Effect of Vitamin D Supplementation among Allergic Rhinitis Patients

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Abstract

Background and aim: **Allergic rhinitis (AR) is thought to affect between 10% and 40% of people worldwide. Vitamin D influences nearly all immune cell types affecting both innate and adaptive immunity. We aimed to compare the clinical outcomes among allergic rhinitis patients treated with vitamin D.** ***Methods:*** **A randomized clinical trial was carried out among 44 patients with persistent AR were included in the study and vitamin D insufficiency (10 to 20 ng/ ml) and. Patients were divided into study and control group. The study group was treated with vitamin D supplementation with antihistaminic, while the control group received antihistaminic only. Patients were evaluated using total nasal symptoms (TNS) score and quality of life (QOL) assessment.** ***Results:*** **Vitamin D supplementation led to a significant improvement in the TNS score as early as 2 weeks after treatment began, whereas improvement in the control group was not recorded until 8 weeks. The study group had a lower TNS score after 8 weeks of treatment compared to the control group (14.9 ± 3.9 versus 18.9 ± 2.9; p < 0.001). There was statistically significant improvement of QOL among patients of both groups, but the improvement was significantly better with vitamin D-treated patients after 2 and 8 weeks of treatment.** ***Conclusion:*** **For allergic rhinitis patients with low vitamin D levels, antihistamine therapy combined with vitamin D supplements can reduce relative symptoms with a notable improvement in clinical outcomes.**

Keywords: allergy, rhinitis, vitamin D, supplementation, adjuvant therapy.

Introduction

Allergic rhinitis (AR) is a significant global health issue, affecting an estimated 10–40% of the worldwide population. Characterized by chronic inflammation of the nasal and paranasal sinus mucosa, AR places a substantial economic and medical burden on healthcare systems. This condition profoundly impacts a patient's quality of life by interfering with their ability to study, sleep, socialize, and be productive at work. The inflammatory response in AR is an IgE-mediated reaction triggered by exposure to specific allergens. Common symptoms include sneezing, nasal pruritus, rhinorrhea, and nasal congestion. Some patients may also experience irritated eyes or post-nasal drip. While pollen exposure leads to seasonal symptoms, allergens such as animal dander, mold spores, and house dust mites are key drivers of perennial symptom exacerbation. It is impossible to completely avoid airborne allergens, and current treatment strategies are often limited to providing symptomatic relief [(1)].

Nasal mucosa serves as the primary site for allergen exposure, initiating the inflammatory cascade that causes allergic symptoms. The pathophysiology of AR involves several complex processes, including

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the activation and migration of effector cells, the release of inflammatory mediators, and the production of chemokines and cytokines by inflammatory cells, leading to damage to nerve endings and the nasal epithelium. Systemic medications, such as antihistamines, are frequently used to treat AR symptoms. However, topical treatments are continually being developed and offer numerous advantages over oral therapies. Topical administration lowers the risk of systemic side effects, allowing for higher doses of medication to be applied directly to the site of inflammation the nasal mucosa [2].

Recent research has focused on the role of vitamin D in the stimulation of allergic responses. These investigations have primarily explored the effects of vitamin D on the immune system and other non-calcemic effects [3–5].

Vitamin D significantly influences nearly all immune cell types, including T, B, and dendritic cells, as well as both innate and adaptive immunity. The regulation by 1,25-dihydroxyvitamin D ($1,25(OH)_2D$) also affects monocytes and macrophages. In addition to its impact on immune cells via cytokine modulation, vitamin D may be a significant factor in the etiology of numerous allergic diseases. Consequently, recent AR research has increasingly focused on the potential preventive benefits of vitamin D intake [6, 7].

Despite a considerable body of research on its preventative effects, a relatively small number of studies have evaluated the efficacy of vitamin D in treating AR [8]. This gap in knowledge is the basis for the current study, which aims to compare the clinical outcomes of allergic rhinitis patients treated with vitamin D to those in a control group.

Patients and methods:

A randomized clinical trial was conducted at Suez Canal University Hospitals. A total of 44 patients aged 18 – 40 years, with persistent AR diagnosed with guideline of AR and its Impact on Asthma presented to the ENT clinic at Suez Canal University Hospitals and diagnosed to have vitamin D insufficiency (vitamin D level: 10 to 20 ng/ ml) were included in study.

Patients who have concomitant chronic medical conditions such as hyperparathyroidism, chronic liver disease, chronic kidney disease, celiac disease or Crohn's disease which can cause a disturbance in the level of vitamin D, its secretion, or its absorption were excluded from the study. Also, patients with history of taking vitamin D supplements within the previous three months, breastfeeding and pregnant women, and the use of antiepileptic and corticosteroids medicines (that can inhibit the body's ability to absorb vitamin D) were excluded from the study.

