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# Vitamins for the Management of Nail Disease: A Literature Review

Kaya L. Curtis[a] Shari R. Lipner[b]

[a]Weill Cornell Medical College, New York, NY, USA; [b]Department of Dermatology, Weill Cornell Medicine, New York, NY, USA



**Keywords**
Nail · Vitamin · Vitamin derivative · Topical vitamin · Oral vitamin

**Abstract**
***Background:*** Vitamins have gained popularity among physicians and patients for purported benefits to hair, skin, and nail health. Safe and efficacious therapies for nail disorders, many of which are chronic conditions, are needed. ***Summary:*** We conducted a literature review of studies assessing the efficacy of oral, topical, and intralesional vitamin/vitamin derivatives for the treatment of nail disorders, including yellow nail syndrome, brittle nail syndrome, onychomycosis, habit-tic nail deformity, periungual/subungual verruca, and nail psoriasis. Forty-nine articles were reviewed. There is good evidence to support the use of topical tazarotene and vitamin D analogs for nail psoriasis treatment. We found overall limited evidence for treatment of other nail disorders with vitamin/vitamin derivatives, and further research is needed to support their use. ***Key Messages:*** Besides topical tazarotene and vitamin D analogs for nail psoriasis treatment, there is limited evidence for treatment of nail disorders with topical, oral, and intralesional vitamin/vitamin derivatives.



## Introduction

Safe long-term therapies are needed for the management of nail diseases, many of which may be chronic conditions. Despite limited evidence for treatment with vitamins, in a 2008 survey-based study, 66% of dermatologists reported recommending vitamin supplements to patients for purported skin, hair, and nail health benefits [1], and self-reported hair, skin, and nail supplement use nearly doubled from 2.5% in 2011–2012 to 4.9% in 2017–2020 [2]. Therefore, we conducted a literature review on the management of nail disorders, including yellow nail syndrome (YNS), brittle nail syndrome (BNS), onychomycosis, habit-tic nail deformity, periungual/subungual verruca, and nail psoriasis, with oral, topical, and intralesional vitamins and vitamin derivatives.

A literature search for peer-reviewed articles using the PubMed/MEDLINE database was performed in March 2023 for treatment of nail diseases with vitamins using the following search terms: "nail disease" AND "vitamin;" "nail" AND "vitamin;" "nail condition" AND "vitamin;" "yellow nail syndrome" AND "vitamin;" "brittle nail syndrome" AND "vitamin;" "onychomycosis" AND "vitamin;" "habit-tic deformity" AND "vitamin;" "periungual warts" AND "vitamin;" "subungual warts" AND "vitamin;" "nail psoriasis" AND "vitamin." Full length

This work is not under consideration at any other journal and has not been previously presented.

karger@karger.com
www.karger.com/sad



Correspondence to:
Shari R. Lipner, shl9032@med.cornell.edu

**Table 1.** YNS studies

| Study | Design | Therapy | Dosage | Sample size | Patient demographics (age/sex) | Nail involvement | Outcomes |
|---|---|---|---|---|---|---|---|
| Williams et al. (1991) [8] | Case report | Topical vitamin E | Topical vitamin E solution twice daily | 1 patient | 64/M | Fingernails | Clinical improvement of thickness, ridging, discoloration, lunula visibility, and nail growth rates when compared to dimethyl sulfoxide alone after 6 months. |
| Lambert et al. (2006) [9] | Case series | Topical vitamin E solution | Topical solution (20,000 IU tocopherol acetate/one fluid ounce of safflower oil) twice daily | 3 patients | 3/M<br>8/M<br>10/M | Fingernails | No effect on fingernail growth rate or clinical appearance when compared to placebo solution (safflower oil) alone after 6 months for all brothers. Only the youngest brother had pulmonary involvement and met the criteria for clinical diagnosis of YNS. |
| Maldonado et al. (2008) [10] | Retrospective cohort | Oral vitamin E | NR | 41 patients | Median age of YNS diagnosis 61 years (18–82) | NR | 14/25 patients (56%) had improvement in yellow nails, of which 5/14 patients were treated with vitamin E therapy. The remaining 9/14 patients had improvement without vitamin E therapy and were thought to be associated with treatment of respiratory symptoms. |
| Ayres and Mihan (1973) [11] | Case report | Oral vitamin E (alpha-tocopherol acetate) | Oral vitamin E (alpha-tocopherol acetate) 800 IU/day | 1 patient | 65/F | Fingernails and toenails | Increased nail growth rate after 2 months, reduced nocturnal leg cramping after 4 months, and complete resolution of all nails after 6.5 months. Bronchial cough persisted but improved. |
| Baran and Thomas (2009) [12] | Clinical trial | Oral vitamin E and pulse-dose fluconazole | Oral alpha-tocopherol 1,000 IU/day and oral fluconazole 300 mg once weekly | 13 patients | NR | NR | Treatment time varied between 18 months and 2 years. Eleven out of 13 patients had a clinical cure, and 2 out of 13 patients showed improved nail regrowth. There was no associated improvement in other systemic YNS manifestations in any study patients. |

