International Journal of Research in Dermatology
Herrick G et al. Int J Res Dermatol. 2025 Mar;11(2):199-207
http://www.ijord.com

DOI: https://dx.doi.org/10.18203/issn.2455-4529.IntJResDermatol20250443

Review Article

Evaluating the impact of high-dose vitamin D3, vitamin C, vitamin E, and zinc supplementation on inflammatory cytokines, lesion severity, and symptom management in hidradenitis suppurativa

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Received: 05 November 2024
Accepted: 18 February 2025

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ABSTRACT

This integrative, holistic review critically evaluates the impact of high-dose vitamin D3, vitamin C, vitamin E, and zinc supplementation on inflammatory cytokine levels, lesion severity, and symptom management in patients with hidradenitis suppurativa (HS). By integrating data from recent clinical trials and observational studies, we explore how these supplements influence key aspects of HS pathology. High-dose vitamin D3 has been shown to significantly reduce levels of inflammatory cytokines and decrease lesion severity, suggesting its role in modulating immune responses and improving disease outcomes. Similarly, the antioxidant properties of vitamins C and E are assessed for their ability to reduce oxidative stress and inflammation, which may lead to improved symptom management and reduced severity of HS lesions. Zinc supplementation, particularly in the form of zinc sulfate, is examined for its effects on enhancing skin barrier function and decreasing the frequency of disease flares. Collectively, these nutritional interventions may offer a multifaceted approach to HS management, highlighting the potential for combining these supplements to optimize therapeutic outcomes. The findings underscore the need for further research to determine the optimal dosing, duration, and interaction of these supplements with standard HS treatments to establish comprehensive management protocols.

Keywords: Integrative, Holistic review, Vitamins C and E

INTRODUCTION

Hidradenitis suppurativa (HS) is a chronic inflammatory disorder characterized by the formation of nodules, cysts, open comedones, and scarring.[1] The pathogenesis of HS is rooted in the occlusion of the follicular portion of the folliculopilosebaceous unit, with common lesion sites including the axillary, inguinal, and perineal regions.[1] The prevalence of HS is approximately 0.40%, and the average age of diagnosis is around 21 years, with a general decline in prevalence observed as individuals age.[3] In addition to its visible symptoms, HS lesions can be painful and malodorous, contributing to significant physical discomfort and a profound psychosocial impact,

leading to diminished self-esteem and quality of life. Due to the chronic and recurrent nature of HS, treatment strategies are continuously evolving, with emerging evidence suggesting that certain supplements may improve disease outcomes.

The pathophysiology of HS is primarily attributed to its classification as a follicular occlusive disease, where the obstruction of the follicle with keratin can lead to rupture and the formation of skin tunnels beneath the surface. These tunnels can later emerge on the skin, perpetuating chronic inflammation.[2] Dysregulation of the immune system further contributes to the disease process, particularly through the action of proinflammatory cytokines such as TNF-α, which has been shown to be elevated in both serum and lesional skin.[4] Additionally, the IL-1β-IL-23/TH17/IL-17 signaling pathway is believed to play a significant role in the pathogenesis of HS, with these cytokines frequently observed in lesional skin.[4] Current treatment modalities for HS focus on preventing the development of new lesions, managing symptoms, and improving the quality of life. However, the varied presentations and progression of HS make treatment challenging. For mild inflammatory lesions, oral tetracyclines, often combined with antiandrogenic drugs or metformin, are the first line of treatment.[2] For more severe cases, oral clindamycin and rifampin are commonly used, with TNF-α inhibitors such as adalimumab considered when antibiotic therapy fails.[2]

Despite the availability of these treatments, the mechanisms by which they exert their therapeutic effects remain under investigation. Moreover, supplementary approaches, such as zinc, Vitamin D3, Vitamin C, and Vitamin E, may provide additional benefits in reducing inflammation and managing symptoms, offering a more holistic strategy for optimizing treatment efficacy. This review aims to explore the efficacy of zinc, Vitamin D3, Vitamin C, and Vitamin E supplementation in HS management, with a focus on their anti-inflammatory and immunomodulatory roles. Evidence suggests that these supplements can positively impact patient outcomes, as Vitamin D3 has been shown to enhance innate immunity and reduce the number of skin nodules, while Vitamins C and E exert anti-inflammatory effects, and zinc offers both anti-inflammatory and antiandrogenic benefits.[2] Beyond the individual benefits of these supplements, this review also explores the potential for synergistic effects when used in combination, aiming to contribute to the development of novel therapeutic strategies that may optimize outcomes for individuals with HS.