Randomization and blinding: Allergic Rhinitis patients were selected from the ENT clinic using the Simple random sample technique. A computer-generated randomized sequence was used for randomization, with stratification based on the doctor and a 1:1 allocation using a block size of 4. Block randomization was employed to maintain an equitable distribution of participants in each group throughout the study. The allocation sequence was created by a research

team member who did not participate in participant interaction or data collection. The assignments were placed in consecutively numbered, sealed envelopes. The patients were unaware of the treatment they were assigned.

The sample size was determined using the following equation [9]:

$$n = 2\left[\frac{(Z_{\alpha/2}+Z_{\beta})*\sigma}{\mu_1-\mu_2}\right]^2$$

Using a power of 80% and 95% CI with the difference between mean TNSS among allergic rhinitis patients with vitamin D supplementation and without was 0.23 [10] and in addition to ten percent for drop-out, the final sample size was 22 subjects per group. Based on earlier research, a minimum sample size of 44 people—22 per group—was determined for this investigation. Prior to the trial, each participant provided written informed consent after being made aware of the study's protocol.

Methods of the study

In a single lab, the electro-chemiluminescent method was used to measure the level of vitamin D. Using a random number system, all patients with vitamin D insufficiency were split into two groups. The intervention group received vitamin D in addition to standard antihistamine medication, while the control group received only antihistamine medication. Vitamin D was administered orally in a daily dose of 6000 IU for 8 weeks.

Subsequently, each participant completed a questionnaire that included demographic information and clinical symptoms such as nasal itching, rhinorrhea, nasal obstruction, sneezing diminished eye pruritus, sense of smell, eye redness, postnasal drip, eyelid edema, nasal tone of voice, and dysphonia. according to the code assigned to every survey.

The questionnaire of clinical symptoms was filled out before the start of trial as well as four and eight weeks following the start of treatment. Since the guidelines of Endocrine Society Clinical Practice recommend an 8-week course of treatment, vitamin D levels were reassessed at that point [11]. However, after the trial was concluded, the control group was provided the recommended course of medication.

Ethical consideration:

The ethical clearance was obtained from ethics committee in Faculty of Medicine Suez Canal University.

Statistical Analysis

The data collected were digitized and analyzed using SPSS version 26. Frequencies and percentages were used to describe qualitative data, with the chi-square test ($\chi 2$) employed to assess relationships between these variables. Quantitative data were summarized using the mean and standard deviation. To compare two distinct groups, the Student's t-test and Mann-Whitney U test were used. The Friedman test was applied to evaluate changes in quantitative variables over different time points within the same group. A P-value of less than 0.05 was considered to indicate a statistically significant difference, while a P-value of 0.05 or greater was deemed non-significant.

Results:

The mean age was 27.6± 6.5 years and 28.4± 6.8 years among groups A and B respectively. There were 63.6% and 59.1% males among groups A and B

respectively. No statistically significant difference was found between the study groups regarding age and gender **(Table 1)**.

Table 1: Basic characteristics of the participants:

		Group A (n=22)	Group B (n=22)	p-value
Age (years)	Mean ± SD	27.6± 6.5	28.4± 6.8	0.851
	Median (Range)	26 (18, 40)	27 (19, 38)	
Sex	Female, n (%)	8 (36.4)	9 (40.9)	>0.999
	Male, n (%)	14 (63.6)	13 (59.1)	

Unpaired t-test **p is significant at <0.05*

The group receiving vitamin D in addition to antihistamines showed an improved TNS score after both 2 and 8 weeks. Antihistamine alone improved total nasal symptoms after 8 weeks, but no significant improvement was observed at 2 weeks. The total nasal symptoms score was 26.1± 2.1 and 24.9± 3.3 among groups A and B with no difference. The total nasal symptoms score after 2 weeks was 21.7 ± 2.6 and 23.1 ± 2.6 among groups A and controls with no difference. Vitamin D combined with antihistamines significantly lowered the total nasal symptoms score compared to antihistamines alone **(Table 2)**.

Table 2: Comparing baseline and follow-up total nasal symptoms among the two studied groups.

Total nasal symptoms score		Group A n=22	Group B n=22	P value
Basic	Mean ± SD	26.1± 2.1	24.9± 3.3	0.184b
	Median (Range)	26 (22, 30)	24 (20, 30)	
P value (basic vs. after 2 weeks)		0.004*a	0.113a	
After 2 weeks	Mean ± SD	21.7 ± 2.6	23.1 ± 2.6	0.194b
	Median (Range)	22 (15, 26)	23 (20, 31)	
P value (after 2 weeks vs. 8 weeks)		<0.001*a	<0.001*a	
After 8 weeks	Mean ± SD	14.9 ± 3.9	18.9 ± 2.9	<0.001*b
	Median (Range)	14.5 (8, 23)	19 (14, 27)	
P value (basic vs. after 8 weeks)		<0.001*a	<0.001*a	

a; Friedmann two-way test (group A= <0.001, Group B= <0.001*), post hoc test (Bonferroni test) b; Student t test *p is significant at <0.05*

In both groups, quality of life was significantly improved after 2 weeks and after 8 weeks. There was no statistically significant difference between the study and the control groups regarding basic total quality of life score. The vitamin D group had a lower two-week and eight-week quality of life score compared to the control group **(Table 3)**.

