

Comparative Study of Recurrence of Allergic Nasal Polyposis after Administration of Vitamin D Supplementation

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Abstract

Background: Chronic rhinosinusitis (CRS) is a sinonasal mucosa inflammation. It's categorised by polyp status. But data implies that chronic rhinosinusitis without nasal polyps (CRSsNP) and CRSwNP are discrete disease entities with distinct inflammatory milieu. **The aim of the study:** to evaluate the impact of vitamin D supplementation (4000 IU/day) on the risk of nasal polyp recurrence in CRSwNP individuals who have had functional endoscopic sinus surgery (FESS). **Methods:** This randomized triple-blinded controlled research was performed on thirty cases presented in Outpatient Clinic of Benha University Hospitals with CRS during the study period of 6 months. The study duration was from September 2022 until March 2023. **Result:** there was a significant variation among the examined groups concerning Six months follow up Meltzer scores, six months follow up SNOT-22 scores and Nasal polyp recurrence. there was no significant distinction among the investigated groups as concern Demographic characteristics, Serum Vit.D level results, Preoperative Meltzer scores and Preoperative SNOT-22 scores.

Conclusion: The current investigation demonstrated the effectiveness and safety of vitamin D supplementation in preventing the recurrence of polyposis in individuals with CRSwNP who had endoscopic sinus surgery. This is the first randomized, triple-blind, placebo-controlled research to examine the effects of VD3 on reducing the recurrence rate of nasal polyposis after endoscopic sinus surgery.

Keywords: allergic nasal polyposis, vitamin D, allergy, Chronic rhinosinusitis.

Abbreviations: CRS: Chronic rhinosinusitis, CRSsNP: chronic rhinosinusitis without nasal polyps, FESS: functional endoscopic sinus surgery, SNOT-22: Sino-nasal outcome test, VD3: vitamin D 3.

Introduction

In CRSwNP, increased eosinophils are a prominent feature, and there is a correlation among the degree of mucosal eosinophilia and the severity of sinonasal illness and the chance of surgical success. (4)

Nasal polyp specimens show mostly epithelial or endothelial cell localization of immunoreactivity for Regulated upon Activation Normal T Cell Express Sequence (RANTES) and production of eosinophil cationic protein. (5) Eosinophils are mobilized into nasal polyp tissues, another function of RANTES. (6)

Perforation of the nasal septum is a potential risk when employing intranasal steroid sprays, and despite their widespread usage, the sprays don't always alleviate symptoms. (7)

In addition to its effects on calcium and bone homeostasis, vitamin D3 (VD3) also modulates the activity of monocytes, macrophages & T cells as an immunomodulatory steroid hormone. VD3 plays an important function in respiratory health and has been shown to have antiproliferative and anti-inflammatory properties as well as possible immunomodulatory activities. (8)

The innate and adaptive immune responses are activated when Toll-like receptors (TLRs) are stimulated. Rapid activation of pro-inflammatory cytokines and chemokines is the end result of intracellular signaling pathways that are activated upon recognition of pathogen-encoded TLR ligands. (9)

CRS is an inflammatory disorder of the sinonasal mucosa. Phenotype, or the presence or absence of polyps, has been utilized for decades as a means of categorization. There is evidence, however, that CRSsNP & CRSwNP are different disease entities with their own specific inflammatory milieu. (1)

Endoscopic sinus surgery (ESS) is a common treatment for CRS for people whose symptoms persist despite conventional medical treatment. The treatment of CRS has significant public health consequences because of the large number of patients who receive surgical surgery each year. (2)

The complex inflammatory etiology of CRS is driven by genetic and environmental factors as well as the microbiome and is influenced by both innate and adaptive immunity. (3)

Furthermore, fibroblasts generated from nasal polyps respond negatively to vitamin D derivatives, reducing their proliferation. (10) In contrast, a lack of VD3 is associated with a higher likelihood of upper respiratory tract infections, while elevated VD3 levels are linked to a decreased risk of asthma-related problems and a reduced need for anti-inflammatory medications. (11)

The purpose of this research was to examine the impact of Vitamin D supplementation (4000 IU/day) on the recurrence rate of nasal polyposis in CRSwNP individuals who had undergone FESS.