DISCUSSION

Impact on inflammatory cytokines

Mechanistic insights

Vitamin D3, a secosteroid hormone, has garnered significant attention due to its role in modulating immune responses, particularly in chronic inflammatory conditions like hidradenitis suppurativa (HS). This hormone influences immune activity by acting on T cells and macrophages to suppress the production of pro-inflammatory cytokines. Researchers such as Campione et al. have discussed how Vitamin D3 can effectively reduce concentrations of TNF-α, IL-1β, and IL-6—cytokines that drive the chronic inflammation observed in HS.[5] Campione et al, also emphasize the significance of elevated levels of TNF-α, IL-1β, IL-12/23, and IL-17, which not only sustain inflammation but also impair normal immune function, contributing to the formation and persistence of HS lesions.[5] In addition to its effects on pro-inflammatory mediators, Vitamin D3 enhances the production of anti-inflammatory cytokines such as IL-10, promoting a more balanced immune response.

The role of TNF-α in HS is particularly critical. Chu et al. illustrate that TNF-α is a primary driver of inflammation in HS, initiating a cascade of immune reactions that exacerbate lesion development.[6] Through binding to TNFR1 and TNFR2 receptors, TNF-α activates pathways like NF-κB, further amplifying inflammatory signals and worsening the skin inflammation that characterizes HS.[6] Modulating these inflammatory pathways by reducing TNF-α activity with Vitamin D3 supplementation creates a less inflammatory environment, which is crucial in preventing lesion formation and reducing disease severity.

In addition to immunomodulatory effects, Vitamin D3 supports the function of epidermal cells, contributing to the maintenance of the skin barrier, which is often compromised in patients with HS. Vitamins C and E complement this process by managing inflammation through their well-known antioxidant properties.[7] Reactive oxygen species (ROS), generated as part of the immune response in HS, contribute to cellular and tissue damage, further perpetuating the inflammatory cycle.

Both Vitamin C and Vitamin E serve as powerful antioxidants, neutralizing these ROS and protecting cells from oxidative stress. This reduction in oxidative damage helps disrupt the cycle of inflammation, which plays a significant role in exacerbating HS lesions. Additionally, zinc is an essential supplement in HS management, playing a multifaceted role in immune regulation. Zinc influences the activity of immune cells, particularly neutrophils and macrophages, which are involved in the early stages of HS lesion development.[8] By inhibiting the release of pro-inflammatory mediators, zinc reduces inflammation and helps restore immune balance in the skin. Together, these supplements target key components of the inflammatory process, offering promising adjunctive strategies for managing HS.

Potential clinical implications

Patients with inflammatory skin disorders who received supplementation showed decreased levels of ROS and a

corresponding decline in cytokine-driven inflammation. Abdulhameed et al, demonstrated vitamin C's ability to scavenge ROS enhances cell survival and promote wound healing by supporting collagen production and reducing inflammatory mediators.[9]

This suggests that Vitamin C supplementation could play a role in decreasing lesion severity in HS by addressing the underlying oxidative stress and inflammation that drive lesion formation. Zinc supplementation has also been explored in both dermatological and systemic inflammatory diseases, with findings highlighting its ability to suppress the production of pro-inflammatory cytokines. Weir et al, report that oral zinc supplementation has been associated with partial remission in over 60% of HS patients, improving the severity of lesions and reducing the frequency of disease flares.[8] This supports the use of zinc as a non-pharmacologic approach to managing HS lesions, especially in patients who are deficient in this mineral.[8] Collectively, these studies underscore the potential for these supplements to reduce inflammation in HS, providing a foundation for their use as adjunct therapies in managing the disease.

The reduction in cytokine levels achieved through supplementation with Vitamin D3, vitamins C and E, and zinc holds significant clinical implications for HS patients. By lowering levels of TNF-α, IL-1β, and IL-6, these supplements could help mitigate the chronic inflammation that drives lesion formation and disease progression in HS. The reduction in inflammation is likely to result in fewer disease flares, a decrease in the severity of lesions, and an overall improvement in patient outcomes.

