

Effect of Vitamin-D Supplementation in Children with Moderate-Severe Persistent Allergic Rhinitis

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ABSTRACT

Objective; To compare serum vitamin D level in pediatric cases of persistent moderate-severe allergic rhinitis with healthy children and to assess efficacy of vitamin D supplementation on treatment of allergic rhinitis in these cases.

Study design, place & duration; Nonrandomized controlled trials. The study was carried out from September 2019 to September 2020 in Combined Military Hospital Mardan and Mardan Medical Complex.

Methodology; One hundred and twenty pediatric cases (5 -15 years) of moderate-severe persistent allergic rhinitis were selected from outpatient department and their serum 25 (OH)D levels were compared with 120 healthy children of same age. The allergic rhinitis children (120) were divided in two groups of 60 each, Group A and Group B. The symptoms of cases were assessed and recorded. Rhinorrhea was assigned score from 0 to 3, 0 for no rhinorrhea, 1 for mild, 2 for moderate and 3 for severe rhinorrhea. Similarly other symptoms of itching, sneezing, nasal obstruction and nasal rubbing were assigned scores and recorded. Group A cases were given daily vitamin D (800IU) in addition to oral antihistamine (loratidine), intranasal corticosteroids (Budesonide), oral leukotriene inhibitors (Montelukast) and intranasal xylometasoline (Xynosine nasal drops). Group B children were given above mentioned medicines only. After four weeks they were assessed in terms of improvements of symptoms and compared. All data was analyzed with help of SPSS 21.

Results; Among allergic rhinitis children, there were 64 (53.3%) males and 56 (46.7%) females. Mean age of children was 9.90 ± 3.06 years. Out of them, 51 (42.5%) were Vitamin D deficient, 46 (38.3%) were Vitamin D insufficient and 23 (19.2%) had sufficient serum Vitamin D levels. Total 80.8% children with allergic rhinitis had low serum vitamin D levels. Among 120 healthy children, there were 61 males (50.8%) and 59 females (49.2%) with mean age 10.41 ± 3.07 years. In healthy children, there were 30.8% cases of vitamin D deficiency and 32.5% cases of vitamin D insufficiency (total 63.3% cases of low serum vitamin D) and 36.7% children had normal serum vitamin D. In contrast 19.2% allergic rhinitis children had normal serum vitamin D levels.

Group A children receiving additional daily Vitamin D (800IU) had significantly better improvement in symptoms of allergic rhinitis (rhinorrhea, nasal itching, sneezing, nasal obstruction) as compared to the group only receiving allergic rhinitis treatment (Group B). Symptom of nasal rubbing also got alleviated after 04 weeks but the improvement was insignificant ($p=0.092$).

Conclusion; Children with persistent moderate-severe allergic rhinitis had significantly lower serum levels of serum vitamin D as compared to healthy children of same age and daily supplementation of vitamin d (800IU) helps alleviating the symptoms of allergic rhinitis in addition to standard therapy of allergic rhinitis.

Keywords; Allergic rhinitis, Vitamin D, Rickets

Introduction

Vitamin D plays important role in decreasing the severity of allergic phenomenon through different mechanisms including effect on immune cells, decreasing the resultant inflammatory reaction and prevention of infections (1,2). Vitamin D is a fat soluble vitamin synthesized in the skin under the effect of sunlight and has two types D2 and D3.

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For activation it undergoes hydroxylation in liver and kidney. It plays important role in the absorption of calcium and phosphorus. It also affects bone growth, immune function, cardiovascular system, pancreas,

muscle, brain and control of cell cycles (3). The main circulating form of vitamin D is 25 hydroxyvitamin D {25(OH)D}. Total serum 25 hydroxyvitamin D {25(OH)D} level is considered a reliable indicator of body vitamin D level.

