RESEARCH ARTICLE

Evaluating the Effects of Vitamin D on Chronic Rhinosinusitis without Nasal Polyposis

Jyothirmayi Kammili[1], Neha Raghuwanshi[2], Muhammad Arshad[3]

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Abstract

Aim: Chronic rhinosinusitis (CRS) poses a substantial challenge for ENT surgeons, affecting a significant portion of the global population. This study aims to enhance our understanding of the interplay between vitamin D and CRS, offering a foundation for future research and contributing to the development of personalized treatment strategies for individuals grappling with this challenging chronic condition.

Materials and methods: This prospective study investigates the potential therapeutic effects of vitamin D supplementation on CRS. We studied the effects of vitamin D on 50 patients with CRS and vitamin D deficiency, utilizing stringent inclusion and exclusion criteria. Participants were randomly assigned to either a test group receiving Vitamin D3 supplementation or a control group with a placebo. The comprehensive evaluation involved three assessments: levels of vitamin D, symptom severity evaluation using the sinonasal outcome test-22 (SNOT-22) questionnaire, and sinus computed tomography (CT) scans employing the Lund-Mackay scale.

Results: The findings of this study suggest that oral vitamin D supplementation, as part of a comprehensive treatment regimen, may be beneficial in managing CRS in individuals with vitamin D deficiency.

Conclusion: The improvements observed in symptomatology and sinus health underscore the potential role of vitamin D in the management of this condition. Further research with larger sample sizes and longer follow-up periods is warranted to validate these findings and explore the long-term effects of vitamin D supplementation.

Clinical significance: This study's clinical significance lies in its potential to enhance CRS management through vitamin D supplementation. Demonstrating the benefits of addressing vitamin D deficiency in CRS patients, it introduces a novel, cost-effective treatment avenue. Implementing vitamin D assessment and supplementation in CRS care could lead to improved symptom control and enhanced quality of life (QoL). Overall, the study's findings offer valuable insights for improving CRS management strategies globally.

Keywords: Chronic rhinosinusitis, Lund-Mackay score, Sinonasal outcome test-22, Vitamin D.

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Introduction

Chronic rhinosinusitis (CRS) is a common issue encountered by ENT specialists, significantly impacting global health by affecting ~ 3–6.4% of individuals worldwide. As per the European Position Paper on Nasal Polyps (EPOS) 2020, CRS is defined as persistent inflammation of the nasal and paranasal sinus regions. This condition requires the presence of at least two symptoms, one of which must be either nasal obstruction, blockage, congestion, or nasal discharge (posterior or anterior). Other associated symptoms can include facial discomfort, pressure, or a diminished sense of smell. Diagnostic tools such as nasal endoscopy often reveal nasal polyps, thick mucous discharge, or inflammation, particularly in the middle nasal passage. Chronic rhinosinusitis is broadly categorized into two forms: Chronic rhinosinusitis with nasal polyps (CRSwNP) and CRS without nasal polyps (CRSsNP).[1]

The highly heterogeneous nature of CRS makes its pathogenesis complex. Multiple factors have been implicated in the onset and progression of CRS like geographical and racial influences, environmental exposures, impaired immune response, imbalanced sinus microbiota, ineffective mucociliary clearance (MCC) or epithelial barrier.[2] Despite advancements in medical and surgical interventions, understanding the root causes and optimal management of CRS remains challenging for researchers and clinicians. A burgeoning area of investigation that has garnered increasing attention revolves around the potential influence of vitamin D in modulating the inflammatory processes associated with CRS. Vitamin D3 plays a crucial role in modulating the immune system by influencing the activity of monocytes, macrophages, dendritic cells, and T lymphocytes. It plays a pivotal role in combating inflammation, is crucial in the prevention and treatment of asthma, and holds particular importance in cases of chronic sinusitis and sinus infections. Additionally, Vitamin D3 positively regulates cathelicidin, an antimicrobial agent unique to humans

[1]Department of ENT, National Health Mission, Vijayawada, Andhra Pradesh, India

[2]Department of ENT, M.G.M.M.C. and M.Y.H., Frisco, Texas, United States of America

[3]Department of ENT, Benazir Bhitto Hospital, Rawalpindi Medical University, Rawalpindi, Punjab, Pakistan

Corresponding Author: Jyothirmayi Kammili, Department of ENT, National Health Mission, Vijayawada, Andhra Pradesh, India, Phone: +91 8374885597, e-mail: saiharshakammili@gmail.com

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produced in the skin, respiratory passages, and throughout the digestive system. The widespread prevalence of vitamin D insufficiency globally contributes to a significant health concern. This deficiency may partly play a part in the rising incidence of CRS and other sinus-related issues.[3] This study explores the potential advantages of vitamin D supplementation in managing CRS. It examines how vitamin D influences symptom severity and enhances the quality of life (QoL) in individuals diagnosed with the condition. A deeper understanding of the interplay between vitamin D and CRS may open new avenues for personalized treatment strategies, ultimately improving outcomes and the overall well-being of patients grappling with this challenging chronic condition.

