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ORIGINAL ARTICLE

The effect of vitamin D on the recurrence of nasal polyposis and the severity of chronic rhinosinusitis after functional endoscopic sinus surgery

Wpływ witaminy D na nawrotowość polipowatości nosa po endoskopowej operacji zatok przynosowych

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ABSTRACT:

Introduction: It is believed that a majority of cases of chronic rhinosinusitis with nasal polyposis (CRSwNP) are related to vitamin D levels.

Aim: The aim of this study was to evaluate the efficiency of vitamin D supplementation in reducing the recurrence of nasal polyps and the severity of chronic sinusitis following functional endoscopic sinus surgery (FESS).

Methods: A prospective, randomized study was conducted in a cohort of 88 adult patients with CRSwNP and vitamin D deficiency treated with FESS and randomized into 2 groups: group A (44 patients), which received vitamin D supplementation, and group B (44), which received a placebo. The severity of symptoms at baseline and 6 months after the surgery, as well as the recurrence status, were assessed using the sinonasal outcome test (SNOT 22), Meltzer nasal endoscopy grading, and Lund Mackay computed tomography (CT) presentation scoring system. Vitamin D levels were also measured at both of the above-mentioned time points.

Results: The average recurrence rate of nasal polyposis was 12.78% in patients aged 18–40, 23.56% in patients aged 41–60, and 34.17% in patients above the age of 60. The average preoperative scores obtained using the SNOT-22 questionnaires were 68.9 in Group A and 53.7 in Group B, while the postoperative scores were 17.4 and 18.6, respectively. The postoperative severity of symptoms was estimated at 14.32 ±8.61 in group A as compared to 28.73 ±15.69 in group B. The Meltzer scores of endoscopic CRSwNP findings were 21.34% in group A and 54.76% in group B. The Lund-Mackay scores were 3.51 ±2.82 in group A and 2.14 ±2.67 in group B. Vitamin D supplementation reduced the recurrence of nasal polyposis (OR [95% CI]: 0.197 [0.086–0.824]; p = 0.032).

Conclusions: Vitamin D3 supplementation was effective in reducing the recurrence of nasal polyposis as well as the severity of symptoms of chronic rhinosinusitis.

KEYWORDS: chronic rhinosinusitis with nasal polyposis, functional endoscopic sinus surgery, vitamin D3

STRESZCZENIE:

Wprowadzenie: Uważa się, że większość przypadków przewlekłego zapalenia błony śluzowej nosa i zatok przynosowych z polipowatością nosa (PZZPzPN) ma związek z poziomem witaminy D.

Cel: Celem niniejszej pracy była ocena skuteczności suplementacji witaminy D w zmniejszaniu nawrotowości polipów nosa, a także w zmniejszaniu nasilenia przewlekłego zapalenia zatok przynosowych po endoskopowej operacji zatok przynosowych (FESS).

Metody: Przeprowadzono prospektywne randomizowane badanie z udziałem 88 dorosłych pacjentów z PZZPzPN i niedoborem witaminy D leczonych FESS podzielonych na 2 grupy: grupę A (44 pacjentów), w której stosowano suplementację witaminy D oraz grupę B (44), której podawano placebo. Przed operacją oraz 6 miesięcy po jej przeprowadzeniu dokonywano oceny stopnia nasilenia objawów i nawrotowość polipowatości oceniano przy użyciu testu oceny dolegliwości nosowo zatokowych (SNOT 22), klinicznej klasyfikacji PZZP endoskopii nosa w ocenie endoskopowej wg Meltzera i obrazów tomografii komputerowej (TK) z wykorzystaniem skali punktowej Lund Mackaya. W obu wymienionych punktach czasowych mierzono również poziom witaminy D.

Wyniki: Średnia częstość nawrotów polipowatości nosa wynosiła w grupie wiekowej 18–40 lat 12,78%, w grupie wiekowej 41–60 lat – 23,56%, natomiast w grupie wiekowej > 60 lat – 34,17%. Średnie przedoperacyjne wyniki ocen z użyciem kwestionariusza SNOT-22 wyniosły 68,9 punktów w grupie A i 53,7 punktów w grupie B, podczas gdy wyniki pooperacyjne wyniosły odpowiednio 17,4 i 18,6. Pooperacyjne nasilenie objawów w grupie A oceniono na 14,32 ±8,61 odchyleń standardowych (SD), natomiast w grupie B na 28,73 ±15,69 SD. Endoskopowa ocena PZZP metodą Meltzera dała wynik 21,34% w grupie A i 54,76% w grupie B. Liczba punktów w skali Lund-Mackaya wynosiła 3,51 ±2,82 SD w grupie A i 2,14 ±2,67 SD w grupie B. Suplementacja witaminą D zmniejsza nawrotowość polipowatości nosa (iloraz szans [OR] [95% CI]: 0,197 [0,086–0,824]; p = 0,032).

Wnioski: Suplementacja witaminą D3 okazała się skuteczna w zmniejszaniu nawrotów polipowatości nosa, a także nasilenia objawów PZZP.