Allergy is defined as the hypersensitivity to a specific antigen resulting in an immune reaction varying in severity from mild to extreme. The incidence of allergy has increased over the past few decades caused by both environmental and host related factors. Vitamin d is known to have been associated with immune function affecting both the innate and acquired aspects by promoting the synthesis of microbicidal peptide in macrophages and regulating T cells. Its deficiency has been linked to increased incidence and recurrence of allergic ailments. The incidence group includes population of all ages including children and pregnant woman. There is no agreed cut off level for vitamin d and is measured by the concentration of 25(OH) in the blood because of longer half-life than the other type (4).

Allergic rhinitis caused by allergens via IGE mediated hypersensitivity causing rhinorrhea, nasal blockage and sneezing affecting over 500 million people around the world. It is the most common type of allergic disease affecting the quality of life and absence from work. The pathophysiology of allergy is considered to be multifactorial including both genetic and environmental causes (5).

Association of vitamin D and allergic rhinitis has always been the subject of interest for decades especially after the discovery of vitamin d receptor (VDR) which helps the aforementioned vitamin to execute its immunomodulatory effect. These receptors¹ are known to be present on all cells of the immune system and takes part in the inhibition of inflammatory processes by inhibiting the toll like² receptors. There is evidence of reduction in the incidence of exacerbation of asthma (which is almost³ similar disease of lower airway as is allergic rhinitis for upper airway) in children by vitamin D supplementation thus improving the quality of life for the patient and reducing the frequent visits to the¹ emergency department (6,7). The occurrence of asthma and wheezing has been associated with a prenatal deficiency of vitamin D in the fetus especially for the² male fetuses and can be overcome by the prenatal supplementation of vitamin D. Moreover it has been noticed that steroid resistance either congenital or³ acquired can be overcome by addition of vitamin D with steroids for managing asthma (7).

This being said there is need of further study in investigate the association between Vitamin D and severity of allergic rhinitis in children and benefits of vitamin D supplementation thus preventing and reducing the severity of allergic rhinitis.

Methods

The study was carried out in CMH Mardan and Mardan Medical Complex from September 2019 to September 2020. The pediatric cases (5 -15 years) of moderate-severe persistent allergic rhinitis who presented in the outpatient department and consented, were included in the subject study. Permission was taken from ethical review board of hospital prior to the study.

According to ARIA (Allergic rhinitis and its impact on Asthma) guidelines, allergic rhinitis is defined as a symptomatic disease induced by immunoglobulin E mediated inflammation after exposure of allergens to the nasal membrane (8). Allergic rhinitis is categorized into persistent and intermittent. In intermittent disease, cases have symptoms for less than 4 days per week and less than 4 weeks per year, in contrast persistent allergic rhinitis patients experience symptoms for more than 4 days per week for more than 4 weeks/year (8). The children who had following symptoms and signs were diagnosed as case of persistent moderate-severe allergic rhinitis, if they had any combination of following symptoms for more than 4 days/week and for more than 4 weeks/year affecting their normal sleep, daily activities or performance at school;

Children ≥ 05 years and ≤ 15 years with rhinorrhea, nasal congestion, repetitive sneezing, itching of nose, eyes, palate or throat, constant clearing of throat
Large pale-bluish turbinates with clear or white nasal discharge
Allergic crease (transverse crease formed at lower part of nose due to upward nose rubbing i.e allergic salute)

Exclusion Criteria

Children with adenoid hypertrophy, nasal polyps, deviated nasal septum, facial asymmetries, syndromic facies
Children with rickets, immunocompromised conditions, liver/renal failure, malabsorption disorders
Children already taking Vitamin D supplements or treatment for allergic rhinitis
To compare serum 25 (OH)D levels of allergic rhinitis children with healthy children, we selected 120

healthy children of same age who were not taking any vitamin supplements, from different houses in Mardan randomly. Consent was taken from their parents for subject purpose; their serum Vitamin D samples were collected and sent to laboratory.

