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Serum Levels of Vitamin D in Patients with Allergic Rhinitis

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Abstract

The association between allergic diseases and vitamin D deficiency is a relatively novel topic that has gained the attention of scientists. In this study, we sought to evaluate the serum levels of vitamin D in patients with allergic rhinitis and compare them with those of healthy volunteers. This case-control study was performed during a one-year period (September 2015 to September 2016) on 100 patients with allergic rhinitis confirmed via the positive skin prick test (patients group) and 100 healthy subjects. The subjects were chosen by using the convenience sampling method, and they were matched with regards to age, gender, and socioeconomic status. The total mean level of vitamin D was 16.17±11.41 nmol/L (n=200), while it was 21.09±13.04 nmol/L in the normal population and 11.25±6.53 nmol/L in the patients with allergic rhinitis. The comparison of vitamin D level between the normal population and patient groups showed a significant difference between them (Z=-5.21, P≤0.0005). The comparison of the presence or absence of polyp in patients with allergic rhinitis showed a significant difference in vitamin D level between the subjects with polyp and those without polyp (t=4.74, P=0.03). The comparison of the subjects with allergic rhinitis showed no significant difference in vitamin D level between the patients with asthma and those without asthma (t=0.23, P=0.62). Based on our study, the level of vitamin D was lower in the patients with allergic rhinitis compared to the normal subjects. The prevalence of vitamin D deficiency was 67% in the allergic rhinitis patients. Our findings could be helpful in the therapeutic management of patients with allergic rhinitis, and in turn, improving their health.

Keywords: Allergic Rhinitis, Serum Level of Vitamin D, Asthma, Polyposis

Introduction

Allergic rhinitis (Hay fever) is an inflammatory reaction, which occurs when the immune system overreacts to some allergens; this disease involves 10-20% of the world population (Dykewicz & Hamilos, 2010). The prevalence of allergic rhinitis varies across different regions, which may be due to geographical and allergenic differences (Arshi and et al., 2012). The prevalence of allergic rhinitis is estimated at 17-25% in the USA (Meltzer, 1997). The prevalence of this condition in the pediatric population is reported to be 10.8%, and its incidence rate is constantly growing (Kong and et al., 2009). In India, allergic disorders are observed in 75% of children and 90% of adults (Bousquet and et al., 2003). A study performed in Japan pinpointed that the prevalence of these disorders has increased by nearly 10% during the past 10 years (Sakashita and et al., 2010). Furthermore, another study carried out in China revealed that the prevalence of this problem has grown in both adults and children over the past two decades (Xu and et al., 2016).

Although allergic rhinitis is not a life-threatening condition, it is a serious a systemic allergic disease that essentially hampers individuals' daily functioning (Lima and et al., 2007; Romano-Zelekha and et al., 2007). Therefore, investigating the etiology and risk factors associated with this disease is highly important. A link between low serum levels of vitamin D and immune system disorders was reported in various studies (Schauber & Gallo, 2008). The increasing rate of involvement with allergic diseases associated with vitamin D deficiency may be accounted for by the limited exposure of people to the sun due to spending more time indoors leading to lower cutaneous production of vitamin D (Litonjua & Weiss, 2007).

A wide range of substances such as cytokines and proteins may be at play in the pathogenesis of immune system disorders. Some cells such as eosinophils, neutrophils, T lymphocytes, macrophages, and epithelial cells contribute to the development of immune system disorders. Both interleukin 5 (IL5) and colony stimulating factor 2 (CSF2), a monomeric glycoprotein secreted by macrophages, are activated by type 2 T helper cells (Th2). This leads to angiogenesis, differentiation, and chemotaxis of eosinophils and IL-13, and consequently, enhanced airway remodeling and inflammation (Ingram & Kraft, 2012; Wolterink and et al., 2012; Muehleisen & Gallo,

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2013; Székely & Pataki, 2012).