SŁOWA KLUCZOWE: endoskopowa operacja zatok przynosowych, przewlekłe zapalenie błony śluzowej nosa i zatok z polipowatością nosa, witamina D3

ABBREVIATIONS

BMI – body mass index
CRP – C-reactive protein
CRS – chronic rhinosinusitis
CRSsNP – chronic rhinosinusitis without nasal polyposis
CRSwNP – chronic rhinosinusitis with nasal polyposis
CT – computed tomography
EPOS 2020 – European Position Paper on Rhinosinusitis and Nasal Polyps 2020
FESS – functional endoscopic sinus surgery
IL-5 – interleukin-5
IL-6 – interleukin-6
INF-γ – interferon-gamma
MMPs – matrix metalloproteinases
MRI – magnetic resonance imaging
OMC – ostiomeatal complex
OR – odds ratio
SD – standard deviations
SNOT-22 – sinonasal outcome test
TNF-α – tumor necrosis factor α

INTRODUCTION

Chronic rhinosinusitis (CRS) is defined as chronic inflammation of the epithelial lining of the nose and paranasal sinuses lasting longer than 3 months; CRS is clinically classified into CRS with nasal polyposis (CRSwNP) and CRS without nasal polyposis (CRSsNP). According to various studies, the prevalence of the condition ranges from 12 to 15%. CRS is a disorder with multifactorial pathophysiology and unknown etiology as well as a significant burden to the health care systems [1, 2].

According to the EPOS 2020 guidelines, CRS is diagnosed on the basis of at least 2 criteria from the group that includes the major criteria, i.e., nasal congestion with nasal discharge (anterior and/or posterior) and headache, and the minor criteria, i.e., pain or pressure in the area of the nose, eyes and forehead, a reduction or complete loss of smell and taste. Endoscopic evaluation reveals the presence of nasal polyps and/or mucopurulent nasal discharge (particularly from the middle meatus) and/or mucosal edema (particularly within the middle meatus) [3, 4].

CRS is a significant burden to health care systems. The pathophysiology of the condition is very complex and includes the impairment of the immune system with the infection by pathogenic microorganisms and changes to the upper respiratory microbiota, as well as the presence of autoimmune disorders such as Sjögren's syndrome and co-occurrence of environmental factors like tobacco smoke and/or elevated concentrations of pollutants in the inhaled air [5].

Cholecalciferol (vitamin D3) is a lipid-soluble secosteroid hormone that modulates calcium and bone homeostasis and exerts immunoregulatory effects on monocyte-macrophages and T cells. It also has anti-infective and anti-inflammatory effects and plays an important role in respiration (passive correlation with upper respiratory tract infections). In addition, cholecalciferol derivatives inhibit the proliferation of fibroblasts derived from nasal polyps [6, 7].

Recently, the role of vitamin D in the development of CRSwNP drew considerable attention of the research community. This is due to its immunomodulatory effects and its essential role in controlling the number of immune cells, including T cells and dendritic cells, as well as in reducing inflammation through a number of mechanisms that switch the Th1/Th17 response to the minimally inflammatory Th2/Treg response. Vitamin D also reduces the *in vitro* release of a number of pro-inflammatory markers, such as tumor necrosis factor α (TNF-α) and interferon-gamma (INF-γ) [8].

Vitamin D deficiency is associated with lowered immunity and increased predisposition to infections; in turn, supplementation with vitamin D may help reduce the effects of inflammation [9].

Vitamin D deficiency has been found to affect the pathogenesis of CRS and the evolution of nasal polyps, whereas administration of vitamin D in high therapeutic doses reduces the size of polyps, improves the symptoms, and restores the normal condition of the nasal mucosa. This finding, on the one hand, makes it possible to develop more effective therapies for nasal polyposis while, on the other hand, providing an argument for the use of vitamin D in postoperative supplementation following functional endoscopic sinus surgery (FESS) to avoid polyp recurrence [10].

The ability to eliminate inflammation in the course of FESS raises the importance of vitamin D, which lowers the levels of inflammatory markers and improves the patients' quality of life. Numerous

studies suggest that vitamin D3 acts as a steroid hormone, exerting anti-inflammatory effects and playing an important role in adjusting the function of dendritic cells, facilitating discontinuation of the production of cytokines and preventing the differentiation of immune cells, thus stopping the progression of the disease [4, 11].

The initial treatment of CRSwNP is aimed at reducing the underlying inflammation and facilitating sinus clearance by means of antibiotics, topical and systemic steroids, and nasal saline irrigations. However, the results of this treatment are frequently disappointing, while the recurrence rates are high; an additional condition for successful treatment is the management of the underlying pathological processes, such as environmental allergies. Unfortunately, some patients do not comply with the recommendations of non-surgical treatment of CRS, resulting in that improving symptoms and increasing quality of life requires endoscopic sinus surgery, which, in turn, has major public health implications [12].

Recently, vitamin D3 deficiency was found to be associated with the presence of nasal polyps in CRS patients [13].

AIM

The aim of this study was to evaluate the efficacy of vitamin D3 supplementation in reducing the recurrence of nasal polyposis following FESS, as well as the possible effect of vitamin D3 levels on the severity of polyp recurrence as assessed by serum vitamin D levels, the Meltzer endoscopic polyp grading score, the SNOT-22 questionnaire results and the results of the Lund-Mackay classification of CT presentation. The potential impact of vitamin D3 supplementation on improved clinical outcomes was also investigated.

METHODS

The study followed a prospective, randomized design. Ethical approval was obtained from the institutional review board of the Mustansiriyah University (protocol no. 183, dated 06/01/2024); written participation consents were obtained from all included subjects. The eligible patients (N = 88) with CRSwNP and vitamin D deficiency, aged ≥ 18 years and subjected to a FESS procedure using 0° and 30° rigid endoscopes (Karl Stores, Germany) with camera connected to the video screen, were randomized into group A (44 patients) to receive oral vitamin D supplementation at a dose of 50,000 IU or group B (44 patients) to receive shape- and color-matched placebo tablets in a double-blind fashion.

Hypothesis

Before and 6 months after surgery, the severity of symptoms and recurrence of polyposis were assessed using the SNOT22 questionnaire, the Meltzer nasal endoscopy grading score, and the Lund-Mackay scale assessment of CT scans. Vitamin D levels were also measured at both of the aforementioned time points.