The allergic rhinitis children (120) selected from the outpatient department were examined thoroughly. These cases were randomly divided in two groups of 60 each, Group A and Group B. The symptoms of cases were assessed and recorded. Rhinorrhea was assigned score from 0 to 3, 0 for no rhinorrhea, 1 for mild, 2 for moderate and 3 for severe rhinorrhea. Itching was also categorized from 0 to 3, 0 for no itching, 1 for mild, 2 for moderate and 3 for severe itching. Nasal blockage/stiffness was also categorized from 0 to 3, 0 for no blockage, 1 for mild, 2 for moderate and 3 for severe blockage. Similarly sneezing was categorized from 0 to 3, 0 for no, 1 for mild (1-3 per hour), 2 for moderate (4 - 6 per hour) and 3 for severe/ marked sneezing (>7 times per hour). The children who did rubbing of nose i.e allergic salute, they were also categorized from 0 to 3, 0 for no, 1 for mild (1-3 per hour), 2 for moderate (4 - 6 per hour) and 3 for severe/ marked rubbing of nose (>7 times per hour). In case of children younger than 10 years, parents were interviewed about the symptoms score. The children were given oral antihistamine (loratidine), intranasal corticosteroids (budesonide), oral leukotriene receptor antagonist (montelukast) and intranasal xylometasoline (Xynosine nasal drops). Group A cases were advised treatment of allergic rhinitis (as mentioned above) along with daily Vitamin D supplement (800 IU daily orally). Group B cases were advised only the treatment of allergic rhinitis. All the cases were sent to laboratory of hospital for Serum Vitamin D level. The main circulating form of vitamin D is 25 hydroxyvitamin D {25(OH)D}. Total serum 25 hydroxyvitamin D {25(OH)D} level is considered a reliable indicator of body vitamin D level. The levels of 25(OH)D are categorized into following(9);

1. Vitamin D deficiency; 25(OH)D level less than 20 ng/mL.
2. Vitamin D insufficiency; 25(OH)D level of 20-29 ng/mL.
3. Vitamin D sufficiency; 25(OH)D level more than 30 ng/mL and above.
4. Vitamin D toxicity; 25(OH)D level more than 150 ng/mL and above.

The cases were advised to review after four weeks of treatment. On follow-up i.e after 4 weeks, any change in severity of symptoms of cases of both groups, was documented according to the criteria/scores mentioned above.

The data was analyzed with SPSS 21. Chi square was used to compare qualitative variables like gender etc and T test was used for quantitative variables like age etc. Consent was taken from parents of all participants and ethical committee approval was taken before the research.

Results

120 children of persistent moderate-severe allergic rhinitis, aged from 5 to 15 years were selected from outpatient department and included in the study. There were 64 (53.3%) males and 56 (46.7%) females. Mean age of children was 9.90 ± 3.06 years. Out of 120 children, 51 (42.5%) were Vitamin D deficient, 46 (38.3%) were Vitamin D insufficient and 23 (19.2%) had sufficient serum Vitamin D levels. Total 80.8% children with allergic rhinitis had low serum vitamin D levels. There was no case of hypervitaminosis D/vitamin D toxicity.

To compare serum 25(OH)D levels of allergic rhinitis cases with healthy children, we selected another 120 children of same age range (5-15 years). Among these healthy children, there were 61 males (50.8%) and 59 females (49.2%). They were comparable with cases of allergic rhinitis as shown in Table 1. Their mean age was 10.41 ± 3.07 . They were almost similar to allergic rhinitis cases in terms of age as well. In healthy children, there were 30.8% cases of vitamin D deficiency and 32.5% cases of vitamin D insufficiency (total 63.3% cases of low serum vitamin D) as compared to 36.7% children with normal serum vitamin D. In contrast 19.2% allergic rhinitis children had normal serum vitamin D levels.