Vitamin D, as a group of lipid-soluble Secosteroids, plays an important role in bone mineralization (Ryan and et al., 2013), which may be explained by its effect on T cells. There is an association between Th1/Th2 ratio and the elevated levels of inflammatory mediators and 25-hydroxyvitamin D (25[OH]D) produced by vitamin D in the liver (Maalmi and et al., 2012). Vitamin D can impact the immune system through the activation of regulatory T-cells and inhibition of B lymphocytes via reduced IgE production (Muehleisen & Gallo, 2013). There is a relationship between vitamin D deficiency and skin inflammation and atopic dermatitis (Vestita and et al., 2015). Considering the role of vitamin D in the prevention of autoimmune and allergic diseases, it can be used in the treatment of allergic reactions (Clifford and et al, 2009; Sidbury and et al., 2008).

The role of vitamin D in allergic rhinitis has been confirmed in some studies (2, Kim and et al., 2016). However, the relationship between the increasing incidence of allergic diseases and vitamin D deficiency and its underlying mechanisms and the impact of vitamin D deficiency on the immune system are still nebulous. Therefore, we aimed to determine the levels of vitamin D in patients with allergic rhinitis and compare them with those of healthy subjects.

Materials and Methods

This case-control study was performed on two matched allergic rhinitis and normal groups (n=100 per group) who presented to Ghaem and Imam Reza hospitals in Mashhad, Iran, for routine examinations during a one-year period (September 2015 to September 2016). The sample size was calculated based on the average of similar studies and considering 10% attrition rate (Thakkar and et al., 2014).

Allergic rhinitis, age 6-40 years, and oral informed consent were the inclusion criteria for participation in the study. The exclusion criteria included the use of any other drugs in addition to prescription drugs, especially anticonvulsants, oral contraceptives, vitamin D or its supplements, corticosteroids, or any other drugs interfering with vitamin D level, pregnancy, infection, immunodeficiency, cutaneous diseases, or allergy to prescription drugs.

We performed this study on 100 patients with allergic rhinitis confirmed via the positive skin prick test (patients group) and 100 healthy subjects. The subjects were chosen by using the convenience sampling method, and they were matched with regards to age (± 5 years), gender, and socioeconomic status.

Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines were used as the diagnostic criteria for allergic rhinitis (Brożek and et al., 2010). The skin prick test was carried out on the patients to determine specific IgE sensitivity to common aeroallergens by expert allergists. Twenty common regional allergens were tested on the skin, and skin reactions to these allergens were considered as a positive test. Based on this test, the patients were classified into the three groups of insufficient, sufficient, and deficient.

Demographic information, risk factors for allergic rhinitis, co-morbid diseases, disease symptoms, and medication history were recorded via a researcher-made questionnaire. This questionnaire was designed by comparing 15 standard allergy questionnaires, and then it was customized to regional characteristics.

To determine the level of vitamin D, blood samples of 2 ml were obtained from the participants. Before testing, the samples were centrifuged and stored at -70ºC. Moreover, 25(OH) D levels were measured by standard competitive protein-binding assay (CPBA) kit (DRG Instruments GmbH, Germany). Based on the standard criteria, 25(OH)D levels < 20 ng/ml, between 20-30 ng/ml, and ≥ 30 ng/ml were considered as deficit, insufficient, and sufficient, respectively (Calatayud and et al., 2009).

Finally, the obtained data were analyzed using SPSS software. The frequencies of all the variables were assessed and the proper statistical tests were used to compare the related variables. Mann-Whitney U test and Chi-square test were run for inter-group comparisons. P-value less than 0.05 was considered statistically significant.

Ethical considerations

Approval was obtained from the Ethics Committee of Mashhad University of Medical Sciences. All the ethical considerations, including confidentiality of the data and obtaining informed consent from the participants were observed. The stages and techniques of this study were clearly explained to the patients prior to the study. They were informed that they could withdraw from the study at any time.

Results

The mean age of the participants was 34.99±12.85 years (age range: 13 to74 years). The mean ages of the patient and normal groups were 34.68±13.31 and 35.29±12.44 years, respectively. The comparison of mean age showed no significant difference between the groups (Z=-0.82, P=0.408), which indicates that the comparison of the groups is acceptable.

Of the 200 patients enrolled in the study, 79 (39.5%) were male and 121 (60.5%) were female. About 44% of the patients with allergic rhinitis were male and 56% of them were female. Moreover, about 35% and 65% of the normal subjects were male and female, respectively. The two groups were not significantly different with respect to gender (χ^2=-1.69, P=0.19).