Objectives

- Evaluate symptom Severity: Evaluate the effects of vitamin D supplementation on CRS symptoms by utilizing the sinonasal outcome test-22 (SNOT-22) questionnaire at three intervals: baseline, 1 month, and 4 months after treatment.
- Assess sinus pathology: Utilize sinus computed tomography (CT) scans and the Lund-Mackay scale to measure changes in sinus pathology severity in response to vitamin D supplementation at baseline and 4 months post-treatment.
- Explore vitamin D levels: Analyze vitamin D levels both prior to and following supplementation to assess the effectiveness of the vitamin D3 regimen and its relationship to symptom improvement.

Materials and Methods

This prospective study was conducted at a primary healthcare center over a 2-year period, from December 2021 to December 2023. The study included 50 patients diagnosed with CRSsNP who also exhibited vitamin D deficiency.

Inclusion Criteria

- Age between 18 and 60 years.
- Presence of diagnostic criteria for CRS without Nasal Polyposis (CRSsNP).
- Vitamin D3 insufficiency (below 20 ng/mL).

Exclusion Criteria

- Patients who refused to consent to participation.
- Patients having nasal polyps or undergone any previous surgical treatment for CRS including functional endoscopic sinus surgery (FESS).
- Patients with known sensitivity to oral vitamin D3.
- History of prolonged systemic steroid use.
- History of systemic disorders, including endocrine, renal, or skeletal conditions, neoplasms, continuous vitamin D3 supplementation Individuals who smoke, and consume alcohol excessively, pregnant women.

Methods

Written informed consent was thoroughly obtained from each patient participating in the study. A total of 50 eligible patients were randomly divided into two groups: The vitamin D3 group and the placebo group, with 25 individuals in each group. Both groups followed a standardized treatment protocol, which included the use of fluticasone nasal spray, a 5-day antibiotic course, and a 1-month regimen of montelukast. The intervention group received a daily oral dose of 400 IU Vitamin D3 tablets for one month, while the control group was given a placebo following the same regimen. Structured questionnaires were distributed to participants for data collection. Clinical outcomes were measured at the onset of treatment and then after 1- and 4-months post-treatment. The questionnaire was designed to evaluate the QoL using the SNOT-22 criteria, a widely recognized tool for assessing QoL in individuals with sinusitis.[4] The SNOT-22 consists of 22 questions, which are divided into four categories: nasal, otologic, sleep, and emotional.

Patients also underwent CT scans of the paranasal sinuses 4 months after treatment. The severity of their condition was evaluated using the Lund-Mackay scale.[5] This scale is a commonly employed technique for radiologic staging of CRS. When interpreting a CT scan of the paranasal sinuses and osteomeatal complex, each sinus is assigned a score from 0 to 2. The score ranges from 0 to 24.

Table 1: This table shows baseline characteristics of both groups of patients

Variables	*Vitamin D3 group*	*Placebo group*
Mean age (Years)	34.7	36.5
Gender		
Male	13	15
Female	12	10
Allergic rhinitis		
Present	9	10
Absent	15	16

Statistical Analysis

Data were collected in Excel sheet.[6] Data were analyzed using MedCalc Software (Version 22.016; accessed December 16, 2023). We present the significant value (p-value) and the 95% confidence interval (CI) of the difference. The p-value indicates the probability of observing the difference between the two samples if the null hypothesis were true. The null hypothesis posits that there is no difference between the two groups (i.e., the difference is 0). If the p-value is less than 0.05 ($p < 0.05$), it suggests that the two means are significantly different.

Results

Of the 50 cases included in our study, 28 were male and 22 were female, resulting in a male-to-female ratio of 1.31. The mean age of participants in the vitamin D3 group was 34.75 years, with a standard deviation of 5.2, while the mean age in the Placebo group was 36.5 years, with a standard deviation of 6.94. The baseline characteristics are presented in Table 1.