Mean serum 25(OH)D levels of healthy children was 27.07 ± 11.45 as compared to 23.31 ± 11.92 of allergic rhinitis cases, having significantly higher serum 25(OH)D levels than allergic rhinitis cases ($p=0.013$). Similarly there were significantly less cases of 25 (OH)D deficiency and insufficiency in healthy children ($p=0.009$) as shown in Table 1.

Table1. Comparison of healthy children with cases of allergic rhinitis

Sr. #	Variable	Allergic Rhinitis Cases (N=120)	Healthy Children (N=120)	P value
1	Gender	Male 64(53.3%) Females 56(46.7%)	Males 61(50.8%) Females 59	0.698
2	Age	9.90 + 3.06 years	10.41 + 3.07 years	P=0.201
3	S. Vitamin D levels 25(OH)D	23.31 +11.92	27.07 + 11.45	P=0.013
4	Vitamin D Status	1. Vitamin D deficiency	37(30.8%)	P=0.009
		2. Vitamin D insufficiency	39(32.5%)	
3. Vitamin D sufficient	44(36.7%)			
	Total	120	120	

The cases of persistent moderate-severe cases of allergic rhinitis were put on treatment. They were divided in 02 groups of 60 each. Group A children were given standard treatment of allergic rhinitis along with daily vitamin D 800 units. However Group

B children were given only standard treatment of allergic rhinitis. Both the groups were comparable in terms of age, gender and serum Vitamin D levels as shown in Table 2.

Table 2. Comparison of the two groups (Group A & group B) of allergic rhinitis cases

Sr. #	Variables	GroupA	Group B	P value
1	Age	10.18+3.05	9.62+3.07	P=0.313
2	Gender	Male 33 Female 27	Male 31 Female 29	P=0.714
3	Serum Vitamin D levels 25(OH)D	22.64+12.85	23.99+10.98	P=0.536
4	Vitamin D Status	Deficient N=29 Insufficient N=21 Sufficient N=10 Total N= 60	Deficient N=22 Insufficient N=25 Sufficient N=13 Total N= 60	P=0.427

The cases of both groups (Group A & Group B) were assessed and their score of symptoms i.e rhinorrhea, itching, sneezing, nasal obstruction and nasal rubbing

were documented. Both the groups (all cases of allergic rhinitis) were comparable in terms of symptoms score and severity, as shown in Table 3.

Table 3. Symptoms score of two groups of allergic rhinitis cases before start of treatment

Sr. #	Symptom	Scores of Symptoms	Group A (N=60)	Group B (N=60)	Total (N=120)	P value
1	Rhinorrhea/ Flu At Start of Therapy	None	1	1	2	0.983
		Mild	10	10	20	
		Moderate	29	27	56	
		Severe	20	22	42	
2	Nasal Obstruction at Start of therapy	None	7	5	12	0.591
		Mild	4	4	8	
		Moderate	31	26	57	
3	Sneezing at Start of therapy	mild	9	4	13	0.293
		Moderate	30	30	60	
		Severe	21	26	47	
4	Itching at Start of therapy	Mild	15	18	33	0.827
		Moderate	34	32	66	
		Severe	11	10	21	
5	Nasal rubbing at start of therapy	Mild	9	13	22	0.557
		Moderate	31	31	62	
		Severe	20	16	36	

After 04 weeks of treatment, both the groups were assessed and their symptom scores were documented. Group A children receiving additional daily Vitamin D (800IU) had significantly better improvement in allergic rhinitis as compared to the group only

receiving allergic rhinitis treatment as shown below in Table 4. There was significant reduction in symptoms score of rhinorrhoea, nasal obstruction, sneezing and itching. There was also improvement in symptom of nasal rubbing but it was not significant (p = 0.092).