The mean level of vitamin D was 16.17±11.41 nmol/L in all the patients. This value was 21.09±13.04 nmol/L (range: 4 to 61.4) in the normal group and 11.25±6.53 nmol/L (range: 3 to 34) in the patients with allergic rhinitis. Characteristics of the subjects with and without allergic rhinitis based on vitamin D level are shown in Table 1. The comparison of mean level of vitamin D between the subjects with and without allergic rhinitis reflected a significant difference (Z=-5.21, P≤0.0005). Similarly, mean level of vitamin D was significantly different between those with asthma and those without this condition (Z=-5.45, P=0.04).

Overall, 26% of the participants with allergic rhinitis have asthma, and the frequency of polyp diagnosis was 42% in these patients. The mean vitamin D level in subjects with allergic rhinitis who have asthma and polyp is presented in Table 2.

The mean level of vitamin D was 10.13±5.28 nmol/L in patients with allergic rhinitis who had polyp, and it was 12.07±7.24 nmol/L in those without polyp. The comparison of patients with allergic rhinitis showed a significant difference in vitamin D level between the subjects with polyp and those without polyp (t=4.74, P=0.03).

The mean of vitamin D level was 10.97±6.82 nmol/L in patients with allergic rhinitis who had asthma, and it was 11.35±6.47 nmol/L in those without asthma. The comparison of the subjects with allergic rhinitis showed no significant difference in vitamin D level between the patients with asthma and those without asthma (t=0.23, P=0.62).

Discussion

We assessed the serum levels of vitamin D in patients with allergic rhinitis and compared them with those of normal volunteers. We found that the level of vitamin D was lower in the patients with allergic rhinitis compared to that in the normal subjects. Moreover, we noted a difference in the mean level of vitamin D between the two groups. The prevalence of vitamin D deficiency was estimated to be 67% in patients with allergic rhinitis.

Similar to our results, the prevalence of vitamin D deficiency was significantly higher in patients with allergic rhinitis compared to normal participants in a study by Moradzadeh et al. (Moradzadeh and et al., 2005). The prevalence rates of mild, moderate, and severe vitamin D deficiency in the normal Iranian population were estimated to be 27.2%, 42.8%, and 5.1% in a study by Moradzadeh et al. (Moradzadeh and et al., 2005). Compared to the findings of Moradzadeh et al., the rate of vitamin D deficiency was higher in our study. Diverse sample sizes and selection methods could account for this discrepancy. Moreover, the study by Moradzadeh et al. was performed on the normal population, while half of our participants had allergic rhinitis. We noted that the level of vitamin D plays a role in allergic rhinitis. Vitamin D deficiency was claimed to have a direct relationship with allergens in children, as such the risk of allergy in children with vitamin D deficiency was 2.4 times higher compared to healthy children (von Mutius and et al., 1998). Therefore, it could be argued that there is an association between serum level of vitamin D and risk of allergic rhinitis. Recently, the evaluation of vitamin D level has been considered a proper method for the diagnosis and management of various allergic diseases.

Multiple environmental factors in combination with different genes can cause autoimmune diseases, especially allergies, and identifying the exact etiology of these diseases is a challenging task due to their diverse forms (Hollis, 2008). There are essential differences between immunologic mechanisms and risk factors for autoimmune diseases and those conditions where allergy and autoimmunity co-occur. For example, Th2 cells are responsible for creating allergic asthma, while non-allergic asthma is characterized by neutrophilic inflammation independent of Th2 cells (Searing and et al, 2010). Proper identification of the causes and the risk factors for this problem is essential for establishing therapeutic strategies for the management of patients with autoimmune diseases and those with both autoimmune diseases and allergies. The association between vitamin D deficiency and allergy has been reported in a number of studies, and this association has been explained by the effect of vitamin D on T cells. Vitamin D regulates type 1 T helper cells (Th1) and induces regulatory T-cell function. The presence of increases the number of regulatory T cells and is responsible for suppressing autoimmune diseases. On the other hand, the stimulation of different cytokines by vitamin D impacts allergic reactions (Cantorna & Mahon, 2004).