Patients and Methods

This randomized triple-blinded controlled trial was performed on thirty

participants presented in Outpatient Clinic of Benha University Hospitals with CRS during the study period of 6 months from August 2020 to January 2021 (Approval code: Ms 2-8-2021).

Type of study: Randomized triple-blinded controlled trial

The cases were assigned randomly by sealed envelopes into two groups: Group A: Vitamin D3 pills, 4000 IU (one daily), were given to the intervention group orally for a period of one month. and **Group B:** The placebo was administered in the same manner to the control group. For group A, patients below 15 ng/ml were received 200,000 IU vitamin D3 [IM injection] once then were given vitamin D3 pills ,4000 IU (one daily)

Inclusion criteria: Individuals with CRSwNP who satisfied the following inclusion criteria were enrolled in the research:

Having a serum VD3 level from ten to thirty ng/ml (i.e. VD3 insufficiency), being >18 years old, fulfilling diagnostic criteria for CRSwNP in accordance with American Academy of Otolaryngology-Head and Neck Surgery standards, having failed routine medical therapy, and being suggested for bilateral FESS.

Exclusion criteria: Participants who were allergic to vitamin D3, smokers, women who were pregnant or breastfeeding, and those who utilized systemic steroids for more than 10 days were not eligible to participate. Having a history or currently taking medicine for endocrine, bone, renal, or gastrointestinal illnesses; or utilizing pharmaceuticals like estrogen, digoxin, thiazide diuretics, antacids, isoniazid, or immunosuppressive drugs.

Tools: All participants provided written informed permission before participation in the study. The following were applied to all patients: Comprehensive history taking (Including Past and Present Nasal Symptoms), To properly examine the nose and to observe the reaction of the mucosa after decongestion, a general and local inspection are performed.

Laboratory investigations (CBC, Liver and kidney function, PT, PTT, INR, Total IgE and Serum level of vitamin D₃) and Radiological investigations.

Methods:

All patients were given 10 milligrams of oral prednisolone for 10 days before to surgery, in addition to 400 milligrams of cefixime daily and two puffs of fluticasone spray in each nostril once daily. Endoscopic sinus surgery was carried out by two seasoned doctors. After surgery, every individual in both groups got standard postoperative care. The statistical analyst did not know which patients belonged to which group until after the data had been decoded.

Results

This table demonstrated that regarding gender, there was no statistically significant variation among the two examined groups ($p= 0.705$). Age (year) in Intervention group varied from 32 to 51 with mean \pm SD = 40.07 ± 5.04 while in Control group the Age (year) varied from 30 to 49 with mean \pm SD = 40.93 ± 5.15 with no statistically significant variation ($p= 0.645$) among the 2 groups. also, showed that Serum Vit. D level in intervention group vary from 13 to 20 ng/mL with mean \pm SD = 16.4 ± 2.16 ng/mL, while in control

group the serum Vit. D level extended from 13 to 20 ng/mL with mean \pm SD = 16.47 ± 2.1 ng/mL with no statistically significant variance ($p= 0.932$) amongst the 2 groups. (Table 1).

This table showed that Preoperative Meltzer score in Intervention group extended from 2 to 4 with mean \pm SD = 3.13 ± 0.52 while in Control group the Preoperative Meltzer score vary from 3 to 4 with mean \pm SD = 3.47 ± 0.52 with no statistically significant distinction ($p= 0.088$) amongst the 2 groups. This table showed that Six months follow up Meltzer score in Intervention group extended from 0 to 1 with mean \pm SD = 0.27 ± 0.46 while in Control group the Six months follow up Meltzer score varied from 2 to 3 with mean \pm SD = 2.33 ± 0.49 with highly statistically significant variation among the 2 groups (Table 2).

