



A Review on Serum Level of Vitamin D in Atopic March

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ARTICLE INFO

Article type

Review article

Article history

Received: 7 Jun 2018

Revised: 28 Jun 2018

Accepted: 17 Jul 2018

Keywords

Allergy

Atopy

Vitamin D

ABSTRACT

Recent studies have reported a relationship between vitamin D and atopic diseases such as asthma, allergic rhinitis, and atopic dermatitis, which is due to the recently discovered vitamin D receptors on many immune system cells. Among all atopic diseases, asthma has been studied the most in this regard. However, the role of vitamin D in other atopic diseases such as allergic rhinitis and atopic dermatitis is a matter of controversy. In this paper, we review the literature on the association between atopic diseases and vitamin D level with a focus on the childhood period. As of today, the role of vitamin D in atopic march is not clear and studies show controversial results. Therefore, further studies with adequate sample sizes and correction for perplexing factors are needed since this could be an innovative treatment in atopic children. It is also advisable to examine high-risk groups of children for vitamin D deficiency.

According to the extracted data, vitamin D has a protecting effect against atopic diseases. At the same time, no evidence was found for such an association in some studies, thus, further studies are needed to clarify this issue.

Please cite this paper as:

Amirian Z, Behmanesh F, Heidari E. A Review on Serum Level of Vitamin D in Atopic March. *Rev Clin Med.* 2018;5(3):111-114.

Introduction

Vitamin D is produced by the human body as a result of skin exposure to sunlight (UVB). In fact, the dietary share of overall vitamin D intake is limited, and endogenous synthesis is estimated to contribute to up to 90% of the total vitamin D in human body (1). Even though Iran is a subtropical country and it is expected to be able to gain enough sun exposure, there is extensive vitamin D deficiency among our children. A cross-sectional study on 196 children (from newborns to 18-year-old children) showed that 3.1% were vitamin D deficient and 19.4% had insufficient serum vitamin D (2). The most recognized role for vitamin D is calcium absorption and bone metabolism. Rickets in children and osteomalacia in adults are the most common presentations of vitamin D de-

ficiency (3).

The discovery of vitamin D receptor (VDR) and the hydroxylation of 25(OH)D on different cell types has led to the recognition of its immunomodulatory role in the human body. VDRs have been detected almost on every cell of the immune system (i.e., T cells, B cells, neutrophils, macrophages, and dendritic cells) (4). The association of vitamin D and reduction of Th1 cytokine secretion and inhibition of T cells proliferation has been revealed in recent studies. However, there are many contradictions about Th2 role and increased and decreased expression of Th2 cytokines, IL-4, IL-5, and IL-10 in adult peripheral blood cell cultures (5,6).

Studies in recent years have examined and re-

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ported the relationship between vitamin D and atopic diseases including asthma (7,8), allergic rhinitis (9), and atopic dermatitis (10). These studies that have investigated the associations of vitamin D status with allergic rhinitis, eczema, and asthma among children have reported contradictory findings (11-13).

Perhaps among different allergic disorders, asthma has been the most frequent one to be studied in association with vitamin D. Nonetheless, the evidence regarding the association between vitamin D status and atopic diseases other than asthma is weak and conflicting (14). Therefore, we performed a brief survey on the association between the serum level of vitamin D and atopic diseases such as asthma, allergic rhinitis, and atopic dermatitis.

Literature Review

Vitamin D and atopy

The contribution of both individual genetic susceptibility and exposure to environmental factors is needed to result in atopic diseases. One of these

environmental factors is the state of nutrition in early ages, which may affect the onset and course of these diseases. Vitamin D may also play a pivotal role as an environmental factor (15).

Males with inadequate vitamin D at 6 and 14 years of age have an increased chance of developing atopy, bronchial hyperresponsiveness, and asthma. Therefore, insufficient vitamin D at the age of 6 years can be a predictor of atopy and asthma at 14 years of age (16).

Investigation of the role of vitamin D in childhood asthma and allergies revealed the inverse correlation of serum 25(OH)D level in children with asthma, allergic rhinitis, and wheezing. Vitamin D insufficiency is a common finding, but it is more significant in children with asthma and allergic diseases than in healthy children (17).

On the other hand, some findings did not exhibit any associations between serum 25(OH)D concentrations and severity or prevalence of atopic diseases (diagnosis made clinically), but the prevalence of eczema is positively associated with serum 25(OH)D concentration (1) (Table 1).

Table 1. Summary of the preformed studies that investigate the association between vitamin D and risk of underlying disease.