**Table 1** (continued)

| Study | Design | Therapy | Dosage | Sample size | Patient demographics (age/sex) | Nail involvement | Outcomes |
|---|---|---|---|---|---|---|---|
| Luyten et al. (1996) [13] | Case report | Oral vitamin E and pulse-dose itraconazole | Vitamin E 800 IU/day for 6 months and itraconazole 400 mg daily for 1 week/month | 1 patient | 27/F | Fingernails and toenails | Slight improvement, with a 1–2-mm healthy growth in proximal nail plate after vitamin E 800 IU daily alone for 6 months. Patient subsequently developed onychomycosis in a few nails, after which a pulse dose regimen of itraconazole was added for an additional 10 months, resulting in complete resolution. |
| Baran et al. (2002) [14] | Case series | Oral vitamin E and pulse-dose fluconazole; oral vitamin E and pulse-dose itraconazole; oral vitamin E and pulse-dose itraconazole | Vitamin E 1,000 IU/day and fluconazole 300 mg once weekly | 3 patients | 57/F; 44/M; 60/F | Fingernails and toenails | Case 1: fingernails had normal appearance, with resolution of over curvature, hardness, and yellow discoloration after 6 months; case 2: complete resolution of fingernail dystrophy and partial improvement of toenail dystrophy after 1 year; case 3: complete resolution of fingernail dystrophy and partial improvement of toenail dystrophy after 1 year. |
| Preston et al. (2018) [15] | Case report | Oral vitamin E and pulse-dose fluconazole | NR | 1 patient | 39/M | Fingernails and toenails | Some improvement after 2 months. |
| Piraccini et al. (2014) [16] | Case series | Oral vitamin E and pulse-dose itraconazole | Oral vitamin E 1,200 IU/day±itraconazole 400 mg daily for 1 week/month | 21 patients | NR | NR | In the vitamin E only group, 3/11 patients had complete resolution and 3/11 patients had clinical improvement after 6 months. In the vitamin E and itraconazole group, 1/9 patients had complete resolution and 3/9 patients had clinical improvement. Clinical improvement included increased nail growth, reduced convexity, reduced detachment, and reduced swelling of the nail fold. |

**Table 2.** Brittle nail syndrome studies

| Study | Design | Therapy | Dosage | Sample size | Patient demographics (age/sex) | Nail involvement | Outcomes |
|---|---|---|---|---|---|---|---|
| Floersheim et al. (1989) [22] | Clinical trial | Oral biotin | 2.5 mg/day | 45 patients | NR | Fingernails | Improved firmness and hardness of fingernails in 41/45 patients (91%) following a 5.5±2.3-month course of therapy. Nail brittleness and ridging returned 10 weeks after biotin discontinuation. |
| Colombo et al. (1990) [23] | Clinical trial | Oral biotin | 2.5 mg/day | 22 patients | NR | Fingernails | In the group of BNS patients from whom nail samples were obtained before and after biotin administration (8 nails), nail thickness increased by 25% from 256±53 μm to 319±86 μm ($p < 0.05$) as assessed by scanning electron microscopy after 9.6±3.6 months of oral biotin. |
| Hochman et al. (1993) [24] | Retrospective study | Oral biotin | 2.5 mg/day | 46 patients | Median age 57 years (21–74); sex NR | NR | Patient reported clinical improvement in nails after 1–4 months (average 2 months) in 22 out of 35 (63%) patients. |
| Piraccini et al. (2005) [25] | Case series | Oral biotin | Oral biotin 5 mg/day and 10% urea ointment once-twice daily | 14 patients | Mean age 42.9 years (32–56); 12 female patients and two male patients | Triangular worn-down nails | At 6 months, clinical improvement and complete clinical resolution was achieved in 6/9 (66.7%) and 3/9 (33.3%) patients, respectively. At 1 year of therapy, 9/9 (100%) of patients had complete resolution. Recurrences occurred in three patients thereafter. |

