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ORIGINAL ARTICLE

Vitamin D: A Modulator of Allergic Rhinitis

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Abstract Allergic rhinitis is a topic of concern among clinicians. Despite of being treated in form of oral medicines, nasal drops and sprays several patients come back with complaint of no relief. This necessitates to review and focus on etiology and to find some other treatment regimen. Established relation of serum vitamin D level and various allergic conditions attracts us to use it as a therapeutic agent for allergic rhinitis. It is a case–control observational study recruited 80 subjects with 40 cases and 40 controls. There was drop out of two subjects among cases. Cases were supplement with oral vitamin D (c-holecalciferol-1000 IU OD) and controls received no treatment. Serum vitamin D level, Total nasal symptom score (TNSS) and total eosinophilic count (TEC) were calculated at 0, 1 and 3 months and compared. Pre-treatment average serum vitamin D level of cases was 20.15 + 10.26 ng/ml and of control was 27.94 + 13.38 ng/ml. The TNSS score of cases was 7.43 + 1.87 and of controls was 5.00 + 1.52. TEC of cases was 546.15 + 113.39 and of controls was 313.33 + 125.08. Post-treatment serum vitamin D level of cases was 38.05 + 14.62 and of controls was 27.43 + 12.76. TNSS of cases was 3.53 + 0.68 and 4.43 + 1.17 in control group, TEC of cases was 68.13 + 38.95 and of controls was 197.03 + 123.36. This study concludes that vitamin D acts as disease modulator in allergic rhinitis In case of allergic rhinitis with vitamin D deficiency its supplementation gives symptomatic relief and also lowers down the values of TNSS and TEC.

Keywords Rhinitis · Allergic · Vitamin D · Total nasal symptom score

Introduction

Allergic rhinitis (AR) is a disease with growing impact on everyday medical practice, as its prevalence has steadily increased during the last decades. It represents a major global health problem which poses significant effect on the quality of life (QOL). It is an immune (IgE) mediated inflammatory reaction of upper airway after allergen exposure. It poses psychosocial and financial burden on society. It affects about 10–25% of population worldwide and in India its incidence is 20–30% [1]. Its prevalence shows geographical variability. Despite of being treated there is lack of satisfaction among patients. Thus, it is necessary to focus on other causes and treatment modalities of allergic rhinitis.

In current scenario, Vitamin D deficiency is increasingly contributed as a potential etiologic or disease-modifying factor in various allergic conditions including allergic rhinitis. The US National Health and Nutritional Examination Survey (NHANES) revealed that mean serum 25-hydroxyvitamin D (25(OH)D) decreased from 30 ng/mL in 1988–1994 to 24 ng/mL in 2001–2004. National population surveys found that both vitamin D deficiency and allergic diseases are increasing year by year possibly due to increased westernization [2]. Previous literatures revealed that Vitamin D plays an important role in decreasing sensitivity to allergens and its deficiency is associated with increased serum IgE levels. Various

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therapeutic studies on allergic diseases including allergic rhinitis have demonstrated that the use of vitamin D supplements can decrease the severity of allergic diseases but still the results are controversial [3].

Limited literature is there which delineate relationship between serum vitamin D level and allergic rhinitis and its use as a therapeutic agent for its treatment. We have conducted a study to evaluate serum vitamin D level in sufferers of allergic rhinitis and also to see the effect of vitamin D supplementation on the course of disease.

Methods

This is an observational case–control study conducted in SMS medical college and attached hospitals, Jaipur, Rajasthan from February 2016 to October 2017. All subjects who were clinically diagnosed allergic rhinitis on the basis of (1) ARIA classification, (2) positive nasal allergic mucin (slide method) and (3) total eosinophilic count (TEC) (> 400 HPF) were included in the study as case population. Cases of perennial allergic rhinitis were included in the study and seasonal allergic rhinitis cases were excluded. Both male and female subjects were included with age range of 15–45 years. Those who had previously received medications including corticosteroids (oral and nasal spray), barbiturates, bisphosphonates, vitamin-D components such as calcium with Vitamin-D and who were not willing to participate in the study were excluded from the study. Age and sex matched subjects with minor ENT ailments except allergic rhinitis reported at ENT outdoor were included in the study as controls for statistical analysis. Total 80 subjects were enrolled in the study after getting written and informed consent.

