CRS. There was significantly more reduction in the TNSS in the group which received vitamin D supplementation as compared to the group which received placebo treatment. The exact mechanism of action is not known but increasing evidence points to an immunomodulatory action of vitamin D in patients of CRS. It improves symptoms directly or indirectly by potentiating the antiinflammatory effects of the medications used to treat allergy. Pichler *et al.* reported an immunoregulatory action of vitamin D in IgE mediated allergy.^[11] Searing *et al.* and Poon *et al.* have also suggested the possibility of a vitamin D effect on glucocorticoid pathway and stated that vitamin D insufficiency promotes the need for higher doses of glucocorticoids to achieve treatment effect.^[12,13] In some more recent studies, Zand *et al.* and Hashemian *et al.* have also highlighted its role in the management of CRS.^[14,15]

Conclusion

If the prevalence of Vitamin D deficiency in general population is brought down, we may succeed in arresting the recent pandemic of allergic diseases and in turn bring down the incidence of CRS. In India, high temperatures during daytime along with high humidity levels act as deterrents for people to follow the advice about sun exposure. Hence, food fortification with Vitamin D is a good option to solve this issue. At the same time, one must be careful not to overenthusiastically treat Vitamin D deficiency without actually monitoring Vitamin D levels and land up with hypervitaminosis D.

While more research and randomized control trials are required to explore the link between vitamin D and CRS, this study of ours shows us that timely detection through screening along with adequate Vitamin D supplementation can go a long way in alleviating their symptoms and bring them back to the path of faster recovery.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patients have given their consent for their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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