**Table 2** (continued)

| Study | Design | Therapy | Dosage | Sample size | Patient demographics (age/sex) | Nail involvement | Outcomes |
|---|---|---|---|---|---|---|---|
| Chiavetta et al. (2019) [26] | Clinical trial | Oral biotin | Hydroxypropyl chitosan-based nail lacquer (HPC-NL) nail lacquer group (once daily); HPC-NL nail lacquer once daily and oral biotin 10 mg daily | 50 patients | Mean age 64±11 years; 21 male patients and 29 female patients | Toenails | At 4 months, proportion of patients with an onychodystrophy global severity score reduction of greater than 50% compared to baseline was 53 and 80% in the nail lacquer arm and combination regimen arm, respectively ($p = 0.05$). |
| Sparavigna et al. (2019) [27] | Clinical trial | Topical biomineral formulation (cystine, panthenol, vitamin E); Oral biomineral formulation (L-cystine, L-arginine, glutamic acid, vitamin C, vitamin E, vitamin B6, vitamin B7, zinc, iron, copper); Combination of topical biomineral formulation and oral biomineral supplement | Topical biomineral formulation; oral biomineral formulation; topical and oral biomineral formulation (dosage NR) | 50 patients | Mean age 39–45 years (18–54); 50 female patients and 0 male patients | Fingernails | At 3 months, nail hardness improved by 40% in the topical arm ($p < 0.01$), 43% in the oral arm ($p < 0.05$), and 50% in the combination arm ($p < 0.05$). Nail roughness decreased by 12% in the topical arm ($p < 0.05$), 18% in the oral arm ($p < 0.05$), and 15% in the combination arm ($p < 0.05$). |
| Sherber et al. (2011) [28] | Clinical trial | Topical tazarotene | Topical tazarotene cream 0.1% twice daily | 20 patients | Mean age 65.7±6.67 years (55–76); sex NR | Fingernails | After 12 weeks therapy and at 12-week post-therapy follow-up, 100% of patients (18/18) achieved assessment score of target nails. |

articles of randomized controlled trials, uncontrolled trials, systematic reviews, cross-sectional studies, cohort studies, case-controlled studies, case reports, and case series were included. Records that were irrelevant, not in English, or did not meet study criteria were excluded. A total of 49 articles were selected for review.

YNS is a rare disorder characterized by a clinical trial of yellow nails, respiratory disease, and lower extremity lymphedema [3]. The etiology of YNS remains poorly understood, although lymphatic impairment is suspected [4]. Nail involvement is characterized by smooth, thick yellow nails with increased transverse curvature, onycholysis, slow nail growth, and loss of cuticles and lunula [5]. Most cases are sporadic [6], although there is a weak association with autoimmune diseases and various cancers [4]. Spontaneous improvement of nail findings is not associated with improvement of other systemic manifestations [6].

Vitamin E has been used to treat YNS topically and systemically (Table 1) [4, 7]. Since lipid oxidation of free radicals results in deposition of lipofuscin pigments, causing yellow discoloration, it is theorized that vitamin E protects against free-radical oxidative damage, reversing yellow discoloration [7].

Evidence for treatment with topical vitamin E is limited. In a 64-year-old male patient with YNS treated with topical vitamin E twice daily for 6 months, there was improvement in fingernail thickness, ridging, discoloration, lunula visibility, and nail growth rates [8]. Conversely, in a case series of 3 pediatric patients with yellow fingernails since birth, treated with topical vitamin E, there was no significant effect on nail growth rate or clinical appearance [9].

Use of oral vitamin E for YNS has been slightly better studied. In a retrospective cohort study of 25 YNS patients, 56% (14/25) had improvement of yellow nails, of which 35.7% (5/14) were treated with vitamin E (9 untreated) [10]. In a case report of a 65-year-old female patient with YNS, there was complete resolution of onychodystrophy with oral alpha-tocopherol acetate 800 IU/day treatment for 6.5 months [11].

Combination regimens of oral vitamin E and pulse-dose triazole antifungals have also been studied. Azole antifungals are thought to improve yellow nails by increasing the linear nail growth rate [13, 17]. In a clinical trial of 13 YNS patients, 84.6% had complete clinical cure with oral vitamin E and pulse-dose fluconazole between 18 months and 2 years [12]. In a case series of 3 patients with YNS, fingernail dystrophy resolved after 6 months to 1 year of vitamin E and pulse-dose fluconazole/itraconazole treatment [14].