All patients were examined by an ENT surgery specialist, who confirmed the diagnosis on the basis of nasal endoscopy and sinonasal CT scan results. The sample size required to achieve the power of 80%, with a 95% confidence interval for the polyp recurrence rate in vitamin D-deficient patients at 0.3 and the error rate of 0.3, amounted to 35 individuals with the assumption of simple randomization.

The inclusion criteria included the age of ≥ 18 years, the diagnosis of CRSwNP as per the American Academy of Otolaryngology-Head and Neck Surgery criteria, inefficacy of previous medical management, vitamin D3 level of < 20 ng/mL, and eligibility for bilateral FESS.

The exclusion criteria included age of < 18 years, nasal tumors such as inverted papilloma, antrochoanal polyp, hemangioma or cancer, history of metabolic bone disease, allergy to vitamin D3, pregnancy or breastfeeding, recent history of steroid use lasting more than 10 days, past or current use of medications for endocrine, bone, kidney or gastrointestinal diseases, as well as the use of estrogen, digoxin, isoniazide, or immunosuppressive drugs, other systemic diseases (comorbid underlying diseases such as asthma, allergic rhinitis, and other immune conditions were acceptable in CRSwNP patients), history of surgery, vitamin D3 supplementation, as well as inability/unwillingness to comply with the treatment and attend regular follow-up visits.

All participants were assigned to either of the 2 groups in a block randomization procedure, which involved assigning approximately the same number of patients to each group by randomly assigning a block of patients to one group and assigning a second block to the other group. As a result, the study groups were similar in size, as well as in terms of baseline parameters such as the SNOT-22 score, the LundMackay score, the Meltzer nasal endoscopic grade, and serum vitamin D3 level, which were recorded and compared between the 2 groups before and after the surgery.

The sinonasal outcome test (SNOT-22)

SNOT-22 [14] is widely utilized for assessing the quality of life of patients with CRSwNP. It is used to assess the severity of symptoms, as well as the impact of sinonasal problems on everyday life of patients.

SNOT-22 provides a validated, 22-item outcome measurement tool suitable for CRS. The possible score range is 0–110; a higher score indicates poorer patient functioning or greater severity of symptoms. The items are scored as follows: 0 = "no problem"; 1 = "very mild problem"; 2 = "mild problem"; 3 = "moderate problem"; 4 = "severe problem"; and 5 = "problem as bad as it can be". The eligible patients were asked to complete the SNOT-22 questionnaire at baseline on the day before FESS as well as 6 months after the procedure. A total of 5 domains were assessed, including nasal symptoms, extra-nasal symptoms, ear/face symptoms, emotional problems, and sleep disturbances (Tab. I.).

The Lund-Mackay computed tomography presentation score

The acquired CT images were evaluated using the Lund-Mackay [15] scoring system, each sinus being assessed as 0 = no opacification, 1 = partial opacification, or 2 = complete opacification, and

Tab. I. SNOT-22 score.

	NO PROBLEM	VERY MILD PROBLEM	MILD PROBLEM	MODERATE PROBLEM	SEVERE PROBLEM	PROBLEM AS BAD AS IT CAN BE	MOST IMPORTANT ITEMS
1. Need to blow the nose	0	1	2	3	4	5	[]
2. Sneezing	0	1	2	3	4	5	[]
3. Runny nose	0	1	2	3	4	5	[]
4. Nasal obstruction	0	1	2	3	4	5	[]
5. Loss of smell or taste	0	1	2	3	4	5	[]
6. Cough	0	1	2	3	4	5	[]
7. Post-nasal discharge	0	1	2	3	4	5	[]
8. Thick nasal discharge	0	1	2	3	4	5	[]
9. Ear fullness	0	1	2	3	4	5	[]
10. Dizziness	0	1	2	3	4	5	[]
11. Ear pain	0	1	2	3	4	5	[]
12. Facial pain/pressure	0	1	2	3	4	5	[]
13. Difficulty falling asleep	0	1	2	3	4	5	[]
14. Waking up at night	0	1	2	3	4	5	[]
15. Lack of a good night's sleep	0	1	2	3	4	5	[]
16. Waking up tired	0	1	2	3	4	5	[]
17. Fatigue	0	1	2	3	4	5	[]
18. Reduced productivity	0	1	2	3	4	5	[]
19. Reduced concentration	0	1	2	3	4	5	[]
20. Frustrated/restless/irritable	0	1	2	3	4	5	[]
21. Sad	0	1	2	3	4	5	[]
22. Embarrassed	0	1	2	3	4	5	[]
Total (for each column):							
Total score (for all columns)							

the ostiomeatal complex (OMC) being assessed as 0 (normal) or 2 (obstructed). The sinuses on the left and the right sides of the face were evaluated separately for the total score, ranging from 0 to 24.

Meltzer nasal endoscopy grading

The Meltzer nasal endoscopy grading [16] is a validated radiological scoring system based on CT scans and intraoperative confirmation. The results are graded as grade 0 = no nasal polyps, grade 1 = small polyps confined within the middle meatus, grade 2 = polyps reaching below the lower border of the middle turbinate, grade 3 = large polyps extending to the lower border of the lower turbinate, and grade 4 = large polyps causing complete nasal obstruction. The total sum score for the right and the left nasal cavities ranges from 0 to 8.

Serum vitamin D3 levels

According to the guidelines from the endocrinology community, serum vitamin D levels [17] were considered normal for values > 30 ng/mL; deficiency was defined as levels < 20 ng/mL, and insufficiency was defined as levels within the range of 21–29 ng/mL. Comparisons between the 2 groups at follow-up were based on the results of Meltzer nasal endoscopy grading, the SNOT-22 questionnaire, the Lund-Mackay scoring of CT images, and serum vitamin D3 levels. The pre-operative and post-operative results were compared.