For patients with mild to moderate HS, supplementing with these vitamins and minerals could offer a less invasive alternative to systemic treatments, potentially delaying the need for more aggressive interventions like surgery or biologics. Molinelli et al, found that zinc, when used as a maintenance therapy, significantly extended disease-free survival and reduced the frequency and duration of acute flares in patients with mild to moderate HS.[10] These findings suggest that zinc could serve as a valuable adjunct to existing treatments, offering a less invasive and cost-effective option for long-term management.

Furthermore, early intervention with these supplements may prove to be a valuable strategy in preventing disease progression. By addressing the inflammatory component of HS early in its course, clinicians may be able to reduce the development of severe lesions and scarring, improving long-term outcomes. These supplements could also enhance the efficacy of existing treatments, such as antibiotics or biologics, by targeting different aspects of the disease. Ultimately, the integration of supplementation into HS management protocols could offer a more comprehensive approach to controlling inflammation and improving patient quality of life.

Effect on lesion severity

Oxidative stress is a key contributor to the pathogenesis and persistence of HS lesions, creating a vicious cycle of inflammation and tissue damage. Lackner et al, found that Vitamin D deficiency correlates with a higher severity of HS lesions, as measured by clinical severity scores such as the sartorius score and international hidradenitis suppurativa severity score system (IHS4).[11] The inverse relationship between Vitamin D levels and lesion severity suggests that correcting Vitamin D deficiency could play a crucial role in reducing both the number and size of HS lesions.[11] In one case study, a 31-year-old African American female with severe Vitamin D deficiency experienced a full resolution of skin lesions, joint pain, and fatigue following high-dose Vitamin D supplementation, further supporting the potential benefits of correcting Vitamin D levels in inflammatory skin conditions like HS.[12]

The report emphasizes the need to recognize and treat vitamin deficiencies as part of HS management, as deficiency can exacerbate inflammatory conditions. In HS, ROS are generated as part of the inflammatory process, causing significant damage to skin cells and contributing to the breakdown of tissue in affected areas. The oxidative environment promotes a continuous immune response, which leads to the exacerbation of existing lesions and the formation of new ones.

By perpetuating inflammation, oxidative stress directly influences the chronicity and severity of HS lesions, making it a critical target for intervention. Another report involving Recurrent Intraoral Herpes (RIH) found that Vitamin D deficiency was associated with persistent mucosal lesions, which healed completely after supplementation, emphasizing the nutrient's role in modulating inflammation and reducing oxidative stress.[13] These cases highlight that Vitamin D supplementation can be a crucial factor not just in managing HS but also in other inflammatory diseases driven by oxidative stress.

Advanced wound management techniques, such as the use of oxygen-enriched oil-based dressings, have been shown to modulate oxidative stress by providing a moist microenvironment and a prolonged release of ROS, which encourages angiogenesis, cell proliferation, and collagen synthesis in HS wounds.[14] These strategies align with the role of zinc and vitamin D3 in reducing inflammation and supporting skin barrier function, as both supplements contribute to the modulation of immune responses and enhancement of wound healing processes. The addition of these supplements may help strengthen the skin's natural defense against further damage and lesions. Additionally, a study on dental implants in a vitamin D deficient patient demonstrated that supplementation improved the healing process,

suggesting a role for vitamin D in wound repair and tissue recovery in HS lesions.[15] NPWT, in particular, has been noted for its ability to decrease inflammatory mediators and promote faster wound closure, further reinforcing the importance of anti-inflammatory interventions in HS management.[14] By targeting both inflammation and oxidative stress, supplementation may address two major drivers of lesion formation, providing a multifaceted approach to disease management. Shen et al. also report that zinc plays a crucial role in modulating the immune system by reducing reactive oxygen species (ROS), matrix metalloproteinases (MMPs), and pro-inflammatory cytokines such as IL-1β and TNF-α.[16]

This modulation of the inflammatory environment can help reduce the number and severity of HS lesions.[16] In this way, the synergistic effect of multiple supplements could provide comprehensive benefits by addressing the root causes of inflammation and tissue damage. By supporting the skin's healing processes, the antioxidants can potentially accelerate recovery from active lesions. These vitamins help stabilize cellular membranes, protect against DNA damage, and reduce the inflammatory signals that drive lesion formation in HS.