BNS affects approximately 20% of the population; women are typically affected twice as frequently as men. Common patient complaints include nail softness, dryness, weakness, breakability, and slow growth rate [18]. BNS is characterized by impaired intercellular adhesion with lamellar splitting of the distal nail plate [19]. Standard treatment is irritant avoidance, water immersion avoidance, and topical emollients [20]. Although there is supporting clinical evidence (Table 2) that biotin is effective for the treatment of BNS, the mechanism of treatment, whether via correction of an underlying deficiency or otherwise, remains unknown [21].

In a clinical trial of 45 patients with BNS of unknown etiology treated with oral biotin 2.5 mg daily, there was improved firmness and hardness of fingernails in 91% (41/45) of patients following a 5.5 ± 2.3-month course [22]. In a retrospective study of 46 patients with oral biotin 2.5 mg/day for 1–4 months, there was clinical improvement in nails in 63% (22/35) of patients [24]. In a case series of 14 patients, clinical improvement and complete resolution were achieved in 66.7% (6/9) and 33.3% (3/9) patients, respectively, at 6 months. At 1 year of therapy, 100% (9/9) of patients had complete resolution [25]. In a clinical trial of 50 patients, 80% of patients treated with nail lacquer and oral biotin 10 mg daily had an onychodystrophy global severity score reduction of greater than 50% compared to baseline, in comparison to 53% of patients treated with nail lacquer alone ($p = 0.05$) [26]. A clinical trial of 50 randomized patients to a topical formulation (including vitamin E) arm, an oral biomineral formulation (including vitamins C, E, B6, and B7), and a topical and oral combination arm. After 3 months of treatment, nail hardness improved by 40% in the topical arm ($p < 0.01$), 43% in the oral arm ($p < 0.05$), and 50% in the combination arm ($p < 0.05$) [27].

Use of topical tazarotene for the management of BNS was studied in a clinical trial of 20 patients. After 12 weeks of treatment with tazarotene cream 0.1% twice daily, 100% (18/18) of patients achieved the primary end-point of improvement measured by the physician global improvement assessment of target nails [28].

Onychomycosis is the most common nail disorder seen in clinical practice. A primary obstacle in onychomycosis management is slow nail growth and the nail plate serving as a barrier to drug permeation and diffusion. Therefore, treatment requires long duration of therapy, typically 12 months or longer for toenails [29]. The vitamins that have been studied for the management of onychomycosis are topical vitamin E, topical tazarotene, and oral acitretin (Table 3).

Vitamin E has antioxidant properties [36] and is thought to increase tissue growth rate via acceleration of fibroblast and epithelial cellular proliferation [37]. The water-soluble derivative of vitamin E, alpha-tocopheryl

**Table 3.** Onychomycosis studies

| Study | Design | Therapy | Dosage | Sample size | Patient demographics (age/sex) | Nail involvement | Outcomes |
|---|---|---|---|---|---|---|---|
| Alessandrini et al. (2020) [30] | Clinical trial | Topical vitamin E and essential oils of lime, oregano, and tea tree | Topical solution once daily | 20 patients | Mean age 45 years; 7 female patients and 13 male patients | NR | At 3 months post-therapy (6 months therapy), 3/17 patients (17.6%) had complete cure (clinical and mycological exam), 13/17 (76.4%) had clinical improvement, and 1/17 patient remained stable (5.8%). At 6 months post-therapy, 7/14 patients (50%) had complete cure, 6/14 (42.8%) had clinical improvement, and 1/14 (7.1%) remained stable. At 6-month follow-up, 11/14 patients had complete cure (78.5%), 2/14 (14.3%) had improvement, and 1/14 (7.1%) remained stable. 4/6 patients dropped out due to patient-reported complete cure of affected nail (2/6 at 3 months; 2/6 at 6 months). |
| Goldsmith (1983) [31] | Case report | Topical vitamin E | Topical 400 IU vitamin E once daily (contents of a vitamin capsule) | 1 patient | 37/M | Toenails | Complete clinical cure after 6 months of treatment. Recurrence occurred in 2 nails and vitamin E application was restarted in nails with recurrence only. At 6-week follow-up, the nails with recurrence had resolved and all other nails remained clinically resolved. |
| Campione et al. (2015) [32] | Clinical trial | Topical tazarotene | Topical tazarotene 0.1% gel daily | 15 patients | 14–70 years; 8 female patients and 7 male patients | Toenails | After 4 weeks, 6/15 (40%) of patients achieved mycological cure. Complete clinical resolution and negative cultures were achieved by 15/15 patients at week 12 ($p < 0.04$), and patients remained clinically cured at 6-month follow-up. The most common side effect was mild nail fold erythema. Disk diffusion assay after 48 h of incubation in tazarotene solution showed a central area of inhibition in all fungal cultures. |