This table showed that Preoperative SNOT-22 score in Intervention group extended from 48 to 71 with mean \pm SD = 58.6 ± 7.51 while in Control group the Preoperative SNOT-22 score vary from 48 to 75 with mean \pm SD = 61.93 ± 7.96 with no statistically significant distinction ($p= 0.248$) among the 2 groups. This table showed that Six months follow up SNOT-22 score in Intervention group extended from 12 to 18 with mean \pm SD = 15.07 ± 1.87 while in Control group the Six months follow up SNOT-22 score ranged from 33 to 52 with mean \pm SD = 44.07 ± 5.48 with highly statistically significant variance amongst the 2 groups (Table 3).

This table showed that regarding nasal polyp recurrence, there was a significant distinction among the 2 investigated groups ($p= 0.046$) (Table 4).

Table (1): Demographic characteristics amongst the study population

	Intervention group (n = 15)	Control group (n = 15)	Test of Sig.	p
Gender				
Male	10 (66.67%)	9 (60%)	$\chi^2 =$	0.705
Female	5 (33.33%)	6 (40%)	0.144	
Age (years)				
Mean \pm SD.	40.07 \pm 5.04	40.93 \pm 5.15	t = -	0.645
Median (IQR)	40 (37 - 42)	40 (38 - 44)	0.466	
Range (Min-Max)	19 (32 - 51)	19 (30 - 49)		
Serum Vit. D level (ng/mL)				
Mean \pm SD.	16.4 \pm 2.16	16.47 \pm 2.1	t = -	0.932
Median (IQR)	16 (15 - 17.5)	17 (14.5 - 18)	0.086	
Range (Min-Max)	7 (13 - 20)	7 (13 - 20)		

χ^2 : Chi- Square test

SD: standard deviation

IQR: interquartile range

t: Independent T test

p: p value for comparing between the studied groups

P-value > 0.05: Non-significant; P-value < 0.05: Significant; P-value < 0.001: Highly significant

Table (2): Preoperative, and six months follow up Meltzer scores amongst the study population

	Intervention group (n = 15)	Control group(n = 15)	Test of Sig.	p
Preoperative				
Mean ± SD.	3.13 ± 0.52	3.47 ± 0.52	t = - 1.768	0.088
Median (IQR)	3 (3 - 3)	3 (3 - 4)		
Range (Min-Max)	2 (2 - 4)	1 (3 - 4)		
Six months follow up				
Mean ± SD.	0.27 ± 0.46	2.33 ± 0.49	t = -11.964	<0.001
Median (IQR)	0 (0 - 0.5)	2 (2 - 3)		
Range (Min-Max)	1 (0 - 1)	1 (2 - 3)		

Table (3): Preoperative SNOT-22 scores among the study population

	Intervention group (n = 15)	Control group (n = 15)	Test of Sig.	p
Preoperative				
Mean ± SD.	58.6 ± 7.51	61.93 ± 7.96	t = -1.18	0.248
Median (IQR)	59 (53 - 64)	61 (57.5 - 68)		
Range (Min-Max)	23 (48 - 71)	27 (48 - 75)		
Six months follow up				
Mean ± SD.	15.07 ± 1.87	44.07 ± 5.48	t = -19.387	<0.001
Median (IQR)	15 (13.5 - 17)	44 (40.5 - 48)		
Range (Min-Max)	6 (12 - 18)	19 (33 - 52)		