The potential to prevent new lesion development, coupled with faster recovery from active flares, makes supplementation a promising addition to HS management protocols. Additional evidence from a clinical trial on diabetic foot ulcers (DFU) demonstrated that Vitamin D supplementation significantly improved wound healing, reducing ulcer depth and inflammatory markers such as C-reactive protein and ESR, reinforcing Vitamin D's role in modulating oxidative stress in chronic wounds.[17] The demonstrated wound healing further supports the idea that Vitamin D's role in managing chronic inflammation extends beyond HS, showing its broader impact on healing persistent wounds.

Integration into HS management For patients who are already receiving systemic therapies, such as antibiotics or biologics, supplements like vitamin D3, vitamins C and E, and zinc may provide additional benefits by addressing inflammation and oxidative stress at a different level. Siregar et al, emphasize the role of vitamin D in the wound-healing process by enhancing the proliferation and differentiation of keratinocytes, modulating immune responses, and reducing inflammation.[18]

These effects are particularly beneficial for HS patients, where wound healing is often delayed, and lesions persist due to chronic inflammation. The non-invasive nature of supplementation makes it an attractive option for patients who are hesitant to pursue more aggressive treatments, such as surgery or laser therapy.[18] Moreover, the timing of supplementation is crucial, with some evidence suggesting that early intervention may prevent the escalation of lesion severity. One study also showed that vitamin D supplementation led to decreased oxidative stress and enhanced fibroblast activity, further supporting its role in tissue regeneration and wound healing.[19] Hewlings et al, work involving chronic wounds reported a significant correlation between low Vitamin D levels and delayed healing, suggesting that Vitamin D supplementation can improve outcomes in hard-to-heal lesions.[20] These findings highlight the importance of early intervention in managing inflammatory skin conditions to prevent lesion progression.

Practical considerations for integrating supplementation into HS management include determining the appropriate dosing, timing, and monitoring of potential interactions with other therapies. High-dose supplementation should be tailored to individual patients, taking into account factors such as baseline nutrient levels, disease severity, and overall health. Clinicians must also be mindful of the potential risks associated with high-dose supplementation, such as hypercalcemia with vitamin D3 or gastrointestinal issues with zinc.

Despite these considerations, the potential for supplements to reduce lesion severity and improve patient quality of life makes them a valuable adjunct to traditional HS therapies. In fact, long-term studies on vitamin D's antioxidant and anti-inflammatory properties have demonstrated its benefits in reducing systemic inflammation and oxidative stress, which are key drivers in chronic inflammatory diseases like HS.[21] By integrating supplements into a comprehensive treatment plan, patients may experience better overall outcomes, including reduced lesion formation and faster recovery times.

Symptom management and quality of life

Patient-reported outcomes

Patients with hidradenitis suppurativa endure a debilitating physical and psychological burden due to symptoms such as pain, odor, drainage, and pruritus. The severity of the disease, location of lesions, and frequency of flares further exacerbate the negative impact on quality of life. A direct relationship between the severity of symptoms and quality-of-life measures, particularly in relation to outcomes such as anxiety, depression, sleep disturbances, sexual dysfunction, work productivity, and leisure activities has been appreciated amongst researchers.[22,23]

Follicular occlusion in HS lesions causes painful, pruritic lesions that often suppurate and release odorous drainage across multiple body sites, including the axillae, inframammary folds, and inguinal and perianal regions.[23] Pain is the most frequently reported symptom, affecting over 95% of patients, often with greater severity than in many other dermatologic conditions.[22] On average, pain scores on the NRS scale (0-10) range from 3.6 (SD 3.2) to 7.7 (SD 2.1), indicating moderate to severe pain levels.[23] Odor, while less studied, has shown patient-

reported scores on the NRS scale ranging from 3.28 (SD 3.58) to 5.6 (SD 3.38), representing mild to moderate levels of discomfort.[22] The hidradenitis suppurativa odor and drainage scale (HODS), a novel tool for measuring drainage severity, shows promising clinical utility but remains in its early stages of development.[24] Nonetheless, HODS scores correlate with other validated quality-of-life measures, including the dermatology life quality index (DLQI).[24] Itching, reported by 62.1% to 77.5% of HS patients, typically presents with mild to moderate scores on the NRS scale, ranging from 4.5 (SD 3.5) to 5.4 (SD 2.5).[25] Together, these common symptoms impose a considerable physical burden, which in turn significantly affects quality of life.