**Table 3** (continued)

| Study | Design | Therapy | Dosage | Sample size | Patient demographics (age/sex) | Nail involvement | Outcomes |
|---|---|---|---|---|---|---|---|
| El-Salam et al. (2020) [33] | Clinical trial | Topical tazarotene | Topical tazarotene 0.1% gel daily; topical tazarotene 0.1% gel once daily; and tioconazole nail paint 28% once daily | 40 patients | 20–40 years | Majority fingernails | After 3 months, clinical improvement, as assessed by onychomycosis severity index, was 25% in the tazarotene alone group and 50% in the tazarotene and tioconazole group ($p$ = 0.039). Tazarotene was most effective against *Aspergillus niger* (negative culture achieved in 3/3 patients). Tazarotene and tioconazole were most effective against *A. niger* (negative culture achieved in 3/4 patients) and *Candida* species (negative culture achieved in 7/9 patients). Reported side effects included irritation (10% tazarotene group, 25% combination group) and skin peeling (15% tazarotene group, 30% combination group). |
| Abd El-Aal et al. (2019) [34] | Clinical trial | Topical tazarotene | Fractional carbon dioxide laser (4 sessions) followed by topical tazarotene; fractional carbon dioxide laser (4 sessions) followed by topical tioconazole 28% | 102 patients | Mean age 33 years; 72 female patients and 30 male patients | Majority fingernails | No difference between groups, with 35.3% of the tazarotene group showing complete resolution and 33.3% of the tioconazole group showing complete resolution ($p$ = 0.33). In the tazarotene group, 91.7 and 100% had negative KOH test and culture result after treatment, respectively. In the tioconazole group, 78.3 and 95.5% of patients had negative KOH tests and culture results after treatment, respectively ($p$ < 0.001). |
| Nasr et al. (2022) [35] | Clinical trial | Oral acitretin | Itraconazole pulse therapy (400 mg/day for 1 week/month); oral acitretin (25 mg/day); combined itraconazole/ acitretin therapy (itraconazole 400 mg/ day for 1 week/month and oral acitretin 25 mg/day) | 135 patients | 24–63 years; majority female patients | Fingernails and toenails | Mycological cure and complete cure were achieved by 51.1 and 20% of the itraconazole group, 28.9 and 28.9% of the acitretin group, and 80.0 and 53.3% in the combined itraconazole/ acitretin group (mycological cure $p \leq 0.05$ and clinical cure $p$ = 0.007). Cheilitis was reported in 44.4% (20/45) of the oral acitretin group and 57.7% (26/45) of the combined itraconazole/ acitretin therapy group. |

**Table 4.** Habit-tic deformity studies

| Study | Design | Therapy | Dosage | Sample size | Patient demographics (age/sex) | Nail involvement | Outcomes |
|---|---|---|---|---|---|---|---|
| Gloster and Kindred (2005) [46] | Case series | Oral multivitamin (vitamin C, B9, B7, zinc, keratin, *para*-aminobenzoic acid, lemon bioflavanoid) | 1 multivitamin/day | 2 patients | 33/F; 39/M | Fingernails | Case 1: Near complete resolution of left thumbnail dystrophy (at baseline had multiple transverse ridges of the nail plate) after 5 months. The patient continued the multivitamin for 1 year and retained normal nails thereafter; case 2: Complete resolution of bilateral thumbnail dystrophy (at baseline had transverse ridges of the nail plates with central depression) after 4 months. Recurrence occurred within 6 months after discontinuing. The patient then took biotin 2.5 mg/day for 6 months without improvement. He subsequently began taking multivitamin again with resolution. |

polyethylene glycol succinate, is a widely used biomaterial in drug delivery systems [38, 39]. Use of vitamin E may, therefore, facilitate antifungal delivery to tissues.

In a clinical trial of 20 patients treated with topical vitamin E and essential oils of lime, oregano, and tea tree, there was a 50% complete cure rate and 78.5% complete cure rate after 3 and 6 months, respectively [30]. In a case report of a patient treated with topical 400 IU vitamin E, there was complete clinical resolution of toenail onychomycosis after 6 months [31].

Tazarotene is a synthetic third-generation retinoid prodrug derived from vitamin A with immunomodulatory and anti-inflammatory properties. It protects keratinocytes from infection by *Propionibacterium acnes* and thus may have defensive activity against infective processes [40]. Tazarotene reduces hyperkeratinization, resulting in high epidermal penetration [41].