A positive history of AR was reported in 19 (38%) cases. At baseline (0 month), the SNOT-22 scores were 69.95 ± 6.9 in the vitamin D3 group and 70.2 ± 8.5 in the placebo group, with no statistically significant difference observed between the two groups ($p = 0.9$). After one month of treatment, the vitamin D3 group had a mean score of 65.3 ± 6.8, while the Placebo group had a mean SNOT-22 score of 66.8 ± 8.44, with no statistically significant difference between the groups ($p = 0.5$). However, at 4 months, both groups showed a notable reduction in SNOT-22 scores. The vitamin D3 group exhibited a significantly lower mean score of 45.9 ± 10.76 ($p < 0.0001$), while the placebo group had a

Table 2: This table shows changes in SNOT-22 and Lund-Mackay scores in both groups score

Test group	*0 month*	*1 month*	*4 months*
Vitamin D3 group			
SNOT22	69.95 ± 6.9	65.3 ± 6.8	45.9 ± 10.76
Lund-Mackay score	16.85 ± 2.32		7.8 ± 2.01
Placebo group			
SNOT22	70.2 ± 8.5	66.8 ± 8.44	54.25 ± 8.16
Lund-Mackay score	15.4 ± 1.77		11.15 ± 2.17
p-values			
SONT22	0.9	0.5	<0.0001
Lund-Mackay score	0.03		<0.0001

Table 3: This table shows vitamin D3 levels before and after supplementation in vitamin D3 group

Time	*0 month*	*4 months*	*p-value*
Mean ± SD	16.5 ± 0.3	30.5 ± 3.31	<0.0001

mean score of 54.25 ± 8.16, indicating a significant improvement in symptoms in the vitamin D3 group compared with the placebo group. In both the vitamin D3 and placebo groups, the Lund-Mackay scores decreased from baseline (0 month) to 4 months. The vitamin D3 group showed a reduction from 16.85 ± 2.32 to 7.8 ± 2.01 ($p < 0.0001$), while the placebo group decreased from 15.4 ± 1.77 to 11.15 ± 2.17 ($p < 0.03$), indicating a more significant improvement in sinusitis symptoms in the vitamin D3 group. The improvement in SNOT-22 and Lund-Mackay scores for the Vitamin D3 group compared with the placebo group is illustrated in the graph and Table 2.

In the group of vitamin D3, the mean vitamin D levels significantly increased from 16.5 ± 0.3 at baseline (0 month) to 30.5 ± 3.31 after 4 months of supplementation ($p < 0.0001$). This is shown in Table 3.

Discussion

The rising incidence of CRS creates a bad impact on the quality of lives of affected individuals and the economic burden on families and societies. Therefore, numerous researchers are focused on discovering treatments that address the various factors involved in the pathogenesis of this condition. The research on the effects of vitamin D supplementation on the symptomatology and pathology of CRS is not a new one but is yet to be concluded.

In our study, we observed that oral vitamin D supplementation was effective in normalizing vitamin D levels, suggesting good patient compliance, proper absorption, and the efficacy of the dosage. Sinonasal outcome test-22 has been shown to be a reliable indicator of symptomatic improvement following CRS treatment,[7] which is why we utilized it to assess the outcomes after treatment. The effects of this supplementation were clearly visible in symptoms, which were measured by the SNOT-22 scores. The improvement in symptoms was more noticeable at the end of 4 months in patients who regularly took vitamin D, compared with those in the placebo group. This suggests that vitamin D3 supplementation may contribute to an amelioration of CRS symptoms over time. The concomitant increase in vitamin D levels in the intervention group adds a biochemical dimension to these findings, affirming the efficacy of the supplementation regimen. Collectively, these results underscore the potential therapeutic role of vitamin D3 in mitigating symptoms and improving the overall health outcomes of individuals with CRS. Tafazzul Hyder Zaidi et al. found that females had higher SNOT-22 scores and thus poorer QoL.[8] However, we did not find any such differences in QoL outcomes based on gender.