They were allocated into two groups: cases and controls. Each group comprised of 40 subjects. The study was approved from the medical research review and ethical board of the institute. Cases were supplemented with oral vitamin D supplements (cholecalciferol-1000 IU OD) and controls were not given any supplementation. The outcomes were assessed in the terms of serum vitamin D levels, TNSS (Total nasal symptom score) and total eosinophilic counts (TEC) at 0, 1 and 3 months and data were compared among two groups. SPSS, version 21 for Windows statistical software was used for statistical analysis. A value of $p < 0.05$ considered statistically significant.

Vitamin D deficiency is defined as $25(OH)D_3$ levels < 15 ng/ml, vitamin D insufficiency if level between 15 and 30 ng/ml. Patients with serum vitamin D levels 30–50 ng/ml are considered as normal and excluded from the study [4] (Table 1). The Total Nasal Symptom Score (TNSS) is the sum of scores for each of nasal congestion, sneezing, nasal itching, and rhinorrhoea at each time point, using a four-point scale (0–3). TNSS is calculated by adding the score for each of the symptoms to a total out of 12 [5] (Table 2).

Results

Total 80 subjects were enrolled in the study who attended outpatient department in our institute. They were divided into two groups (cases and controls) with 40 subjects in each group. Out of 40 cases, 2 were dropped in follow up. Thus, there were 38 cases. The age range was 15–45 years. Among 80 subjects, 50 were males and 28 were females. Thus, this study shows male preponderance (M: F = 1.78: 1).

Baseline (at 0 month) i.e. before supplementation, serum vitamin D level, TNSS and TEC were calculated and later same parameters were calculated at 1 and 3 months in both groups and compared (Table 3). At the initial point of study average serum vitamin D level in 38 cases was 20.15 ± 10.26 ng/ml and after 3 months of supplementation it was 38.05 ± 14.6 ng/ml i.e. there was statistically significant ($p = 0.0001$) increase. In controls no significant change was noted.

All 38 cases were experiencing signs and symptoms of allergic rhinitis with baseline TNSS 7.43 ± 1.87. After 3 months of vitamin D supplementation it was 3.53 ± 0.68. This difference was measured as statistically significant ($p < 0.05$). Thus, the study revealed significant decrease in TNSS with symptomatic improvement after vitamin D supplementation. Serum vitamin D level and TNSS follow inversely proportional relation. On other hand, 40 controls didn't show any significant difference in TNSS.

TEC was calculated in all 78 subjects. In cases pretreatment TEC was 546.15 ± 113.39 and after 3 months of taking oral vitamin D it was 68.13 ± 38.95. This post treatment decrease in TEC was statistically significant ($p < 0.05$).

We observed that nasal symptoms (calculated by TNSS) and TEC had correlation with serum vitamin D level as TNSS and TEC both got decrease as serum vitamin D level increased (Table 3).

Likewise, study of parameters mentioned above shows significant post treatment differences along with symptomatic improvement. These study results are in favour of use of vitamin D as treatment modality of allergic rhinitis. In the light of above findings, it can be suggested that multicentric studies on large sample sizes should be encouraged to find out role of vitamin D supplementation in case of allergic rhinitis.

Table 1 Serum vitamin D level in body

Vitamin D status	Serum vitamin D level (ng/ml)
Normal	30–50
Insufficiency	15–30
Deficiency	<15

Table 2 TNSS grading

TNSS	Symptoms
0 (None)	No symptoms
1 (Mild)	Mild symptoms that are easily tolerated
2 (Moderate)	Awareness of symptoms which are bothersome but tolerable
3 (Severe)	Severe symptoms that are hard to tolerate and interfere with daily activity

Minimum score = 0; maximum score 12

Table 3 Comparison of serum vitamin D level, TNSS and TEC among cases and controls

