Editorial
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The Clinical Impact of Vitamin D in Children With Atopic Dermatitis

Jae-Won Oh*

Department of Pediatrics, Hanyang University College of Medicine, Guri, Korea

Recently there have been a number of reports that vitamin D plays a role in the pathogenesis of many diseases including atopic dermatitis (AD).[1,2] Considering the purported immunologic mechanisms that contribute to AD, it is possible that vitamin D may influence this disorder through its immunomodulatory properties.[3,4] It was well known the active form of vitamin D [1,25(OH)2 D3] enhanced expression of antibacterial peptides, and prevented skin infections. Some studies demonstrated a link between vitamin D–mediated activation of Toll-like receptors, the production of cathelicidin, and diminished sensitivity to bacterial infections.[5,6] In addition, vitamin D stimulates protein synthesis, such as filaggrin, that is necessary for stratum corneum barrier formation. Therefore, vitamin D deficiency might exacerbate AD via disturbed epidermal barrier function and immunologic dysregulation, with subsequent impaired defense against infections. Clinical observations indicate that the disease usually worsens in winter season as a result of less exposure to solar radiation. Epidemiologic investigations have shown a higher prevalence of AD in countries with higher geographic latitude.[7,8] This is consistent with other observations that inhabitants of urban countries at high latitudes often have low vitamin D levels. Javanbakht et al revealed that additional factors, besides geographic locations, may influence vitamin D level in patients with AD.[9]

Lee's study in this issue found an inverse correlation between serum concentration of vitamin D and severity of the disease expressed by SCORAD index in children with AD associated with food allergy.[10] The result from this study also did not prove such a correlation in SCORAD index and any of its parameters and it could be explained by the influence of other environmental factors on the course of the disease. Perhaps other extrinsic factors, such as sweat or clothing, can irritate and exacerbate skin inflammation in a setting of low vitamin D levels. The deficiency of vitamin D is responsible for the most intensive skin lesions localized on body regions not exposed to sun. Vitamin D is poorly produced by cloth-covered skin, which suggests a possible local beneficial effect of vitamin D generated in the skin to protect against the development of AD lesions.

Furthermore significantly higher rates of food allergy in children born autumn/winter compared to spring and summer suggest a relationship between relative food allergy rates and monthly UV irradiation. Mullins et al. hypothesized that UV light exposure and vitamin D status may be one of many potential factors contributing food allergies in childhood.[10] Multiple reports suggested which the lack of vitamin D impairs the epithelial barrier integrity leading to increased and inappropriate mucosal exposure to food antigens. Thereby vitamin D deficiency would also promote a pro-sensitization immune imbalance that compromises immunologic tolerance. The authors hypothesized that early correction of vitamin D deficiency might promote mucosal defense, maintain a healthy microbial barrier and food allergen tolerance in children.[11,12]

The fact that vitamin D stimulates keratinocytes to produce antimicrobial peptides may explain why skin infections may occur more often during the winter season. 3-week supplementation with 1,000 IU/day vitamin D resulted in an increased expression of cathelicidin belonging to antimicrobial peptides family. These observed improvement of SCORAD index, with a decrease in mean index for lichenification and pruritus, and reduction of AD severity.[13] Possibly, it demonstrates a regulatory effect of vitamin D on the immune response. Vitamin D stimulates production of antimicrobial peptides in the epidermis and, in turn, reduces skin colonization by *Staphylococcus aureus*.[14]

Correspondence to: Jae-Won Oh, MD, PhD, Department of Pediatrics, Hanyang University College of Medicine, 153 Gyeongchun-ro, Guri 471-701, Korea.
Tel: +82-31-560-2254; Fax: +82-31-552-9493; E-mail: jaewonoh@hanyang.ac.kr
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Vitamin D has become the subject of intensive research as an immune regulator both of the innate and adaptive immune system.[15,16] Interestingly, vitamin D affects different aspects of innate immunity. On the one hand, vitamin D decreases the expression of immune receptors and co-stimulatory molecules inhibiting dendritic cell activation by LPS. Furthermore cytokine secretion declines and leads to reduced antigen presentation. On the other hand, vitamin D helps to defend opportunistic infections by inducing autophagy in human macrophages and to support the innate skin barrier by stimulating endogenous AMP expression in resident epithelial cells of the skin and lung. As a consequence, vitamin D decreases pro-inflammatory cytokine released from T cells. Therefore Vitamin D inhibits T cell proliferation through decreased Th1 cytokine secretion. Vitamin D suppresses adaptive immunity by inhibition of antigen presenting cells. B-cell proliferation and immunoglobulin production can be inhibited by vitamin D. Vitamin D also effects B lymphocyte functions and modulates the humoral immune response including secretion of immunoglobulin E (IgE).

In conclusion, it was suggested that supplementation of vitamin D might improve barrier function and thus inflammation in AD. Vitamin D plays an important role in antimicrobial cutaneous immunity when identifying a vitamin D response element in the promoter region of the cathelicidin gene. Multiple elements in the molecular mechanisms of vitamin D mediated cathelicidin expression have been characterized. Thus, a direct connection between vitamin D metabolism and cutaneous innate defense function was established. Thus, elevating vitamin D levels in the serum may help to strengthen the innate cutaneous and mucous defense barriers to prevent cutaneous infections which could serve as cofactors for allergic sensitization as well as to maintain food allergen tolerance as Lee's study suggested.

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