Table 3: Quality of life among the study the participants.

QOL		Group A n=22	Group B n=22	P value
Basic	Mean ± SD	40.1± 4.0	40.3 ± 3.4	
	Median (Range)	40 (31, 47)	40 (32, 47)	0.880b
P value (basic vs. after 2 weeks)		0.001*a	0.001*a	
After 2 weeks	Mean ± SD	30.4± 2.7	34.0± 3.7	
	Median (Range)	30 (25, 35)	33 (28, 40)	0.001*b
P value (after 2 weeks vs. 8 weeks)		0.001*a	0.001*a	
After 8 weeks	Mean ± SD	13.7 ± 2.6	16.2 ± 3.3	
	Median (Range)	14 (9, 18)	16 (9, 23)	0.012*b
P value (basic vs. after 8 weeks)		<0.001*a	<0.001*a	

QOL: quality of life

a; Friedmann two-way test (group A= <0.001, Group B= <0.001*)), post hoc test (Bonferroni test) b; Student t test *p is significant at <0.05*

Discussion:

Allergic rhinitis (AR) is a chronic allergic disorder characterized by inflammation of the nasal mucosa, significantly affecting patients' daily lives, including their work performance, academic achievement, and overall quality of life [12]. Vitamin D has recently gained attention for its immunomodulatory effects, with a wide range of cells expressing vitamin D receptors [13-15].

The primary objective of this study was to compare the clinical outcomes of allergic rhinitis patients treated with vitamin D to a control group. This randomized controlled trial was conducted at Suez Canal University Hospitals and included patients between 18 and 40 years old who had a vitamin D deficiency (10–20 ng/ml) and were diagnosed with persistent AR according to the ARIA guidelines. A total of 44 patients were enrolled and randomly divided into two groups of 22. We have evaluated patients for clinical improvement using TNS score and QOL.

This study found that after two weeks, there was no significant difference in the TNS score between the two groups. However, after two months, the vitamin D group showed a significant reduction in the total nasal symptoms score compared to the control group. This improvement was consistent across several specific symptoms, including rhinorrhea, nasal itching, sneezing, and nasal obstruction.

These findings are consistent with other studies. Kalsotra et al., [16] reported a statistically significant difference in TNSS between the groups after treatment, with the vitamin D group showing a greater symptom reduction. [16]. Similarly, Bakhshaee et al., [17] found that while there was no significant difference in symptom severity after four weeks, a significant difference emerged after eight weeks, a finding that strongly aligns with the delayed but significant effect observed in our study [17]. El Maghraby et al., [18] also found a significant difference in end nasal symptoms, with patients receiving vitamin D plus immunotherapy showing better results than those on immunotherapy alone [18]. Furthermore, both Jerzynska et al., [19] and Malik et al., [20] concluded that vitamin D supplementation significantly improved nasal symptoms in their respective studies [19, 20].

In contrast, some studies present conflicting findings. For example, Bhardwaj et al., [21] reported a greater increase in post-treatment symptom scores in their vitamin D group, though this difference was not statistically significant. This could be attributed to the relatively short four-week follow-up period in their study [21]. Additionally, Shrestha et al., [22] found no symptom improvement with vitamin D supplementation, a discrepancy that may be due to their use of a different outcome measure, the Sino-nasal Outcome Test (SNOT-22), instead of TNS score [22].

A unique aspect of this study was the assessment of quality of life in relation to vitamin D supplementation. The results showed that the total quality of life score was lower (indicating improvement) in the study group after two weeks ($p < 0.001$) and remained significantly lower after eight weeks. The improvement was particularly noted in the domains of memory and sleep.

While these findings are encouraging, they are not universally consistent across the limited existing literature. For example, a study by Columbo and Rohr [23] found no significant difference in quality of life between AR patients receiving vitamin D and those on a placebo [23]. This discrepancy could be due to variable vitamin D dosage used in both studies or the older average age of the participants in the Columbo trial (77.5 ± 7.3 years), which is significantly different from the younger population in the current study.

The main limitations of the current study were the short follow up duration, the limited age range and the absence of immunological evaluation as the study did not measure immune cells or cytokines, preventing a clear understanding of the biological mechanisms behind vitamin D's effects.

Conclusion:

this study demonstrates that the addition of vitamin D supplementation to standard antihistamine therapy significantly improves total nasal symptoms and overall QOL in patients with AR over a two-month period. These findings align with growing evidence supporting the immunomodulatory role of vitamin D in allergic diseases. The results suggest that vitamin D could be a valuable adjunctive treatment for AR, especially for patients with a co-existing vitamin D deficiency.

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