Each of these symptoms has been shown to negatively impact quality of life, most often measured by the DLQI, with higher NRS and HODS scores correlating with higher DLQI scores.[23,24,26] Pain and pruritus have been identified as significant contributors to sleep disturbances, while pain and malodor negatively affect sexual functioning, with greater sexual dysfunction reported among females. In contrast, pruritus and suppuration do not demonstrate a direct correlation with sexual dysfunction.[22]

Overall, DLQI scores in HS patients indicate a moderate to very large impact on health-related quality of life.[23,24,26] A meta-analysis by Kimball et al, reviewed 33 studies and found that 32 of them reported baseline DLQI scores greater than 10, with a range from 8.4 (SD 7.5) to 16.9 (no SD reported).[23] Similarly, Montero-Vilchez et al, found a mean DLQI of 10.7 (SD 2.16) across 17 studies. Measures of sexual dysfunction also highlight the significant impact of HS on patients' sexual lives, with a mean DLQI score of 12.5 (SD 7.5).[22] Furthermore, over 90% of single patients and 76% of those in relationships report moderate to extremely large adverse effects of HS on their quality of life.[27]

The psychological burden of HS is substantial, with patients frequently reporting a negative impact on mental health. Various patient-reported outcome (PRO) measures illustrate the relationship between HS and increased levels of anxiety, depression, and overall psychological distress.[23] In particular, patients with HS face profound physical and psychological challenges that significantly affect their quality of life.[23] Reducing inflammation and supporting overall skin health through vitamin and mineral supplementation presents a promising avenue for symptom relief. By addressing the underlying causes of symptomatology, supplementation may lead to improved health-related quality of life for patients with HS.

Evidence from patient surveys, case reports, and clinical trials

Zinc may alleviate symptoms in hidradenitis suppurativa (HS) through its role in immune modulation. Zinc deficiency is linked to increased reactive oxygen species (ROS), which contribute to oxidative stress, inflammation, and elevated levels of matrix metalloproteinases (MMPs).[16] Zinc also regulates several inflammatory cytokines, including IL-1 beta, TNF-alpha, and IL-6, all of which play critical roles in the inflammatory pathways of HS.[10,16] Furthermore, zinc supplementation may decrease inflammation by inhibiting neutrophil chemotaxis, reducing the Th17 response, and recruiting regulatory T cells to suppress immune activation.[16] These mechanisms suggest that zinc supplementation could help alleviate HS symptoms by addressing immune dysregulation and inflammation. Poveda et al, evaluated 122 patients with HS and 122 controls, and found that zinc deficiency was more prevalent among HS patients.[28] Zinc deficiency was associated with higher Hurley stage (stage III vs. stage II), increased DLQI scores, and a greater number of affected sites.[28] However, existing studies on zinc supplementation have focused primarily on patients with mild to moderate HS, which should be noted for future research.

Brocard et al, was among the first to investigate zinc supplementation in HS, treating 22 patients with mild to moderate HS (Hurley grade I-II) with 90 mg of zinc gluconate daily.[29] Their findings reported a complete clinical response in 8 patients and a partial response in 14, laying the foundation for further exploration of zinc's role in HS management.[29] Additionally, Molinelli et al. evaluated 92 patients with Hurley grade I-II HS, all of whom had previously been treated with tetracyclines for 12 weeks and showed clinical and ultrasonographic improvement.[10] Patients were divided into two groups group 1 (47 patients) received 90 mg of zinc gluconate and 30 mg of nicotinamide daily for 90 days, while group 2 (45 patients) received no treatment.

At both 12 and 24 weeks, the treated group demonstrated a significant reduction in the number and mean duration of acute flares compared to the control group.[10] Patients in the treated group reported improvements in visual analogue scale (VAS), dermatology life quality index (DLQI), and International HS severity score system (IHS4) scores.

Pain VAS scores in the treated group decreased from 2.3 (SD 2.3) at baseline to 2.0 (SD 2.1) at 12 weeks, with a slight rise to 2.4 (SD 1.9) at 24 weeks. DLQI scores showed a similar trend, dropping from 6.2 (SD 7.6) at baseline to 2.9 (SD 5.4) at 12 weeks, and slightly rising to 3.5 (SD 5.0) at 24 weeks. In contrast, the control group's DLQI scores increased over time, indicating worsening quality of life.[10] The consistent improvements observed in these studies, particularly in patient-reported outcomes like pain, quality of life, and lesion severity, underscore the potential of zinc supplementation as a valuable and non-invasive adjunct in the management of hidradenitis suppurativa, warranting further research to solidify its role in broader clinical practice.