Statistical analysis

Statistical analysis was carried out using the SPSS software (version 25; SPSS Inc., Chicago, Illinois, US); variables were expressed using means, standard deviations (SD), frequencies, and percentages (%). Differences in quantitative variables between the study groups were assessed using the Student's ttest for independent samples, while differences in pre- and post-operative values of quantitative variables within the groups were assessed using the Student's ttest for dependent samples. Gender differences and differences in the recurrence of nasal polyposis between the 2 groups were assessed using the chisquared test with odds ratio (OR) calculations. Statistical significance was defined as $p < 0.05$.

Tab. II. SNOT-22 scores across the 2 groups.

SNOT-22 SCORE	GROUP A		GROUP B		*P*
	AVERAGE	SD	AVERAGE	SD	
Pre-operative	68.93	14.75	53.74	16.82	0.67
Post-operative at 1 month	45.72	10.43	34.36	10.54	< 0.043*
Post-operative at 3 months	21.95	09.93	31.20	09.21	< 0.021*
Post-operative at 6 months	17.43	01.12	26.18	06.78	0.013

*Statistically significant result.

Tab. III. Meltzer endoscopic scores across the 2 groups.

MELTZER NASAL ENDOSCOPY SCORE	GROUP A		GROUP B		*P*
	AVERAGE	SD	AVERAGE	SD	
Pre-operative	78.92	13.67	81.76	16.48	0.74
Post-operative at 1 month	41.73	10.43	79.87	10.54	0.036
Post-operative at 3 months	29.85	09.32	68.20	09.36	0.0478
Post-operative at 6 months	21.34	0.17	54.76	0.39	0.019

*Statistically significant result.

RESULTS

A total of 88 eligible patients with CRSwNP and vitamin D deficiency, aged ≥18 years, and subjected to FESS, were included in the study. Group A (44 patients) consisted of 23 men (52.27%) and 21 women (47.73%), with a mean age of 41.57 ±1.89 years. Group B (44 patients) consisted of 24 men (54.54%) and 20 women (45.46%), with a mean age of 39.62 ±1.87 years; no statistical difference was observed between the groups (p = 0.065).

In relation to age, patients with vitamin D deficiency (< 20 ng/ml) were characterized by a significantly higher rate of disease recurrence (47.36%); however, that rate was reduced as the result of vitamin D supplementation to reach 12.78% in patients aged 18 through 40, 23.56% in patients aged 41 through 60, and 34.17 in elderly patients (> 60 years). The differences were statistically significant. Vitamin D supplementation sustainably reduced the incidence of polyp recurrence following FESS procedures by regulating inflammation and the immune response.

The preoperative SNOT-22 scores were 68.93 ±0.15 in group A and 53.74 ±0.62 in group B; there was no statistically significant difference between the 2 groups (p = 0.67). Six months after the surgery, a significant reduction in scores was observed, with a significant difference in both groups after surgery as compared to baseline values, and with patients in group A presenting with lower SNOT-22 scores than patients in group B (p = 0.013). As shown in Tab. II., the study groups did not significantly differ in terms of preoperative Meltzer scores, with a significant difference being observed after the procedure: at 6 months, the polyp recurrence rate was lower in group A (21.34%) than in group B (54.76%) (Tab. III.).

The symptom severity was significantly lower in group A, with the mean score of 14.32 ±8.61 compared to 28.73 ±15.69 in group B (p = 0.024). Extending the clinical criteria to include nasal endoscopy grading increased the precision of CRS diagnosis (sensitivity of 45.72% and specificity of 93.87%).

With regard to the Lund-Mackay scoring of CT images, no significant difference was observed between the 2 groups in the preoperative results while a significant improvement in the severity of nasal polyposis was achieved as a result of the surgery: for grade 1, 100% of polyps resolved to the undetectability level and sinus clearance was achieved; for grade 2, grade 3, and grade 4, the percentage improvement rates were 76.41%, 52.68%, and 47.32%, respectively. The Lund-Mackay scoring system is frequently used in clinical trials with improvements in disease severity and polyp recurrence being assessed by means of endoscopy. The average Lund-Mackay scores and the corresponding SD are given in Tab. IV.

Vitamin D supplementation can statistically significantly reduce the risk of the recurrence of nasal polyposis (OR [95% CI]: 0.197 [0.086–0.824], p = 0.032).

DISCUSSION

FESS is the most efficient treatment of CRSwNP; however, it is impossible to eradicate all microscopic inflammatory pathologies, and consequently, residual inflammation within the nose and sinuses contributes to the recurrence of polyps. Vitamin D3 has been found to be safe and effective in preventing recurrence of nasal polyps after FESS [2].

In the present study, the parameters associated with the recurrence of nasal polyps after FESS included patient age, the SNOT-22 score, the Meltzer endoscopy grading score, the Lund-Mackay score, and serum vitamin D levels.

Gender of patients in studies associated with nasal polyp recurrence after functional endoscopic sinus surgery

Gender is a frequent subject of research as a potential factor influencing surgical outcomes due to its possible impact on the immune response, inflammatory pathways, and pathology of nasal polyps.

Tab. IV. Lund-Mackay scoring of CT images.

CT-BASED SEVERITY	AVERAGE (SD)		*P*
	GROUP A	GROUP B	
Pre-operative	18.43 ±1.76 SD	17.62 ±4.52 SD	0.061
Post-operative at 1 month	6.75 ±3.28 SD	15.23 ±3.67 SD	0.045
Post-operative at 3 months	4.38 ±1.27 SD	14.61 ±2.53 SD	0.037
Post-operative at 6 months	3.51 ±2.82 SD	2.14 ±2.67 SD	0.011

*Statistically significant result.