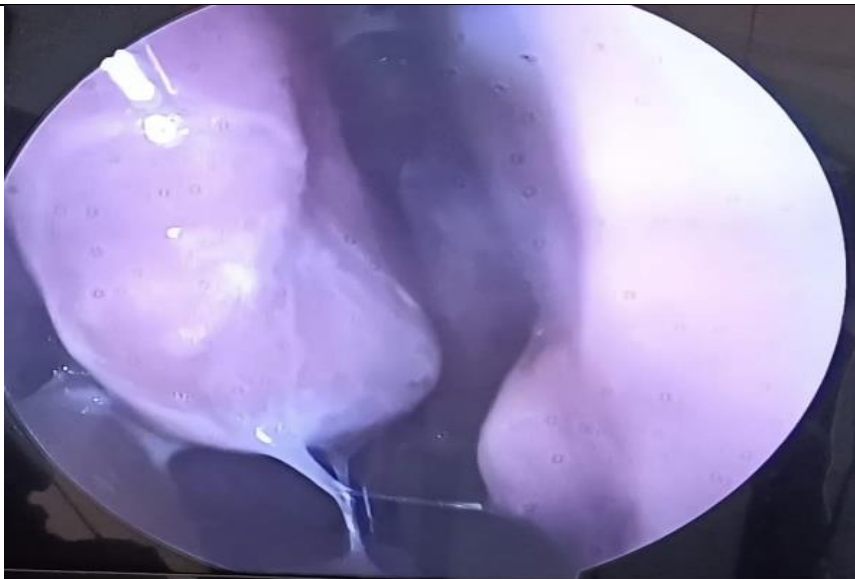
Table (4): Nasal polyp recurrence among the study population

	Intervention group (n = 15)	Control group (n = 15)	Test of Sig.	p
Nasal polyp recurrence				
- Yes	2 (13.33%)	7 (46.67%)	X2 = 3.968	0.046
- No	13 (86.67%)	8 (53.33%)		

Case presentation (Figure 1 – Figure 2).



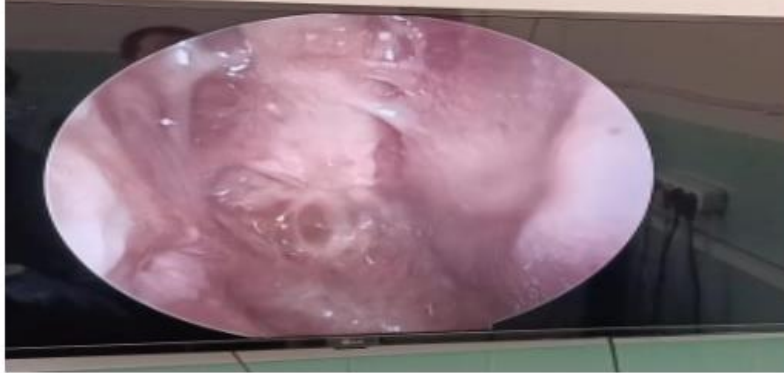
Preoperative patient with vitamin D administration.



Patient with vitamin D administration One month follow up.



Patient with vitamin D administration Three months follow up



Patient with vitamin D administration Six months follow up

Fig. 1: patients with vitamin D administration.