Author Year Reference	Country	Patients: number and age	Underlying disease	Association between vitamin D and risk of underlying disease
Hollams 2011 (16)	Australia	989 6-yr-olds and 1,380 14-yr-olds	BHR, Atopy HDM sensitization	Inversely
Wawro 2014 (1)	Germany	2815 10-years old	eczema, allergic rhinitis, and asthma	positive association for eczema No association With atopy in general
Cairncross 2016 (18)	New Zealand	1329 children aged between 2 and <5 years	eczema, allergic rhinitis, and asthma	No associations
Sidbury 2008 (24)	Norway	11 2-13 years	Atopic dermatitis	Inversely
Aryan 2017 (20)	Tehran	21 observational studies	allergic rhinitis	Inversely
Tian 2017 (19)	China	Review article	allergic rhinitis	Inversely
Bener 2014 (17)	UK	1833 Qatari children	asthma, allergic rhinitis and wheezing	Inversely
Yao 2014 (3)	Taiwan	1315 Children aged 5-18 years	asthma, rhinitis, eczema, atopy	No associations
Mirzakhani 2015 (15)	USA	Review article	asthma, rhinitis, eczema, atopy	Inversely
Hoxha 2014 (14)	Albania	Review article	Asthma, and Allergic Rhinitis	Inversely
Kim 2016 (23)	Korea	Meta-Analysis	Atopic Dermatitis	Inversely
Vestita 2015 (22)	Italy	Review Article	Atopic Dermatitis	Inversely
Mesquita 2013 (26)	Brazil	Review Article	Atopic Dermatitis	controversial
Manousaki 2017 (27)	UK	33,996 children	atopic dermatitis asthma elevated IgE level	No associations

Studies performed on children aged between 2 and 5 years did not indicate any association between vitamin D level and eczema, atopic asthma, or allergic rhinoconjunctivitis (diagnosis made by parental acquired reports) (18).

Vitamin D and allergic rhinitis

Both experimental and clinical studies show a slight inverse correlation between allergic rhinitis and serum vitamin D concentration, although findings are very conflicting and inconsistent (19). Children with serum 25(OH)D \geq 75 nmol/L had significantly reduced the odds of aeroallergen sensitization compared to those with serum 25(OH)D $<$ 50 nmol/L, who did not receive vitamin neither during gestation nor during infancy, which can affect allergic rhinitis (AR) prevalence. Also, the risk of aeroallergen sensitization and allergic rhinitis in association with vitamin D is significantly related to age and sex as it is mainly observed in adult men (20).

It is claimed that 100 IU/day dietary intake of vitamin D during the first and second semesters of pregnancy is associated with 21% and 20% reduced risk of developing allergic rhinitis in future (21).

Studies discovered a high prevalence of vitamin D deficiency in children with asthma and allergic diseases. There is a strong correlation between asthma, allergic rhinitis, wheezing and vitamin D deficiency (17).

Vitamin D and atopic dermatitis

Recent studies have stressed the possible effect of vitamin D on atopic dermatitis, and therefore, the possible therapeutic role of vitamin D supplementation in the course of atopic diseases. Data obtained from basic studies support these findings by indicating that vitamin D plays a role in many aspects of the immune system on a molecular level (22). Serum 25(OH)D level in atopic dermatitis patients is significantly lower compared to healthy population in all ages. This is more prominent in children with atopic dermatitis (23).

Low levels of vitamin D have an inverse correlation with atopic dermatitis. Additionally, the low level of vitamin D at birth is a risk factor for developing atopic dermatitis in future. Moreover, a therapeutic course of vitamin D supplementation performed on children seemed to reduce the symptoms of atopic dermatitis during winter (24). This effect is probably due to the induction of endogenous antimicrobial peptides in the skin in atopic diseases by oral vitamin D supplementation (25).

Other articles concluded the role of vitamin D and its metabolites in maturation of the immune system either in prenatal or postnatal periods, but

its role in the development of cutaneous and respiratory allergic reactions remains controversial. They also suggested the enhancing and protecting effects of vitamin D against atopic diseases (26).

Another study found no evidence granting an increased risk of asthma, atopic dermatitis, or elevated total serum IgE due to low vitamin D levels, suggesting that it may not have therapeutic effects to reduce the risk of atopic diseases and addition of supplementation to patients' diet may not be beneficial (27).

Conclusion

In recent years, many studies have been published that described the role of vitamin D in various parts of the human body and its responsibility in developing diverse diseases. Furthermore, several studies have examined its effect on the immune system, and particularly allergic diseases. Different studies have shown this effect in developing asthma and airway hypersensitivity. Data obtained from basic studies support these effects of vitamin D on the immune system on a molecular level, showing that vitamin D acts on many different immune cell functions. It corroborates the idea that vitamin D can be used as a new treatment for these conditions that are gradually becoming more common. Studies present controversial results and further studies with adequate sample sizes and correction for perplexing factors such as sun exposure, food intake, or drug effects are currently much needed. It is also advisable to examine high-risk groups of children for vitamin D deficiency. These groups include children with a history of respiratory viral infections or atopy in early life.

Acknowledgements

We would like to thank Dr. Ezzat Khodashenas and Dr. Shirin sadat Ghiasi for their technical help.

Conflict of Interest

The authors declare no conflict of interest.

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