In this study, a slight male predominance was observed; this observation appears to be consistent with the results of several other studies that have discussed the role of gender and its relationship to recurrent nasal polyposis; for example, Brescia et al. [18] showed that the male gender is a risk factor for the development and recurrence of nasal polyposis after surgery. This is thought to be related to the higher incidence of CRSwNP in men, in addition to the differences in immune response. Due to the differences in immune response, hormonal factors, and genetic predisposition, males are at a significantly higher risk of the recurrence of nasal polyposis after FESS; the results of the cited study indicated that testosterone levels and the immune system in men may contribute to a more aggressive course of inflammation and polyp regrowth.

On the other hand, some studies, such as the one by Ryan et al. [19], showed lower polyp recurrence rates following the FESS procedures, with a higher percentage of women showing complete postoperative resolution of symptoms. The researchers noted that estrogen may have anti-inflammatory effects that benefit recovery after surgery. Estrogen may be involved in modulating the immune response and inflammation of the nasal mucosa, leading to better healing and reduced recurrence.

Some studies focused on potential hormonal mechanisms influencing the differences in nasal polyp recurrence after FESS between men and women, suggesting that estrogen, which is thought to modulate the immune response, makes women potentially less susceptible to severe polyps and polyp recurrence, while testosterone, which is believed to promote a pro-inflammatory immune response, may contribute to polyp persistence and recurrence as well as affect the inflammatory response and tissue regeneration [20].

Statistically insignificant differences in relation to gender were also observed in our study ($p = 0.065$). With the mean age in the fourth decade of life, these results were almost similar to those obtained in other studies, such as that by Kazem et al. [21], who had found no statistically significant differences in gender between the 2 study groups ($p = 0.705$).

A direct inverse relationship between the serum vitamin D levels and the recurrence of nasal polyposis was found in the present study, suggesting that vitamin D supplementation was instrumental in this reduction. Hashemian et al. [2] attempted to assess the relationship between blood vitamin D levels in CRSwNP patients and the recurrence of nasal polyposis. According to their findings, vitamin D prevents polyp recurrence after FESS.

With regard to the Meltzer endoscopy grading, statistically significant differences were obtained to show that the severity of nasal polyps was significantly reduced in the vitamin D3 supplementation group as compared to the placebo group. These results are supported by findings from other studies, such as those by Kazem et al. [21] or Abdelaal et al. [22]. In conclusion, vitamin D3 supplementation was found to be potentially helpful in the reduction of the size of nasopharyngeal polyps in individuals with vitamin D3 deficiency.

The SNOT-22 questionnaire results as obtained in the present study are indicative of a significant reduction in the SNOT22 scores in both groups, with group A scores being significantly lower than those in group B ($p = 0.013$). These observations were consistent with those obtained by Kazem et al. [21], Ghazavi et al. [7], and Jiao et al. [23], who found that supplementation with vitamin D as a compound with anti-inflammatory and antioxidant properties leads to a reduction in the rate of recurrence of nasal polyposis, as well as to an improvement in CRSwNP symptoms by promoting healing after FESS.

The relationship between the age and the recurrence of nasal polyposis after FESS in the context of vitamin D supplementation, as observed in this study, had also been the subject of several other studies. For example, Ali et al. [24] found that vitamin D levels play an important role in preventing polyp recurrence, especially in older patients, who tend to have lower baseline vitamin D levels as compared to younger adults (< 40 years old), who generally have higher baseline vitamin D levels and thus lower rates of nasal polyp recurrence after FESS. The researchers observed that vitamin D supplementation was associated with a noticeable reduction in the recurrence of nasal polyps in the age group in question. Similarly, Brociek-Piłczyńska et al. [25] and Pantazidou et al. [26] reported that age and vitamin D levels were strongly correlated with polyp recurrence after FESS. Those with vitamin D deficiency had the highest risk of recurrence, while vitamin D supplementation reduced this risk, especially in the elderly.

Zand et al. [27] reported that vitamin D plays an important role in regulating the immune response and inflammation by affecting the production of pro-inflammatory cytokines that are involved in the pathogenesis of nasal polyps; as a result, vitamin D supplementation significantly reduces the polyp recurrence rate.

The results of the studies cited above highlight the significant role of vitamin D in reducing the recurrence of nasal polyps, with the age of the patients being an important factor influencing the results. Vitamin D supplementation may therefore potentially reduce the rate of recurrence after FESS by modulating inflammation and the immune response as observed in this study.

Several studies focused on measuring serum vitamin D levels and their association with nasal polyp recurrence after FESS. In a number of studies, vitamin D deficiency (< 20 ng/mL) was described as strongly associated with higher rates of the recurrence of nasal polyposis after FESS. For example, in the studies by Hashemian et al. [2], Li et al. [11], and Schlosser et al. [28], patients with vitamin D deficiency presented with significantly higher rates of recurrent nasal polyposis compared to those with normal vitamin D levels. Thus, as suggested by the authors of the aforementioned papers, severe vitamin D deficiency contributes to a higher recurrence

rate, and therefore vitamin D supplementation before and after FESS may lead to a reduction in the recurrence of nasal polyps, especially in vitamin D-deficient patients, by preventing the formation of new polyps after surgery.