S. no.	Duration	Serum vitamin D level (ng/ml)		TNSS		TEC	
		Cases	Controls	Cases	Controls	Cases	Controls
1.	Baseline	20.15 ± 10.26	27.94 ± 13.38	7.43 ± 1.87	5.00 ± 1.52	546.15 ± 113.39	313.33 ± 125.08
2.	After 1 month	26.03 ± 9.45	27.23 ± 12.61	5.13 ± 1.40	4.78 ± 1.49	192.10 ± 81.37	241.75 ± 129.81
3.	After 3 months	38.05 ± 14.62	27.43 ± 12.76	3.53 ± 0.68	4.43 ± 1.17	68.13 ± 38.95	197.03 ± 123.36

Discussion

Allergic rhinitis is a health problem of concern as it affects day-to-day life of people. Allergens responsible for it include: domestic allergens (mites, domestic animals, insects or of plant origin), outdoor allergens (pollens and moulds), occupational allergens (latex), tobacco smoke, automobile exhaust (ozone, oxides of nitrogen and sulphur dioxide) aspirin and other non-steroidal anti-inflammatory drugs (NSAIDs). It comprises four major symptoms–rhinorrhoea, sneezing, nasal itching, and nasal congestion, which result in sleep disturbance, fatigue, depressed mood, irritability and cognitive function impairment. Various other conditions like—conjunctivitis, postnasal drip, Eustachian tube dysfunction, otitis media, sinusitis and in children, dental malocclusions & facial deformities may be associated with it [6].

Although there are several treatments options for allergic rhinitis in form of oral antihistaminic and topical steroids, which give good results but still there is need of some more options to improve quality of life of affected people. Many of the times patient doesn't get satisfactory relief by these drugs so we should have some other therapeutic agent for its treatment with minimal or no side-effects. On other hand allergic rhinitis has a long course even after taking treatment and most of the patients get relief till, they take treatment. So, we have to pay attention on this also that one can continue it for a long time without any harmful effect on body and drug interactions. Vitamin D fulfils these criteria perfectly. Being a vitamin one can continue it for a long time.

In Indian scenario, AR does not receive the attention it deserves, neither by patients nor by clinicians. It significantly affects the quality of life (QOL). Thus, it is an evolving topic which requires attention by clinicians to find out its causes and management modalities along with the other factors involve in its etiopathogenesis directly or indirectly. Being a multi-factorial disease, it is difficult to approach its exact cause. Various literatures indicate that allergic diseases are associated with low-serum Vitamin D levels and AR is one of them. Recent studies have suggested its plausible role as an immuno-modulator in allergic rhinitis. It plays an important role in the regulation of immune system, lymphocyte function, T cell antigen receptor signalling or activation, cytokine production.

Vitamin D deficiency is pandemic now-a-days may be due to westernization, sedentary lifestyle which lead to less sun exposure and less cutaneous vitamin D production. The International Study of Asthma and Allergies in Childhood (ISAAC) demonstrated the highest prevalence of asthma symptoms in countries such as the United Kingdom, Australia, New Zealand, and the Republic of Ireland. This data helped to form the foundation for the description that people living in more westernized, developed nations have higher reported rates of allergic diseases [7–9].

In a study conducted by Hollams et al. in Australia, in 2012, serum vitamin D level was calculated and its association with allergic rhinitis was studied. This study got success to establish association between vitamin D deficiency and allergic rhinitis. Similarly, another study conducted by Gupta et al. in India in 2016 in which 27 patients of allergic rhinitis with mean age of 26.47 ± 9.25 years were enrolled. Their treatment regimen included oral antihistaminic which was supplemented by oral vitamin D in 14 patients and in rest 13 patients no vitamin D supplementation was added. This study revealed overall symptomatic improvement in nasal symptoms score (NSS) in patients receiving vitamin D along with antiallergic medication and quote the role of vitamin-D in modulating the immune system [9, 10].

There are many more studies which denote worldwide increase in allergic diseases such asthma, allergic rhinitis and food allergy and their association with low serum vitamin D levels. The aim of our study is to measure serum vitamin D levels in patients with allergic rhinitis and in deficient patients observe the effect of vitamin D supplementation.