Preoperative patient without vitamin D administration



**Patient without vitamin D administration
One month follow up**

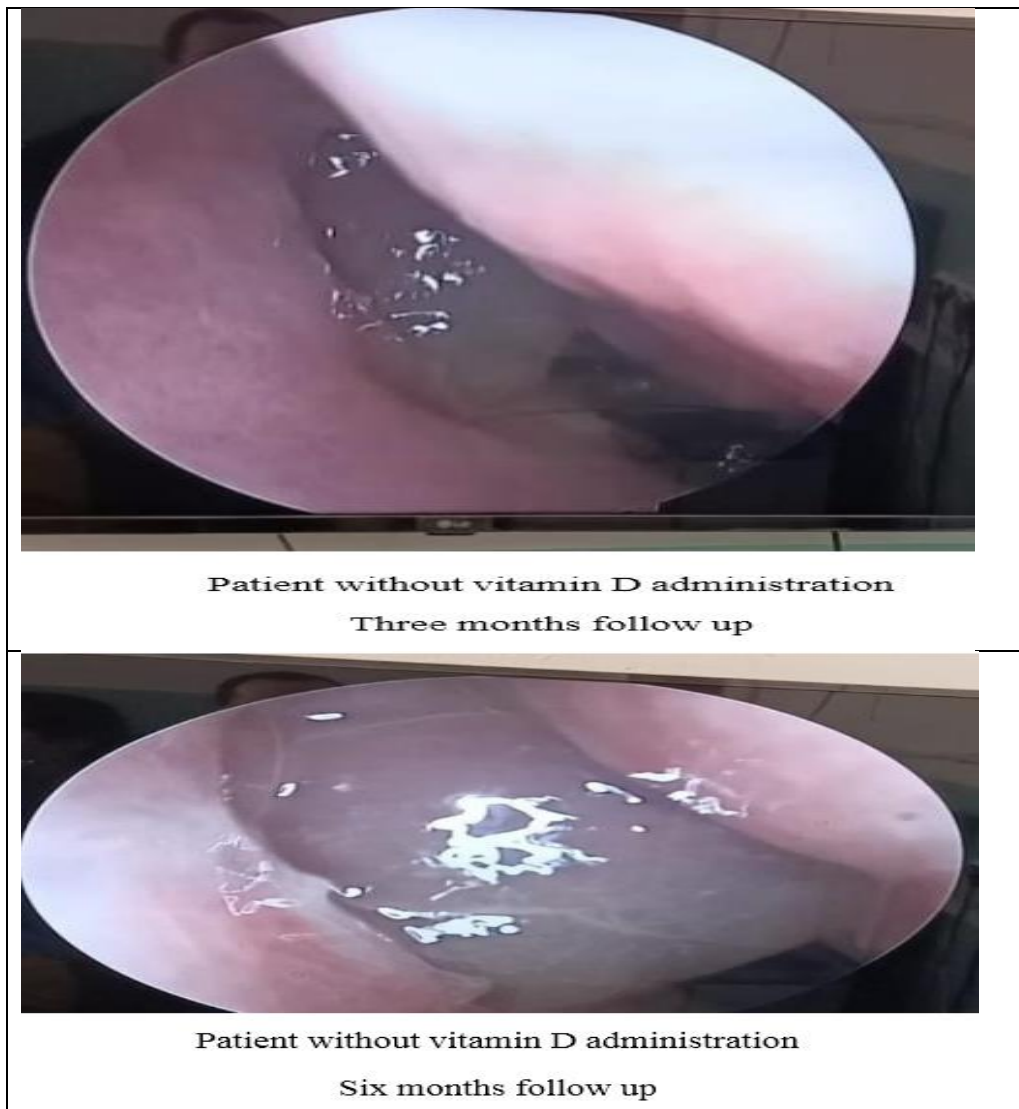


Fig. 2: patients without Vitamin D administration.

Discussion

Mucosal inflammation in the nose and sinuses that lasts longer than three months characterizes a frequent disorder known as CRS, which is further classified as either CRSwNP or CRSsNP (12).

Individuals with CRS who continue to experience symptoms despite receiving proper medication treatments may undergo functional sinus surgery. The treatment of CRS has significant public health consequences due to the large

number of people who receive surgical therapy each year (13).

The main results as follows:

Regarding gender, there was no statistically significant distinction amongst the two examined groups ($p=0.705$). Age (year) in Intervention group extended from 32 to 51 with mean \pm SD = 40.07 ± 5.04 while in Control group the age (year) varied from 30 to 49 with mean \pm SD = 40.93 ± 5.15 with no

statistically significant variation ($p=0.645$) amongst the 2 groups.

Our results supported with Hashemian et al. who want to find out if taking VD3 orally would prevent polyps from returning following FESS. 46 participants were involved in the research. Twenty-two patients were given vitamin D (4000 IU) and twenty-four were given a placebo, for a total of 46 cases. individuals in the VD3 group had a mean age of 41.35 ± 13.58 years, whereas those in the placebo group had a mean age of 42.5 ± 13.79 years (14).