Christensen et al.'s investigation highlights the complex local regulation of vitamin D within sinonasal tissue during CRS, suggesting potential independence from serum 25(OH)D levels.[9] The findings indicate a complex dysregulation of the vitamin D pathway, characterized by reduced transcription of the metabolic gene *CYP27B1* and increased transcription of the catabolic gene *CYP24A1* in sinonasal tissue. This localized dysregulation implies a tissue-specific modulation of vitamin D metabolism in CRS, distinct from systemic levels. The observed decrease in *CYP27B1* transcription may limit the synthesis of active vitamin D, while increased *CYP24A1* transcription could enhance its degradation. Such imbalances may contribute to altered local vitamin D availability and activity in sinonasal tissues, potentially influencing the pathophysiology of CRS. These novel insights underscore the importance of considering local tissue-specific factors in understanding vitamin D dynamics and its potential implications for CRS.

Abuzeid et al.'s study highlights vitamin D's pivotal role in regulating immune response mechanisms and influencing immune cell differentiation. The study highlights the potential therapeutic benefits of vitamin D supplementation in reducing inflammation and enhancing clinical outcomes in chronic upper airway conditions.[10] In a similar vein, Sansoni and colleagues investigated the novel role of vitamin D3 in regulating CRS with nasal polyposis, specifically examining its effect on basic fibroblast growth factor (bFGF). Their study found that vitamin D3 acts as a regulator of bFGF, a crucial factor in tissue repair and inflammation, offering a molecular insight into the anti-inflammatory properties of vitamin D in nasal polyposis. This discovery of vitamin D3 as a modulator of bFGF enhances our understanding of its immunomodulatory effects in CRS, potentially opening new therapeutic options for treating nasal polyposis.[11]

The Lund-Mackay score, used to assess changes in disease severity with treatment,[12] was applied in our study to evaluate the impact of vitamin D supplementation on sinus pathology. Initially, both groups showed similar results after 1 month of treatment; however, after 4 months of consistent vitamin D supplementation, a more pronounced and statistically significant reduction in sinus pathology was observed in the vitamin D group. This suggests a positive effect of vitamin D on improving sinus conditions in CRS patients.

The study conducted by Baruah et al. explored the impact of oral vitamin D3 supplementation as a preventive measure against allergies and CRS. The contextualization of the study within the unique environmental conditions of India, where high temperatures and humidity impede adherence to sun exposure recommendations, underscores the importance of alternative strategies such food fortification with vitamin D has been explored as a potential strategy for improving overall vitamin D status and reducing health risks.[13] Mulligan et al. demonstrate that a deficiency in vitamin D worsens sinonasal inflammation, highlighting the complex interplay between vitamin D levels and nasal health.[14] In their meta-analysis, Li and colleagues examine the link between serum vitamin D levels and CRS, concluding that there is a significant correlation between low vitamin D levels and the prevalence of CRS.[15]

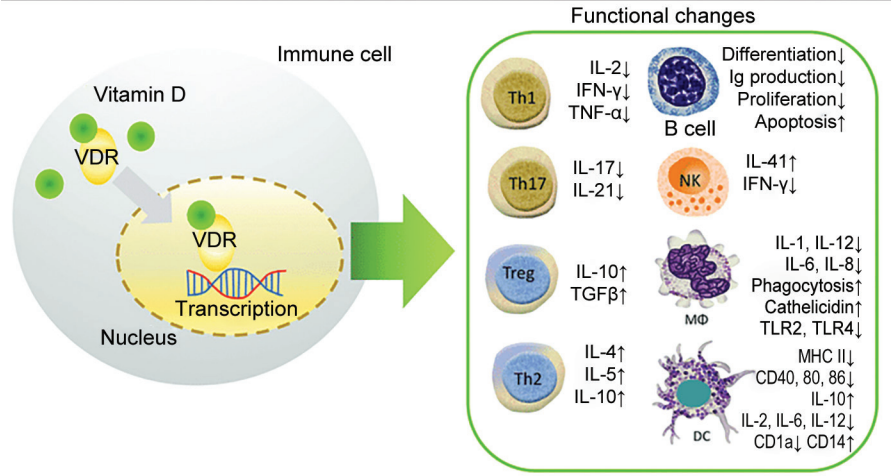

Fig. 1: Immunomodulatory effects of vitamin D ($1,25(OH)_2 D_3$) on multiple immune cell lineages
DC, dendritic cell; M, macrophage; NK, natural killer; R, receptor; VDR, vitamin D receptor[19]