Modh et al. conducted a study "Role of vitamin D supplementation in allergic rhinitis" in 2011–2012 in 21 allergic rhinitis patients with vitamin D deficiency. They used total nasal symptoms score (TNSS) to categorise patients according to severity of symptoms. Pre-treatment TNSS was 10.6 ± 2.65 and post-treatment it was 2.76 ± 1.6 i.e. there was significant symptomatic improvement. Thus, this study shows that vitamin D supplementation alters natural course of AR toward significant clinical improvement [11]. Our study also concludes same results.

Previous studies quote that the hormonal form of vitamin D3 is immunoregulatory. Experimental studies have demonstrated that $1,25(OH)_2D3$ affects a wide range of immune cells and cytokines and is associated with many immune diseases. Previous reports have shown that T cells, B cells, dendritic cells, monocytes and macrophages are influenced by the regulation of $1,25(OH)_2D3$ [12–26]. Therefore, experimental and clinical studies have shown that being an immunomodulator, vitamin D is associated with AR, although the results are inconsistent and even conflicting.

In 2016, Zahra Aryan et al. published a systemic review and meta-analysis which included 21 observational studies. This study aimed to investigate the association of vitamin-D status with risk of two main outcomes: aeroallergen sensitization and allergic rhinitis (AR). This study revealed that serum vitamin-D is inversely associated with prevalence of aeroallergen-specific IgE sensitization in children and adolescents. Prevalence of AR is lower in adults with serum vitamin-D $\geq$ 75 nmol/L compared to serum $<$ 50 nmol/L. They also found sex disparity in association of serum vitamin-D with AR; serum vitamin-D $\geq$ 75 nmol/L is associated with lower prevalence of AR in men, while no significant association is observed in women. They suggested Vitamin D as a modifiable risk factor for aeroallergen sensitization and AR development in boys but not girls [27].

Our study results are nearly identical to various studies which shed light on association of serum vitamin-D and allergic rhinitis. They concerned that the prevalence of severe vitamin D deficiency was significantly higher in patients with allergic rhinitis than the normal population. Supplementation of vitamin D may be beneficial in the prevention of the pathogenesis of AR [28–30].

Some observational studies calculated serum level of vitamin D and TNSS in allergic rhinitis patients and then supplement them by oral vitamin D (1000 IU). Same parameters were calculated after supplementation and compared. These studies as well as our study, found significant increase in serum vitamin D level along with decrease in TNSS [31, 32]. Thus, there has been speculative role of Vitamin-D supplementation in deficient patients with improvement in symptoms of allergic rhinitis (Table 4).

Table 4 Comparison of results of various studies

S. no.	Study	Serum vitamin-D (ng/ml)		TNSS		*p* value
		Pre-treatment	Post treatment	Pre-treatment	Post treatment	
1.	Malik et al.	17.32 ± 8.26	29.71 ± 2.28	9.92 ± 1.37	2.81 ± 3.04	0.0001
2.	Modh et al.	18 ± 5.61	23.91 ± 9.73	10.6 ± 2.65	2.76 ± 1.6	0.0001
3.	Our study	20.15 ± 10.26	38.05 ± 14.62	7.43 ± 1.87	3.53 ± 0.68	0.0001

We also measured TEC in AR patients and noted decrease in its values but in previous literatures we didn't got any comment on this parameter so we are mentioning our data in this study without any comparison with previous studies.

Conclusion

This study reveals overall symptomatic improvement along with increase in TNSS in allergic rhinitis patients after vitamin D supplementation. Total eosinophilic count (TEC) is also supportive in diagnosis of allergy, our study results show decrease in TEC after vitamin D supplementation. This study suggests that vitamin D acts as an immunomodulator and can be used as a therapeutic agent in AR. We recommend to estimate serum vitamin D level in AR patients and supplements should given in case of deficiency.

Compliance with Ethical Standards

Conflict of interest All co-authors and corresponding author declare that we have no conflicts of interest.

Ethical Approval All investigations done in presented study involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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Informed Consent Informed consent was obtained from all individual participants included in the study.

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