Commentary

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Potential Role of Vitamin D Supplementation in Systemic Vasculitis

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Vitamin D (VD) plays a significant immunomodulatory role in various autoimmune diseases, including systemic vasculitides. This short review evaluates the existing literature on VD supplementation (VDS) in systemic vasculitis. A systematic search identified two studies focusing on Kawasaki disease (KD) and Henoch-Schönlein purpura (HSP). Both studies suggest potential benefits of VDS in reducing disease onset and recurrence, as well as modulating immune responses. Although current evidence is limited, findings support further investigation into VD as an adjunctive therapeutic strategy in vasculitis.

Keywords: vitamin D; vasculitis; Kawasaki disease; Henoch-Schönlein purpura; supplementation; immunomodulation

Introduction

Vitamin D (VD), traditionally recognized for its role in calcium and bone metabolism, has garnered substantial attention due to its immunomodulatory effects. VD deficiency is a global health issue, prevalent even in regions with adequate sunlight exposure. Its deficiency has been consistently reported in autoimmune diseases such as systemic lupus erythematosus, rheumatoid arthritis, and multiple sclerosis [1]. In recent years, systemic vasculitides, a group of disorders characterized by inflammation of blood vessels, have also been associated with low VD levels [2]. These findings raise the hypothesis that VD supplementation (VDS) could modulate disease activity or outcomes in vasculitis.

Systemic vasculitides, including Kawasaki disease (KD), Henoch-Schönlein purpura (HSP), Takayasu arteritis, and antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis, present diagnostic and therapeutic challenges [3]. The search for safe and effective adjunctive therapies remains essential. Given the known anti-inflammatory properties of VD, its supplementation may hold potential as a supportive intervention. This review evaluates the current evidence on VDS in systemic vasculitis.

Methods

A comprehensive literature search was performed using PubMed, Scielo, and LILACS databases from January 1965 to April 2024. The search terms included "vitamin D", "supplementation", and "systemic vasculitis". Inclusion criteria encompassed studies that evaluated the impact of VDS in patients with systemic vasculitis, regardless of patient age, study design, or language. Exclusion criteria included studies focusing on VD levels without intervention and case reports. The review adhered to PRISMA guidelines to ensure methodological rigor.

Two studies [4,5] met the inclusion criteria and were included in this review. Data extracted included study design, population characteristics, type of vasculitis, VD formulation and dosage, outcomes measured, and adverse effects.

Results

The two studies that met the criteria are summarized in Table 1 (Ref. [4,5]). The first study by Meyer *et al.* (2019) [4] was a population-based case-control study from Germany involving 308 children with KD and 326 controls. It investigated the role of breastfeeding and VDS as protective factors against the onset of KD. VD supplementation (400–500 IU/day) and breastfeeding were negatively associated with KD. Importantly, children with KD had a shorter duration of VDS than controls.

The second study by Fu *et al.* (2021) [5] was a prospective randomized controlled trial conducted in China with 200 children diagnosed with HSP. Patients receiving oral alfacalcidol (0.25 µg/day) for 4 weeks had a lower recurrence rate and reduced incidence of renal complications compared to controls. Immunological assessment revealed increased levels of CD3+ and CD4+ T cells and NK cells, along with decreased levels of IL-6, IL-17, IL-21, and TNF.

Table 1. Summary of studies on vitamin D supplementation in systemic vasculitis.

Author, reference	Study design	Country	N, age, gender	Systemic vasculitis	Disease duration	Treatment regimen	Follow-up	Outcome	Side effects
Meyer *et al*., 2019 [4]	Population based case-control study	Germany	308 KD and 326 controls, 6.5 yo, 63% males	Kawasaki disease	ND	400–500 IU/day	2012–2014	VDS and breastfeeding were negatively associated with KD. VDS duration was shorter in KD. There are no differences regarding developing coronay aneurism, being refractory to intravenous immunoglobulin treatment, age at onset of the disease, and levels of inflammatory laboratory values.	ND
Fu *et al*., 2021 [5]	Prospective randomized controlled trial	China	200 (100 VDS and 100 controls), 6.5 ± 6.1 yo, 59% males	Henoch-Schönlein purpura	3.5 ± 1.1 years	Alfacalcidol (0.25 µg/d) orally for 4 weeks	6 months	The recurrence rate and the incidence of renal damage in the VDS group were lower than in the control. Higher VD, percentages of CD3+T cells, CD4+T cells, and NK cells, and lower levels of IL-6, IL-17, IL-21, and TNF.	ND

KD, Kawasaki disease; N, number; ND, not described; yo, years old; VDS, vitamin D supplementation; VD, vitamin D.

Discussion

The reviewed studies suggest a potential immunomodulatory role for VD in systemic vasculitis, particularly in pediatric populations. In the KD study [4], VDS appeared to reduce the risk of disease development, though causality cannot be inferred. It is plausible that VD may exert protective effects through modulation of innate and adaptive immunity, given its ability to suppress pro-inflammatory cytokines and enhance regulatory T cell responses.

In the HSP trial [5], the impact of VD on recurrence and renal involvement is particularly noteworthy. The observed changes in T cell subsets and cytokine profiles underscore the biological plausibility of VD's immunomodulatory actions. These findings align with broader research suggesting that VD deficiency correlates with increased disease activity in autoimmune conditions.

Nevertheless, these data should be interpreted cautiously due to the limited number of studies and the heterogeneity in study design, population, and outcomes. The lack of studies in adult populations and in other forms of vasculitis, such as Takayasu arteritis and ANCA-associated vasculitis, represents a significant gap.

Despite the limitations, the review highlights several strengths: use of well-defined disease criteria, inclusion of all available research without language restriction, and application of a systematic search strategy. Future studies should aim to investigate VD's impact across diverse vasculitis subtypes, utilizing standardized dosing regimens and long-term follow-up.

Conclusion

VD supplementation shows potential as an adjunctive strategy in the management of systemic vasculitis, particularly in pediatric cases of KD and HSP. The current evidence, though limited, supports further investigation through well-designed randomized controlled trials in both pediatric and adult populations. Identifying optimal dosing, treatment duration, and immunological markers of response will be crucial to establishing VDS as a viable therapeutic approach in vasculitis.

Author Contributions

JFdC designed the commentary; JFdC and ATAM performed the commentary. JFdC and ATAM have been involved in drafting the manuscript and both authors have been involved in revising it critically for important intellectual content. Both authors gave final approval of the version to be published. Both authors have participated sufficiently in the work to take public responsibility for appropriate portions of the content and agreed to be accountable for all aspects of the work in ensuring that questions related to its accuracy or integrity.

Ethics Approval and Consent to Participate

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Conflict of Interest

The authors declare no conflict of interest. Jozélio Freire de Carvalho is serving as one of the Editorial Board members of this journal. We declare that Jozélio Freire de Carvalho had no involvement in the review of this article and has no access to information regarding its peer review.

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