Regarding the results of the SNOT-22 questionnaire surveys, as also used in this study, numerous studies are available that evaluate the effect of vitamin D levels on SNOT-22 scores in individuals with recurrent nasal polyposis after FESS. Accordingly, Cho et al. [29] investigated the effect of serum vitamin D levels on SNOT-22 scores and recurrence of nasal polyposis after FESS in a cohort of 120 patients with CRSwNP to find that the preoperative SNOT-22 scores were significantly higher, reflecting poorer quality of life due to the disease symptoms, in patients with severe vitamin D deficiency. In contrast, with regard to postoperative outcomes, SNOT-22 scores remained relatively high after surgery in the vitamin D-deficient group, with a significant rate of polyp recurrence (45% at 12 months). The observed improvement in SNOT-22 results was modest, in contrast to the significant improvement observed in the group with sufficient vitamin D levels. In this group, the SNOT-22 score after FESS was reduced by 35%, and a lower recurrence rate (20%) was observed. The authors concluded that adequate preoperative vitamin D levels were associated with better postoperative outcomes, as reflected in better results obtained using the SNOT-22 questionnaire.

Bavi et al. [30] studied the SNOT-22 scores in patients with severe vitamin D deficiency, concluding that minimum serum vitamin D levels were associated with high SNOT-22 scores and thus associated with poor symptom control and quality of life ($p < 0.001$, $r = -0.49$). Ghazavi et al. [7] observed a greater change in mean SNOT-22 scores in the patient group compared to the control group (36.03 ±10.71 *vs.* 29.90 ±11.99, $p = 0.041$), which indicated a significant reduction in the SNOT-22 score in those who had received vitamin D supplementation compared to the control group (without supplementation). The authors found that vitamin D supplementation after surgery led to significant improvements in the quality of life as assessed by SNOT-22 scores, confirming the role of vitamin D in improving outcomes after FESS.

In turn, Al-Morsy et al. [31] found that vitamin D was effective in reducing the recurrence of nasal polyposis after its endoscopic removal, with better control of post-operative symptoms and improved quality of life as indicated by a greater decrease in SNOT-22 scores between the pre- and post-operative timepoints.

The aforementioned studies provide evidence that supports the results obtained in this study, namely, that adequate vitamin D levels can significantly improve SNOT-22 scores, as patients with vitamin D deficiency were consistently found, both preoperatively and postoperatively, to have higher SNOT-22 scores (indicating poorer quality of life). Vitamin D supplementation in patients with vitamin D deficiency was associated with significant improvements in postoperative SNOT-22 scores, reflecting better patient outcomes and recovery, thus improving the quality of life of patients having undergone FESS.

The results of the Meltzer nasal endoscopy grading as obtained in the present study were also observed in several other studies that had evaluated the results of nasal endoscopy in relation to serum vitamin D levels and the recurrence of nasal polyps after FESS. Vitamin D deficiency was found to be associated with more severe and extensive nasal polyposis and more severe inflammation, as also observed in the present study; patients with the above symptoms presented with a higher rate of recurrence of nasal polyposis after the FESS procedure. Based on the results of Meltzer nasal endoscopy grading, Abdelaal et al. [22] reported on an improvement in the vitamin D3 group being achieved in 68.3% of cases as compared to 20% of cases in the placebo group; the severity of nasal polyps in the vitamin D3 group was found to be significantly lower than in the placebo group, and therefore vitamin D deficiency was correlated with a more severe course of nasal polyposis and worse postoperative outcomes. On the other hand, vitamin D supplementation facilitated improved surgical outcomes and reduced recurrence of polyposis. The researchers concluded that lower vitamin D levels are directly correlated with more severe endoscopic evaluation results, and therefore, vitamin D supplementation should be implemented in patients with vitamin D deficiency after surgery to reduce polyp recurrence and improve mucosal healing.

Murdaca et al. [32] also investigated the role of nasal endoscopy findings in predicting the recurrence of nasal polyps after FESS in correlation with serum vitamin D levels to find extensive polyps and significant recurrence of polyposis 6–12 months after surgery in patients with severe vitamin D deficiency.

A similar observation was made by Ghazavi et al. [7], who reported that vitamin D supplementation was associated with improved postoperative endoscopic evaluation, reduced polyp recurrence, and improved mucosal inflammation (severity of symptoms). Theirs was an epidemiological study in which, unlike in most of the other studies, vitamin D deficiency was not considered a risk factor when assessing the association between vitamin D levels and CRS [33]. Instead, serum vitamin D levels were found to be influenced by factors such as race, gender, body mass index (BMI), geographic region, and season, leading to the conclusion that the conduct of a well-designed study requires the use of analogous cohorts [11].

Research Trends

Biomarkers of inflammation and immune response

Increasing attention is being paid to the links between chronic inflammation, immune system dysfunction, and the development of nasal polyposis. Several biomarkers are currently being studied as potential predictors of polyposis recurrence after the surgery, such as eosinophil counts and interleukin-5 (IL-5) levels.

Mucosal thickness and the healing process of sinus mucosa on imaging studies

Advances in imaging technologies, such as high-resolution CT and magnetic resonance imaging (MRI), have facilitated detailed assessment of mucosal thickness and sinus mucosal healing (which had been previously difficult to quantify) to predict which patients are at higher risk for polyp recurrence.

Nasal microbiome

Examination of the nasal microbiome is an emerging area of research, particularly directed at determining how imbalances in the microbial community may affect the recurrence of nasal polyps after FESS. Imbalance (dysbiosis) in the nasal microbiome was found to be associated with chronic inflammation, which can contribute to polyp recurrence by promoting bacterial or fungal infections that prolong inflammation, leading to polyp formation. Some microbial species can also enhance the immune responses that lead to tissue remodeling and regrowth of polyps.

Gene expression and epigenetics

There is a growing body of research into the role of genetic and epigenetic factors in the development and recurrence of nasal polyps. The studies focus on the expression profiles of genes correlated with CRSwNP and the profile changes as a result of FESS treatment.

Systemic inflammatory markers (CRP, IL-6, and TNF-a)

C-reactive protein (CRP), interleukin-6 (IL-6), and TNF-α are systemic markers of inflammation that are finding use in other inflammatory diseases and are now being investigated as possible predictors of the recurrence of nasal polyposis after FESS.