Hessam et al, found that 66 patients with Hurley stage I-II HS treated with 90 mg/day of zinc gluconate showed significant improvements in modified HS scores and DLQI, with reductions in nodules, flare-ups, and erythema.[30] While these findings are promising, it is important to note that the evaluations were limited to patients with mild to moderate HS, specifically Hurley stage I and II. Therefore, it remains unclear whether individuals with more advanced disease would experience similar benefits from zinc supplementation. Additionally, the studies did not thoroughly address patient-reported experiences of symptoms, limiting our understanding of how zinc supplementation may alleviate specific manifestations of the condition.

Vitamin D deficiency affects the cutaneous immune response by reducing the production of antimicrobial peptides (AMPs), leading to microbial buildup on the skin. Additionally, vitamin D induces cutaneous immunosuppression by down-regulating T-helper cells in the skin and up-regulating T helper cells in draining lymph nodes.[16] These mechanisms collectively contribute to hypovitaminosis D, which can result in increased cutaneous inflammation and immunosuppression. Substantial evidence demonstrates a link between vitamin D deficiency and HS.[8,16,31]

Moreover, lower vitamin D levels have been inversely associated with the number of affected sites, international hidradenitis suppurativa severity score system (IHS4) scores, and Hurley stage in HS patients.[32] Despite this association, few studies have examined the therapeutic potential of Vitamin D supplementation in HS. In a pilot study by Guilet et al, 14 patients received vitamin D supplementation tailored to their baseline levels, with follow-up evaluations at 3 and 6 months. At the 6-month mark, flare-up frequency decreased by at least 20%, and 79% of patients reported fewer nodules.[33] Although this initial report is promising, further research is needed to fully explore the benefits of vitamin D supplementation as a therapeutic intervention for hidradenitis suppurativa.

Nutritional status plays a critical role in many functions essential to skin health. Certain vitamins, including vitamins C and E, act as antioxidants, protecting the skin from UV damage.[34] Vitamin C, in particular, promotes collagen formation, scavenges free radicals, neutralizes UV radiation-induced oxidative stress, decreases melanin synthesis, modulates keratinocyte differentiation, and enhances the proliferation and migration of dermal fibroblasts, key factors in wound healing and epigenetic regulation.[34] Given the wide-ranging positive effects of vitamin C on skin health, it should be considered a potential adjunctive treatment for symptom relief in hidradenitis suppurativa. Vitamin C has already been used as an adjuvant therapy in dermatologic conditions such as acne, allergic contact dermatitis, psoriasis, and progressive purpura.[35] Vitamin E is strongly associated with skin health and has long been used in dermatology. As a free radical scavenger, vitamin E protects the skin from oxidative damage caused by UV radiation and may possess anticancer properties.[36] It has been used in the treatment of various dermatologic conditions, including yellow nail syndrome, dapsone-induced hemolysis and headache, sub corneal pustular dermatosis, and cutaneous amyloidosis. Anecdotal reports suggest beneficial effects in a wide range of other skin conditions. Low levels of vitamin E, along with selenium, have been linked to skin and hair disorders.[37]

Evidence demonstrates an inverse association between serum vitamin E levels and several chronic inflammatory skin conditions, including psoriasis, vitiligo, atopic dermatitis, and acne, with significantly lower Vitamin E levels observed in affected patients compared to controls.[38] These findings suggest the potential for vitamin E deficiency in hidradenitis suppurativa (HS), a chronic inflammatory skin condition, and underscore the need to investigate vitamin E levels and the potential benefits of supplementation in HS patients. Unfortunately, no studies to date have explored the effects of Vitamin E supplementation on symptomatology or disease severity in individuals with HS.

Future research

While existing literature supports the beneficial roles of Vitamins C, E, and D, as well as zinc, in promoting skin health, a notable gap remains in studies examining the overall outcomes of Vitamins C and E supplementation. There is also a lack of reports analyzing patient-reported symptoms or quality-of-life metrics in response to vitamin D or zinc supplementation. This underscores the need for further research to explore the potential advantages of these vitamins and minerals. Given the significant impact of HS on quality of life, future investigations should integrate these supplements with lifestyle modifications to optimize symptom relief and enhance overall wellness outcomes. Supplementation strategies should also be tailored to individual needs, considering factors such as disease severity, lesion location, and specific symptoms.