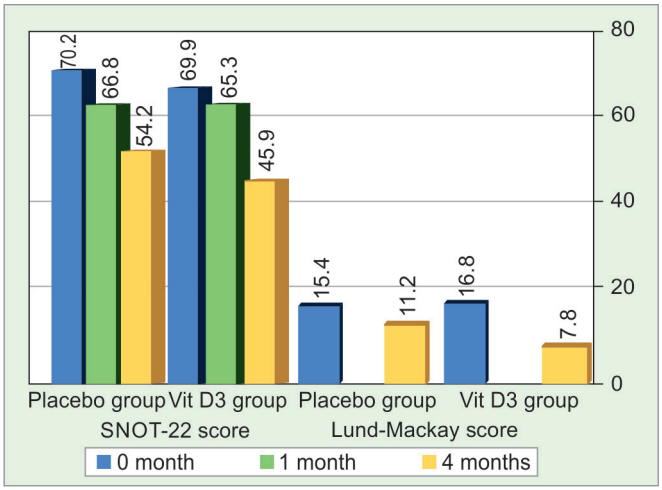

Fig. 2: SNOT 22 and Lund-Mackay scores before and after treatment

Heaney's comprehensive review of vitamin D emphasizes its broad physiological roles beyond bone health, underlining its significance in immune function and general health. His work provides a crucial framework for understanding the diverse functions of vitamin D, particularly its impact on immune modulation and its relevance to conditions affecting the sinonasal system.[16]

Various studies have analyzed the relationship between CT severity scores and VD3 levels in patients with CRS. Schlosser et al.[17] found a significant association between decreased VD3 levels and increased bone remodeling observed in CT scans. Zand V et al. evaluated the impact of vitamin D supplementation in patients with chronic sinusitis, noting a reduction in disease symptoms after administering 4000 IU of vitamin D for at least 4 weeks. In patients with severe inflammation, high inflammatory markers, and low vitamin D levels, these markers decreased following vitamin D supplementation.[18] Figure 1 illustrates the effects of vitamin D on the immune system (Fig. 2).[19]

Conclusion

The findings of this study suggest that oral vitamin D supplementation, as part of a comprehensive treatment regimen, may be beneficial in managing CRS in individuals with vitamin D deficiency. The improvements observed in symptomatology and sinus health highlight the importance of vitamin D in the management of this condition. Further research with larger sample sizes and longer follow-up periods is warranted to validate these findings and explore the long-term effects of vitamin D supplementation.

Clinical Significance

The clinical significance of this study lies in its potential to transform the management of CRS by introducing vitamin D supplementation as an effective therapeutic option. By highlighting the benefits of addressing vitamin D deficiency in CRS patients, the study offers a novel, cost-efficient treatment approach. Integrating vitamin D assessment and supplementation into CRS care could lead to better symptom management and improved QoL for patients. This personalized medicine approach emphasizes the importance of tailoring treatment based on individual patient characteristics, ultimately enhancing treatment effectiveness and reducing healthcare costs associated with ineffective therapies. In summary, the findings from this study provide crucial insights that could shape CRS management practices worldwide, benefiting both patients and healthcare systems.

Limitations

While your study offers valuable insights into the potential benefits of vitamin D supplementation in managing CRS without nasal polyposis, it is important to recognize certain limitations: The study included a relatively small sample size of 50 participants, which may limit the generalizability of the findings. Larger sample sizes are typically required to account for variations in demographics, disease severity, and response to treatment across different populations. Additionally, the follow-up period of four months may not be adequate to capture the long-term effects of vitamin D supplementation on CRS symptoms and sinus health. Further studies with extended follow-up durations could provide a more comprehensive understanding of the lasting impact of vitamin D supplementation on CRS. Chronic conditions like CRS often require extended observation periods to assess treatment efficacy and potential relapse.

Participants received a standardized treatment regimen, including nasal spray, antibiotics, and montelukast, in addition to

either vitamin D supplementation or placebo. While this approach reflects real-world clinical practice, it makes it challenging to isolate the specific effects of vitamin D on CRS outcomes.

Measurement tools: While the SNOT-22 questionnaire and Lund-Mackay scale are widely used tools for assessing CRS symptoms and sinus pathology, they rely on subjective reporting and radiological interpretation, which may introduce variability in measurements.

While serum vitamin D levels were measured before and after supplementation, the study did not investigate potential biomarkers of inflammation or immune response associated with CRS. Including biomarker analysis could provide additional mechanistic insights into the role of vitamin D in CRS pathogenesis and treatment.

Addressing these limitations in future research could further elucidate the potential role of vitamin D supplementation in the management of CRS without nasal polyposis and guide the development of more effective treatment strategies.

Orcid

Neha Raghuwanshi https://orcid.org/0000-0002-8820-5259

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