Matrix metalloproteinases and tissue remodeling

Matrix metalloproteinases (MMPs) are enzymes involved in tissue remodeling and are associated with the formation and recurrence of nasal polyps.

Limitations

The limitations of this study consisted in its single-center character and limited follow-up period. Another limitation consisted in a selection bias: participants included in this study may have presented with certain characteristics that could have influenced the results, such as more severe disease and/or better compliance with treatment protocols. In addition to compliance with the prescribed vitamin D3 supplementation regimen, its serum levels can be affected by various factors, such as diet, sun exposure, and seasonal changes.

CONCLUSIONS

Vitamin D3 supplementation was effective in reducing the recurrence of nasal polyposis as well as the severity of symptoms of CRS. The variables associated with the recurrence of nasal polyposis after FESS included the age, the SNOT-22 questionnaire score, the Meltzer nasal evaluation grade, the Lund-Mackay score, and serum vitamin D levels; despite a slight predominance of male study subjects, the gender differences were not statistically significant; age, on the other hand, appeared to be an important factor influencing the results. Vitamin D supplementation has the potential to reduce the recurrence rate of nasal polyposis after FESS as based on the fact that adequate vitamin D levels can significantly improve the SNOT-22 scores; at the same time, as demonstrated by Meltzer endoscopic grading and the Lund-Mackay CT presentation assessment scores, vitamin D deficiency is associated with more severe and extensive diffuse nasal polyposis and more severe mucosal inflammation; in addition, a direct inverse relationship between serum vitamin D levels and the recurrence of nasal polyposis was found, suggesting that vitamin D supplementation was beneficial for reducing this recurrence.

REFERENCES

1. Fokkens W.J., Lund V.J., Hopkins C., Hellings P.W., Kern R. et al.: European position paper on rhinosinusitis and nasal polyps 2020. Rhinology., 2020; 58 (Suppl S29): 461–464. doi: 10.4193/Rhin20.600.
2. Hashemian F., Sadegh S., Jahanshahi J., Rabiei M.A.S., Hashemian F.: Effects of vitamin D supplementation on recurrence of nasal polyposis after endoscopic sinus surgery. Iran J Otorhinolaryngol., 2020; 32(108): 21–28. doi: 10.22038/ijorl.2019.37766.2241.
3. Kalińczak-Górna P., Radajewski K., Burduk P.: Relationship between the severity of inflammatory changes in chronic sinusitis and the level of vitamin D before and after the FESS procedure. J. Clin Med., 2021; 10(13): 2836. doi: 10.3390/jcm10132836.
4. Faghih Habibi A., Gerami H., Banan R., Kazemnezhad Leily E., Khoshkhat P. et al.: Serum 25-hydroxy vitamin D in chronic rhinosinusitis with and without nasal polyposis: A case-control study. Iran J Otorhinolaryngol., 2019; 31(102): 19–24.
5. Zblewski J., Kozakiewicz B., Dalke K., Górna A.: The role of probiotics in modulating the microbiota of the nose and paranasal sinuses and reducing chronic inflammation of the paranasal sinuses. Pol Otorhino Rev., 2025; 14(1): 26–31. doi: 10.5604/01.3001.0054.9412.
6. Fraczek M., Rostkowska-Nadolska B., Kusmierz D., Zielinska A., Rok J. et al.: Vitamin D analogs decrease in vitro secretion of RANTES and enhance the effect of budesonide. Adv Med Sci., 2012; 57(2): 290–295. doi: 10.2478/v10039-012-0043-5.
7. Ghazavi H., Hashemi S.M., Jafari S.: The effect of Vitamin D supplement on the relapsing incidence of rhinosinusitis with nasal polyposis after functional endoscopic sinus surgery. Adv Biomed Res., 2023; 12: 29. doi: 10.4103/abr.abr_237_21.
8. Magboul N.A., Alotaibi M., Aldokhayel F., Almazyad L.M., Alkwai K. et al.: Association between serum vitamin D level and uncontrolled chronic rhinosinusitis with nasal polyposis. Ear Nose Throat J., 2024; 27: 1455613241302892. doi: 10.1177/01455613241302892.
9. Aranow C.: Vitamin D and the immune system. J Invest Med., 2011; 59(6): 881–886. doi: 10.2310/JIM.0b013e31821b8755.
10. Stokes P.J., Rimmer J.: The relationship between serum Vitamin D and chronic rhinosinusitis: A systematic review. Am J Rhinol Allergy., 2016; 30(1): 23–28. doi: 10.2500/ajra.2016.30.4267.
11. Li B., Wang M., Zhou L., Wen Q., Zou J.: Association between serum vitamin D and chronic rhinosinusitis: A meta-analysis. Braz J Otorhinolaryngol., 2021; 87(2): 178–187. doi: 10.1016/j.bjorl.2019.08.007.
12. Flint P.W., Haughey B.H., Lund V.J., Robbins K.T., Thomas J.R. et al.: Cummings otolaryngology-head and neck surgery e-book. Elsevier Health Sciences., 2014; 70(1): 1–2.
13. Konstantinidis I., Fotoulaki M., Iakovou I., Chatziavramidis A., Mpalaris V. et al.: Vitamin D_3 deficiency and its association with nasal polyposis in patients with cystic fibrosis and patients with chronic rhinosinusitis. Am J Rhinol Allergy., 2017; 31(6): 395–400. doi: 10.2500/ajra.2017.31.4484.
14. Kennedy J.L., Hubbard M.A., Huyett P., Patrie J.T., Borish L. et al.: Sino-nasal outcome test (SNOT-22): a predictor of postsurgical improvement in patients with chronic sinusitis. Ann Allergy Asthma Immunol., 2013; 111(4): 246–251.e2. doi: 10.1016/j.anai.2013.06.033.
15. Glick Y., Knipe H., Hirano Y.: Lund-Mackay score. https://doi.org/10.53347/rID-51934 (16.02.2025).
16. Meltzer E.O., Hadley J.A., Lanza D.C., Lanza D.C., Marple B.F. et al.: Rhinosinusitis: developing guidance for clinical trials. J Allergy Clin Immunol., 2006; 118(5 Suppl): S17–S61. doi: 10.1016/j.jaci.2006.09.005.