In a clinical trial of 15 patients with toenail onychomycosis treated with topical tazarotene 0.1% gel daily, mycological cure rate was 40% at 1 month, and complete clinical cure and negative cultures were achieved in 100% (15/15) of patients at 3 months. Disk diffusion assay after 48 h of incubation in tazarotene solution showed a central area of inhibition in all in vitro fungal cultures [32]. In a comparative cross-sectional study of 40 patients, clinical improvement as assessed by the onychomycosis severity index was 25% in patients treated with tazarotene alone, compared to 50% in patients treated with tazarotene and tioconazole ($p = 0.039$) after 3 months of therapy [33]. In a clinical trial of 102 patients treated with fractional carbon dioxide laser-assisted delivery of topical tazarotene or topical tioconazole, there was no difference in clinical cure between groups ($p = 0.33$). In the tazarotene group, 91.7 and 100% had negative KOH and cultures, respectively, compared to 78.3 and 95.5% in the tioconazole group ($p < 0.001$) [34].

Retinoids have immunomodulatory and fungistatic activity against dermatophytes and *Candida albicans* [42] and increase nail growth rate via increased epidermal

**Table 5.** Periungual and subungual verruca studies

| Study | Design | Therapy | Dosage | Sample size | Patient demographics (age/sex) | Nail involvement | Outcomes |
|---|---|---|---|---|---|---|---|
| Priya et al. (2019) [49] | Clinical trial | Intralesional vitamin D3 | 0.2–0.5 mL/session | 14 patients | Mean age 28.57 years (12–49); sex NR | NR | Injections were performed at 2-week intervals till either complete resolution or maximum of 4 total sessions. Mean number of injection sessions till complete clearance was 3.05±0.83. 13/14 patients (92.9%) had complete clinical cure, 1/14 (7.1%) had moderate response (50 to <100% reduction in number of warts), and 0% (0/14) had mild response (<50% reduction in number of warts). No recurrences reported at 6-month follow-up. |
| Jakhar et al. (2019) [48] | Therapeutic pearl | Intralesional vitamin D3 | 0.2 mL/session | 1 patient | NR | Fingernails | Clinical resolution of filiform wart of the thumbnail at 1-month post-therapy following 2 injections of vitamin D3 (0.2 mL) over 2-week intervals. |
| Raghukumar et al. (2017) [50] | Case series | Intralesional vitamin D3 | 0.2–0.5 mL (600,000 IU; 15 mg/mL)/session | 2 patients | NR | NR | Injections were performed at 3-week intervals until complete resolution or for a maximum of 4 total sessions. 1/2 patients had complete resolution (100% regression) and 1/2 had partial resolution (>50% regression). |
| Xu et al. (2022) [51] | Retrospective observational | Topical tretinoin | Superficial X-ray therapy (total dose 16 Gy over 28 days); combination regimen of superficial X-ray therapy with topical tretinoin (occluded 8 h/day for 20 days) | 36 patients | Mean age 32.58 years (6–86); 11 female patients and 25 male patients | NR | In the superficial X-ray therapy arm, 75% (18/24) of periungual warts achieved complete response, while 25% (6/24) of warts had a partial response. In the combination regimen arm, 92.7% (38/41) of periungual warts achieved complete clinical cure, while 7.3% (3/41) of warts had a partial response ($p < 0.046$). |

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**Table 6.** Nail psoriasis studies

