Letter to the Editor

Vitamin D and diabetic foot ulcers: A missed topic

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Dear Editor,

Diabetic Foot Ulcers (DFU) is the most catastrophic complication of diabetes mellitus affecting more than 25% of diabetic patients. DFU is the first cause of non-traumatic lower extremity amputation. Amputation following DFU has a negative impact on a patient's quality of life and a high economic burden on the healthcare system [1, 2].

In the past few years, there has been growing evidence for the role of vitamin D and its metabolites in many biological processes, such as wound healing [3].

Vitamin D is a fat-soluble hormone that is basically synthesized in the human skin from 7-dehydrocholesterol after exposure to sun ultraviolet B light. Although vitamin D is available in some foods and supplements, its primary source is sun exposure. Then, vitamin D will be hydroxylated to 25-hydroxyvitamin D (25(OH)D3) in the liver. Finally, via the action of 1α-hydroxylase, it will be hydroxylated to 1, 25 dihydroxy vitamin D (1, 25(OH)2D3), which is the active form of vitamin D in many cells [3, 4]. The major circulating form of vitamin D is 25(OH)D3. Its normal plasma range is about 30–80 ng/mL, and 25(OH)D3 values below 30 and 10 ng/mL will be considered vitamin D insufficiency and deficiency, respectively [5].

Previous studies have shown that vitamin D has an important role in immune system regulation and signaling pathways involved in wound healing [6, 7]. It has been reported that patients with diabetes have lower circulating vitamin D levels than healthy controls [8]. However, recent studies found that patients with DFU have lower vitamin D levels than diabetic patients without foot complications [9, 10]. For example, a meta-analysis on 1644 diabetic patients showed that the odds of vitamin D deficiency were 3.6 greater in patients with DFU than diabetic patients without foot complications [11].

25(OH)D3 and its active metabolite 1, 25(OH)2D3 play a crucial role in the growth and differentiation of fibroblasts and keratinocytes by modulating growth factors and cytokines such as transforming growth factor beta (TGF-β), epidermal growth factor (EGF), platelet-derived growth factor (PDGF), interleukin 1-α (IL-1α), IL-6, and IL-8, respectively [10].

Moreover, the role of vitamin D in the prevention of DFU infection through the stimulation of antimicrobial peptides such as cathelicidin and some defensins has been recognized in recent studies [12, 13]. Vitamin D has the ability to induce the expression of cathelicidin in many cells, such as keratinocytes. Cathelicidin has many pleiotropic roles in immunomodulation (immune cells chemotaxis, production of cytokines and chemokines), cell growth and proliferation, increasing vascular permeability and, wound healing [12, 14].

Patients with chronic DFU have lower vitamin D levels and cathelicidin production, resulting in infection and delayed wound healing [14]. To conclude the importance of vitamin D status and considering the beneficial effects of vitamin D on the immune system and wound healing, measurement of vitamin D and its supplementing is recommended to improve the outcomes of patients with diabetic foot complications.

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Conflict of interest
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