17. Rosen C.J., Abrams S.A., Aloia J.F., Brannon P.M., Clinton S.K. et al.: Committee members respond to Endocrine Society vitamin D guideline. J Clin Endocrinol Metab., 2012; 97(4): 1146–1152. doi: 10.1210/jc.2011-2218.
18. Brescia G., Contro G., Ruaro A., Barion U., Frigo A.C. et al.: Sex and age-related differences in chronic rhinosinusitis with nasal polyps electing ESS. Am J Otolaryngol., 2022; 43(2): 103342. doi: 10.1016/j.amjoto.2021.103342.
19. Ryan M.T., Patel K., Fischer J.L., Tolisano A.M., McCoul E.D. et al.: Gender differences in outcomes following endoscopic sinus surgery: a systematic review and meta-analysis. Rhinology., 2024; 62(5): 514–525. doi: 10.4193/Rhin24.009.
20. Abuduruk S.H., Sabb Gul B.K., AlMasoudi S.M., Alfattani E.H., Mohammad M.A. et al.: Factors contributing to the recurrence of chronic rhinosinusitis with Nnasal polyps after Endoscopic Sinus Surgery: A systematic review. Cureus., 2024; 16(8): e67910. doi: 10.7759/cureus.67910.
21. Kazem N.G., Elaskarany A.A., Abdelazim H.E.M.: Comparative study of recurrence of allergic nasal polyposis after administration of vitamin D supplementation. BMFJ., 2024; 41(1): 141–152. doi: 10.21608/bmfj.2024.253652.1974.
22. Abdelaal A.S., Elhadidy S.S., Ibrahim M.A.E.: Comparative study between vitamin D and placebo in patients with nasal polyps. Int J Med Arts., 2021; 3(4): 1849–1854. doi: 10.21608/ijma.2021.86879.1345.
23. Jiao J., King T.S., McKenzie M., Bacharier L.B., Dixon A.E. et al.: Vitamin D3 therapy in patients with asthma complicated by sinonasal disease: Secondary analysis of the Vitamin D add-on therapy enhances corticosteroid responsiveness in asthma trial. J Allergy Clin Immunol., 2016; 138(2): 589–592.e2. doi: 10.1016/j.jaci.2015.12.1329.
24. Ali S.A., Ali O.A.: Vitamin D deficiency contributes to development of nasal polyps in Iraqi patients suffering from chronic rhinosinusitis. J Popul Ther Clin Pharmacol., 2023; 30(8): 349–356. doi: 10.47750/jptcp.2023.30.08.038.
25. Brociek-Piłczyńska A., Trebinska-Stryjewska A., Jurkiewicz D.: Preoperative serum 25(OH) D status and its correlation with an early endoscopic sinus surgery outcome and chronic rhinosinusitis severity. Otolaryngol Pol., 2024; 78(6): 1–8. doi: 10.5604/01.3001.0054.7429.
26. Pantazidou G., Papaioannou I., Skoulakis C., Petinaki E., Hajiioannou J.: Vitamin D levels in chronic rhinosinusitis in patients with or without nasal polyposis: A systematic review. Cureus., 2023; 15(9): e46275. doi: 10.7759/cureus.46275.
27. Zand V., Baradaranfar M., Vaziribozorg S., Mandegari M., Mansourimanesh M. et al.: Correlation of serum vitamin D levels with chronic rhinosinusitis disease severity. Iran J Otorhinolaryngol., 2020; 32(108): 35–41. doi: 10.22038/ijorl.2019.31926.2050.
28. Schlosser R.J., Soler Z.M., Schmedes G.W., Storck K., Mulligan J.K.: Impact of vitamin D deficiency upon clinical presentation in nasal polyposis. Int Forum Allergy Rhinol., 2014; 4(3): 196–199. doi: 10.1002/alr.21274.
29. Cho S.W., Kim D.W., Kim J.W., Lee C.H., Rhee C.S.: Classification of chronic rhino sinusitis according to a nasal polyp and tissue eosinophilia: limitation of current classification system for Asian population. Asia Pac Allergy., 2017; 7(3): 121–130. doi: 10.5415/apallergy.2017.7.3.121.
30. Bavi F., Movahed R., Salehi M., Hossaini S., Bakhshaee M.: Chronic rhinosinusitis with polyposis and serum vitamin D levels. Acta Otorhinolaryngol Ital., 2019; 39(5): 336–340. doi: 10.14639/0392-100X-2439.
31. Al-Morsy M., Ibrahim M.: Benefits of vitamin D supplementation after functional endoscopic sinus surgery for recurrent nasal polyposis. Pan Arab J Rhinol., 2023; 12(2): 64–68. doi: 10.58595/2090-7559.1209.
32. Murdaca G., Paladin F., Gangemi S.: Role of Vitamin D in the Clinical Course of Nasal Polyposis. Biomedicines., 2021; 9(8): 855. doi: 10.3390/biomedicines9080855.
33. Lee E.J., Hwang C.S., Kim K.S.: Lack of correlation between serum 25(OH) D level and endoscopy-based chronic rhinosinusitis in Korean adults. Rhinology., 2019; 57(2): 139–146. doi: 10.4193/Rhin18.110.

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