Our findings showed that the level of vitamin D was lower in allergic rhinitis patients with asthma compared to those without asthma; however, this difference was not significant. Although we found no association between the serum level of vitamin D and asthma in patients with allergic rhinitis, in a similar study, vitamin D level was lower in patients with asthma compared to healthy subjects, which highlights the role of vitamin D in the pathogenesis of asthma (Tamašauskienė and et al., 2015). This finding was in line with the results of other studies (Tamašauskienė and et al., 2015; Li and et al., 2011). The discrepancy between our findings and those of other similar studies may be attributed to subjects' conditions or other confounding variables; therefore, further studies in this regard are recommended.

Vitamin D can influence the proliferation of airway smooth muscle cells via adjustment of gene transcription patterns (Bossé and et al., 2007). In a study by Tamašauskienė et al., eosinophils and IgE antibodies were ascribed to play an important role in allergic reactions, such that eosinophil count and total IgE were higher in allergic asthma patients compared to non-allergic asthma patients. The mentioned study did not find any correlation between eosinophil count in peripheral blood and total IgE in serum and vitamin D level. However, a negative correlation was noted between vitamin D level and eosinophil count in patients with multiple allergens (Tamašauskienė and et al., 2015).

IL-10, as an anti-inflammatory cytokine, adjusts cellular sensitivity to glucocorticoids in several types of leukocytes, and reduction in the level of this cytokine results in vitamin D deficiency (Urry and et al., 2012). Moreover, the secretion of some interleukins, which affect the pathogenesis of inflammation, is decreased due to vitamin D deficiency (Poon and et al, 2013). This mechanism contributes to the development of asthma. However, some studies did not find any association between vitamin D deficiency and the incidence of asthma (Mai, ans et al., 2012; Menon and et al., 2012). Overall, vitamin D deficiency may have an impact on the pathogenesis of allergic asthma. Nonetheless, considering the discrepant findings in this regard, no definitive conclusion can be drawn regarding the relationship between eosinophil count and total IgE and vitamin D (Li and et al, 2011; Ma and et al., 2011). Therefore, further studies are required to assess the relationship of eosinophil count in peripheral blood and total IgE with the level of vitamin D.

We also found that the level of vitamin D in allergic rhinitis patients with polyp was lower compared to those without polyp. Based on similar studies, VD3 deficiency is common in patients with chronic rhinosinusitis with nasal polyps (CRSwNP) compared to those without nasal polyps and healthy controls (Mulligan and et al, 2011; Schlosser and et al., 2014; Mulligan and et al., 2012). The incidence of VD3 deficiency is estimated at 55% in all CRSwNP patients, which varies across races (Schlosser and et al., 2014).

IgE and IFN-, IL-4, and IL-10 cytokines are indicators of Th1/Th2 balance in patients with allergic rhinitis and nasal polyposis. There is limited data on vitamin D level in patients with nasal polyposis and even on the association of polyposis and allergic rhinitis (Litonjua & Weiss, 2007; Ingram & Kraft, 2012; Wolterink and et al., 2012). Mulligan et al. reported that vitamin D deficiency is reported in chronic rhinosinusitis and allergic fungal rhinosinusitis patients with nasal polyps (Mulligan and et al, 2011). Moreover, the treatment of vitamin D deficiency in patients with nasal polyposis has been emphasized in some studies (Ozkara and et al., 2012; ostkowska-Nadolska and et al., 2010).

We suggest measuring the serum levels of vitamin D in the routine examination of allergic rhinitis patients. Our findings provide a deeper insight into the pathophysiology of allergic rhinitis and help experts to manage and choose the most efficient type of treatment. Future studies are recommended to be performed on various populations due to the lack of sufficient evidence in this regard.

Limitations and Strengths

The use of a control group is the main strength of our study, which allows comparison of the effect of serum levels of vitamin D with allergic rhinitis patients, while the only study performed on this issue compared serum levels of vitamin D in the general population. Limited sample size was the main limitation of this study. Lack of evaluation of systemic diseases and other intervening variables was another drawback of this study.

Conclusion

Comparison of vitamin D levels in subjects with and without allergic rhinitis showed that the level of vitamin D was lower in the patients with allergic rhinitis relative to the normal subjects. The prevalence of vitamin D deficiency was high in the allergic rhinitis patients. The results of this study can be helpful in the therapeutic management of patients with allergic rhinitis, and as a result, improving these patients' health. To gain a deeper understanding of the pathophysiology of allergic rhinitis, further extensive studies on the disease could be performed.

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Conflicts of interest: None declared.

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