| Study | Design | Therapy | Dosage | Sample size | Patient demographics (age/sex) | Nail involvement | Outcomes |
|---|---|---|---|---|---|---|---|
| Scher et al. (2001) [62] | Randomized, double-blind, controlled trial | Topical tazarotene | Vehicle gel; tazarotene 0.1% gel nightly to 2 target nails, one nail occluded, one nail not occluded | 31 patients | Mean age 43 years; 9 female patients and 22 male patients | Fingernails | Compared to vehicle gel, tazarotene resulted in significantly greater reduction in onycholysis in occluded nails ($p \leq 0.05$ at weeks 4 and 12) and a significantly greater reduction in onycholysis in nonoccluded nails ($p \leq 0.05$ at week 24). The tazarotene treatment arm also had significantly greater decrease in nail pitting in occluded nails ($p \leq 0.05$ at week 24). There was no difference between treatment arms for subungual hyperkeratosis, leukonychia, nail plate crumbling, splinter hemorrhage, and nail growth rate. 5/21 tazarotene gel patients reported adverse events, including proximal nail fold skin peeling, skin irritation, periungual irritation, paronychia, and proximal nail fold erythema. |
| Rigopoulos et al. (2007) [63] | Randomized, double-blind trial | Topical tazarotene | Tazarotene 0.1% cream occluded nightly; clobetasol propionate 0.05% cream | 46 patients | Age NR; sex NR | Fingernails and toenails | Both treatment arms showed improvement in pitting, onycholysis, hyperkeratosis, and salmon patches ($p < 0.001$) after 12 weeks of therapy. There was no statistically significant difference in improvement between treatment arms at 12 weeks. At 24 weeks, tazarotene treatment had a greater reduction in hyperkeratosis ($p < 0.001$). Adverse events were reported in 3/16 (18.75%) patients in the tazarotene arm (desquamation and erythema of nail fold, periungual irritation, paronychia). |
| Bianchi et al. (2003) [64] | Open, prospective | Topical tazarotene | Tazarotene 0.1% gel nonoccluded nightly | 25 patients | 22–66 years; 5 female patients and 20 male patients | Fingernails and toenails | At 12 weeks, 19/25 (76%) patients had reduction in onycholysis, hyperkeratosis, oil spots, and pitting ($p < 0.0001$). Initial improvements were noted in the fingernails after only 4 weeks of therapy. Hyperkeratosis and oil spots showed the most drastic and fastest improvement. Pitting was the most persistent sign. Moderate recurrences noted at 24 weeks post-therapy. The main recurrent sign was mild relapsing hyperkeratosis. Reported side effects included mild erythema (70%), proximal nail fold peeling (15%), burning (15%). |
| Diluvio et al. (2007) [65] | Case report | Topical tazarotene | Tazarotene 0.05% gel nonoccluded daily | 1 patient | 6/F | Fingernails | At 8 weeks, hyperkeratosis improved, fragility completely resolved, and nail growth was normal. Nail pitting persisted. No relapses were reported at follow-up. There was local skin irritation during the first week of treatment. |
| Fischer-Levancini et al. (2012) [66] | Open, prospective | Topical tazarotene | Tazarotene 0.1% ointment nightly | 6 patients | Age NR; sex NR | NR | Mean nail psoriasis severity index was 14.3±6.3 at baseline. At 3 months, the average nail psoriasis severity index decreased to 8±3.29 ($p = 0.007$), and at 6 months, the average nail psoriasis severity index decreased to 2.3±1.21 ($p = 0.003$). At 6 months, complete resolution occurred for subungual hyperkeratosis in 5/6 (83.3%) of patients, splinter hemorrhages in 4/6 (66.7%), onycholysis in 3/6 (50.0%), pitting spots in 3/6 (50.0%), and oil spots in 2/6 (33.3%). Pain remission was observed in most cases. No adverse events were reported. |

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**Table 6** (continued)

| Study | Design | Therapy | Dosage | Sample size | Patient demographics (age/sex) | Nail involvement | Outcomes |
|---|---|---|---|---|---|---|---|
| Piraccini et al. (2014) [67] | Case series | Topical tazarotene | Tazarotene 0.1% gel daily | 2 patients | 77/F; 38/M | Fingernails | Two patients with nail psoriasis developed pyogenic granulomas after treatment with topical tazarotene. Case 1: pyogenic granulomas observed after 3 months of tazarotene. Lesions were 0.5–1.5 cm in diameter and very painful. Tazarotene therapy was discontinued and after clobetasol propionate ointment twice daily for 2 weeks, the pyogenic granulomas regressed; case 2: pyogenic granuloma observed after 2 months of tazarotene. The lesion was 0.5 cm in diameter and mildly painful. The granuloma resolved after 4 weeks. |
| Tosti et al. (2009) [68] | Open, prospective | Oral acitretin | Oral acitretin 0.2–0.3 mg/kg daily | 36 patients | Mean age 41 years; 9 female patients and 27 male patients | Fingernails | At 6 months, average fingernail psoriasis severity index score was reduced from baseline 31.5 to 18.6 (41% mean percent reduction, no *p* value reported). At 6 months, 9/36 (25%) had complete resolution, 9/36 (25%) had moderate improvement, 12/36 (33%) had mild improvement, and 11/36 (11%) had no improvement. One patient experienced adverse effects (severe dryness of periungual skin and multiple pyogenic granulomas 2 months after therapy). |
| López et al. (2009) [69] | Case report | Oral acitretin | 25 mg daily | 1 patient | 60/M | Fingernails and toenails | Baseline physical exam was notable for oil drop discoloration, subungual hyperkeratosis, onycholysis, nail pitting, and paronychia. Clinical improvement after 2 months. |
| Ricceri et al. (2013) [70] | Case report | Oral acitretin | Oral acitretin 25 mg daily and 5% urea nail lacquer | 1 patient | 73/F | Fingernails and toenails | Baseline exam was notable for oil drop discoloration, subungual hyperkeratosis, nail pitting, paronychia, and onychogryphosis. Toenail involvement impeded the patient's ability to walk. Clinical improvement was noted at 2 months of therapy, and improvement progressed 6 months later. Cheilitis was a reported side effect. The patient did not have relapse at 5 month follow-up. |
| Krajewska-Włodarczyk et al. (2021) [71] | Prospective, controlled observational | Oral acitretin | Oral acitretin 0.6–0.8 mg/kg daily | 41 patients | Age 32–64 years; 24 female patients and 17 male patients | Fingernails | After 6 months of treatment, reduction of nail bed and matrix thickness was noted via ultrasound exam ($p = 0.046$, $p = 0.031$, respectively). Although thickness of nail plates decreased, this was statistically insignificant ($p = 0.059$). Modified nail psoriasis severity index decreased in over 80% of patients. |
| Graceffa et al. (2020) [72] | Case report | Oral acitretin and topical tacalcitol | Oral acitretin 10 mg twice daily and tacalcitol ointment once daily | 1 patient | 37/F | Fingernails and toenails | Paronychia remission with minimal improvement of nail dystrophy after 3 months. The patient was started on apremilast and clobetasol, which moderately improved nail dystrophy. Acitretin was decreased to 10 mg daily due to cheilitis, and apremilast was continued with the addition of tacalcitol ointment once daily. 2 months later, apremilast was discontinued due to nausea, and combination oral acitretin/tacalcitol ointment was continued. Between the baseline visit and 16-months, modified nail psoriasis score had decreased by 80% from 45 to 9; psoriasis area and severity index had declined from 3.2 to 0.6. |