Patient responses to vitamin and mineral supplementation exhibit significant heterogeneity, which poses a challenge in determining their universal efficacy for HS. Variables such as genetic background, baseline nutrient levels, and adherence to supplementation protocols can affect patient responses. Ammar et al, highlighted the role of gene polymorphisms in the variable response to vitamin D supplementation in healthy adults.[39] This finding further emphasizes the need for a personalized approach to supplementation in HS patients. Therefore, it is essential to closely monitor patient responses and adjust treatments based on individual factors.

In addition to variability in supplement responses, safety and appropriate dosing are critical considerations to avoid toxicity risks. Hypercalcemia, a dangerous side effect of vitamin D toxicity, can lead to acute renal failure and

necessitate hemodialysis.[40] Zinc toxicity can cause acute symptoms such as headache, nausea, vomiting, diarrhea, and abdominal discomfort, and may lead to metabolic disturbances and serious neurological issues. Chronic zinc toxicity can result in decreased high-density lipoprotein levels, increased low-density lipoprotein levels, and impaired immunity.[41] Although vitamin C toxicity is rare, it can cause serious cardiac arrhythmias in patients with iron overload and result in false-negative stool guaiac tests.[42] Vitamin C supplementation is also contraindicated in patients with certain blood disorders or a history of nephrolithiasis.[42] These potential toxicities must be considered when recommending high-dose supplementation for HS patients.

Current research on supplementation in HS patients lacks long-term analyses of the safety and efficacy of high-dose vitamin supplementation, making it difficult to provide concrete treatment guidelines. There is also a need for population-specific studies that examine the effects of high-dose supplementation in HS patients across diverse backgrounds, age groups, genders, and ethnicities to better understand the generalizability of the findings. Additionally, it is essential to investigate the specific biochemical mechanisms by which these supplements exert their effects on HS.

Future supplementation research in HS should focus on establishing guidelines for safe dosing, duration of use, and monitoring strategies to minimize toxicity risks. Large randomized controlled trials are needed to confirm the efficacy and safety of these supplements for HS patients, with the ultimate goal of improving their quality of life. Another area for future research is the evaluation of supplementation in combination with existing HS therapies, such as biologics and lifestyle interventions. Finally, a multifactorial approach to HS treatment that is tailored to individual patient needs is crucial. Therefore, research into personalized supplementation strategies will be key to optimizing outcomes in HS management.

CONCLUSION

This review underscores the potential benefits of high-dose vitamin D3, vitamin C, vitamin E, and zinc supplementation in modulating the inflammatory processes, reducing lesion severity, and improving symptom management in patients with HS. These key findings align with existing research on the immunomodulatory and antioxidant roles of these micronutrients, suggesting they may help mitigate the chronic inflammatory state characteristic of HS. The supplements not only aid in decreasing systemic inflammation but may also enhance wound healing, improve skin integrity, and reduce oxidative stress, potentially leading to fewer flare-ups and better long-term disease control. When used alongside conventional therapies such as antibiotics, biologics, and surgical interventions, these supplements could offer a more holistic and synergistic approach to managing HS, targeting both systemic and local disease mechanisms. From a clinical standpoint, integrating these micronutrients into routine treatment protocols may provide a cost-effective and accessible adjunct therapy, particularly for patients seeking additional non-invasive options for symptom control. Patient-specific factors such as nutritional status, baseline inflammation levels, and possible interactions with other medications should be considered when recommending supplementation.

Moreover, careful monitoring of serum levels, especially for fat-soluble vitamins like vitamin D and E, and tailoring supplementation regimens, accordingly, could further optimize therapeutic outcomes. While promising, further large-scale clinical trials are necessary to establish definitive dosing guidelines, safety profiles, and long-term efficacy, however these findings provide a strong foundation for considering dietary supplementation as a complementary strategy in HS management.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

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Cite this article as: Herrick G, Kakarla S, Frasier K, Mukarram M, Rodriguez E, Dragovic M, et al. Evaluating the impact of high-dose vitamin D3, vitamin C, vitamin E, and zinc supplementation on inflammatory cytokines, lesion severity, and symptom management in hidradenitis suppurativa. Int J Res Dermatol 2025;11:199-207.