Our results were supported by others who sought to assess the link among vitamin D levels in the blood of individuals suffering from CRS and nasal polyps and the severity of their condition. There were 88 participants in the research, with ages varying from 18 to 72 (mean = 43). In terms of age and gender, there were not any significant variations among the three groups (15).

Meltzer scores among the study population. Preoperative Meltzer score in Intervention group vary from 2 to 4 with mean \pm SD = 3.13 ± 0.52 while in Control group the Preoperative Meltzer score vary from 3 to 4 with mean \pm SD = 3.47 ± 0.52 with no statistically significant variance ($p=0.088$) amongst the 2 groups (15).

Six months follow up Meltzer score in Intervention group extended from 0 to 1 with mean \pm SD = 0.27 ± 0.46 while in Control group the Six months follow up Meltzer score extended from 2 to 3 with mean \pm SD = 2.33 ± 0.49 with highly statistically significant distinction amongst the two groups.

Our results supported with Abdelaal et al. who wanted to see if vitamin D3 may help individuals with vitamin D3

deficiency reduce the size and severity of their sino-nasal polyps. Forty-six people with CRS and nasal polyps & vitamin D3 insufficiency [low levels of vitamin D3 <30 ng/ml] participated in their research. In the first group, 22 cases received vitamin D3 [200,000 IU] intramuscularly [IM], whereas the other group, consisting of 20 cases, received a placebo in the same fashion. Endoscopic Meltzer grading score and CT scan were used to compare the two groups before and after 3 months of vitamin D3 and placebo treatment. The severity of sino-nasal polyps was shown to be significantly reduced in the vitamin D3 group when compared to the placebo group, with 68.3 percent of the vitamin D3 group demonstrating improvement against 20percent of the placebo group (16).

SNOT-22 scores among the study population. Preoperative SNOT-22 score in Intervention group ranged from 48 to 71 while in Control group the Preoperative SNOT-22 score ranged from 48 to 75 with no statistically significant variance ($p=0.248$) amongst the 2 groups.

Six months follow up SNOT-22 score in Intervention group ranged from 12 to 18 while in Control group the Six months follow up SNOT-22 score ranged from 33 to 52 with highly statistically significant variation amongst the two groups.

Ghazavi et al. who sought to see if VD supplementation may help stop CRSwNP from returning following endoscopic treatment. Patients with CRSwNP and a vitamin D deficiency who were eligible for endoscopic sinus surgery were split into two distinct categories for the clinical trial. All

patients had endoscopic sinus surgery, and then the cases received VD supplementation (50,000 IU) once weekly for 8 weeks whereas the controls received no additional treatment. Sino-nasal outcome test (SNOT-22) and recurrence of NP were utilized to estimate the severity of symptoms before and after treatment. Their findings revealed that the average SNOT-22 change was greater in the case group than in the control group (36.03 ± 10.71 vs. 29.90 ± 11.99 ; $P = 0.041$). (17)

On contrast with our results Hashemian et al. who reported that Prior to treatment, there were insignificant variations in SNOT-22 ($P=0.53$) or Meltzer ($P=0.165$) scores among each of the groups concerning the degree of Sino nasal polyposis (14).

Nasal polyp recurrence amongst the study population. Regarding Nasal polyp recurrence, there was a significant variation among the two examined groups ($p= 0.046$).

Ghazavi et al. who reported that the recurrence rate of NP was lower in cases than in controls, suggesting that VD supplementation substantially lessens the likelihood of NP (odd ratio [95% confidence interval]: 0.298 [0.099-0.900]; $P = 0.032$) (17).

Conclusion

Recent research has shown that vitamin D supplementation is an effective and safe method of lowering the risk of polyp recurrence in individuals with CRSwNP who have had endoscopic sinus surgery.

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