Table 4. Symptoms score of two groups of allergic rhinitis cases after 04 weeks of treatment

Sr. #	SYMPTOMS	SCORE OF SYMPTOMS	Group A (N=60)	Group B (N=60)	Total (N=120)	P value
1	Rhinorrhoea/ flu 04 weeks after Therapy	None	29	3	60	0.000
		Mild	31	57	60	
2	Nasal obstruction after 04 weeks therapy	None	25	11	36	0.010
		Mild	35	47	82	
		Moderate	0	2	2	
3	sneezing 04 weeks after Therapy	None	32	11	60	0.000
		Mild	28	49	60	
4	Itching 04 weeks after Therapy	None	32	19	51	0.016
		Mild	28	41	69	
5	Nasal rubbing 04 weeks after Therapy	None	49	41	90	0.092
		Mild	11	19	30	

Discussion

Deficiency of vitamin D is common in third world countries as well as developed countries and causes can be attributed to factors affecting UVB light, medical and nutritional. The former category involves people with dark skin colour, use of sun-block or other skin care products, inadequate exposure to sunlight either due to season or indoor routine and elderly due to the lack of 7-dehydrocholesterol in their skin. The second category involves a wide array of causes including nutritional deficiency, inadequate absorption due to certain pathological conditions including celiac disease, cystic fibrosis and surgical removal of intestinal part all leading to poor fat absorption affecting vitamin d as well as other fat soluble vitamins level. Other causes include obesity, chronic kidney disease and use of certain medications like anticonvulsants (10).

Allergic rhinitis is a common illness in children visiting outpatient department (11). It is associated with poor work performance and affects quality of life (12). Ahmad F et al reported that allergic rhinitis is prevalent in 24.62% of our population in Pakistan (13). Worldwide, prevalence of allergic rhinitis has been reported 9-42% (14) and 18-44% in parts of Asia (15). As already mentioned, Vitamin D is known to have role in immune and allergic phenomenon. Vitamin D deficiency is very common in our country. In South Asia, nearly 70% population has Vitamin D deficiency

and insufficiency (16) and 84% of healthy asymptomatic population in our country is Vitamin D deficient (17). According to another study, 78% of our population is vitamin D deficient (18). Immunoglobulin E (a mediator of allergy/hypersensitivity) has been documented to be inversely related to serum Vitamin D levels, ie increase in immunoglobulin E levels with decrease in serum Vitamin D levels (19).

In our study, we saw that patients with moderate-severe persistent allergic rhinitis had significantly lower serum levels of 25(OH)D levels than healthy children. Similarly, we found that group taking Vitamin D along with anti-allergy medication had significantly better improvements in symptoms. Many researchers have linked vitamin D with allergic diseases especially asthma. Tachimoto et al compared vitamin D supplementation with placebo in asthmatic children and found a significant improvement in vitamin D supplementation group (20). Similarly Uysalol et al had shown increased severity of asthma with decrease in Vitamin D levels (21).

Dogru and Suleyman compared serum 25(OH)D levels in children with allergic rhinitis and nonallergic rhinitis with control group and they reported that mean serum 25(OH)D levels were lower in children with allergic and nonallergic rhinitis as compared to control group (22). Similarly Arshi et al found significantly higher prevalence of serum 25(OH)D

level deficiency in allergic rhinitis patients than general population (23). Similarly other studies have shown lower serum 25(OH)D levels in allergic rhinitis cases as compared to healthy individuals (24).

This is the first study where we have not only compared serum vitamin D levels of healthy children with allergic rhinitis children (moderate-severe persistent disease) and also assessed efficacy of daily vitamin D supplementation on alleviation of symptoms of allergic rhinitis. We recommend prescription of daily vitamin D supplementation of such cases by doctors for better outcome and improving their quality of life and performance in our setups/country.

Conclusion

Children with persistent moderate-severe allergic rhinitis had significantly lower serum levels of serum vitamin D as compared to healthy children of same age and daily supplementation of vitamin D (400IU) helps alleviating the symptoms of allergic rhinitis in addition to standard therapy of allergic rhinitis.

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