**Table 6** (continued)

| Study | Design | Therapy | Dosage | Sample size | Patient demographics (age/sex) | Nail involvement | Outcomes |
|---|---|---|---|---|---|---|---|
| Brazzelli et al. (2004) [73] | Case report | Oral acitretin | Oral acitretin 0.5 mg/kg daily | 1 patient | 39/M | Fingernails and toenails | Complete clinical resolution after 6 months. There was no relapse at 5-month post-therapy follow-up, and the patient reported complete resolution of prior functional disability. Cheilitis and palmoplantar scaling were reported side effects. |
| Tosti et al. (2006) [74] | Case report | Oral acitretin | Oral acitretin 0.3 mg/kg daily | 1 patient | 38/M | 20 fingernails and toenails | At 3 months, roughness, riding, subungual hyperkeratosis, and pitting had almost completely resolved. No side effects were reported. Therapy was discontinued after 7 months with complete resolution. |
| Tosti et al. (1998) [58] | Randomized, double-blind trial | Topical calcipotriol | Topical calcipotriol ointment 50 μg/g twice daily; betamethasone dipropionate (64 mg/g) and salicylic acid (0.03 g/g) ointment | 58 patients | Mean age 51.8±14.8 years; 23 female patients and 35 male patients | Fingernails and toenails | After 3 months, fingernail subungual hyperkeratosis decreased by 26.5% in the calcipotriol group and 51.7% in the betamethasone group ($p < 0.001$ from baseline, no difference between groups). After 5 months, fingernail responders showed a 49.2% reduction in hyperkeratosis in the calcipotriol group and 51.7% in the betamethasone group ($p < 0.001$ from baseline, no difference between groups). After 3 months, toenail subungual hyperkeratosis decreased by 20.1% in the calcipotriol group and 22.9% in the betamethasone group ($p < 0.001$ from baseline, no difference between groups). After 5 months, toenail responders showed a 40.7% reduction in hyperkeratosis in the calcipotriol group and 51.9% in the betamethasone group ($p < 0.0001$ from baseline, no difference between groups). 3/4 patients underwent adverse events (erythema, periungual irritation, local burning sensation, and diffuse urticaria) in the calcipotriol arm. |
| Zakeri et al. (2005) [75] | Case series | Topical calcipotriol | Topical calcipotriol ointment 50 μg/g twice daily | 24 patients | Mean age 33 years (18–68); 18 female patients and 5 male patients | Fingernails and toenails | At 3 months, 14/24 (58.3%) patients showed clinical improvement. At 5 months, 2/24 (8.3%) had complete resolution. Reduction in hyperkeratosis, onycholysis, and discoloration was especially notable. Fingernails had greater response than toenails. Two patients reported adverse effects (periungual irritation and pruritus/oozing). Most patients experienced recurrence of lesions with reduced severity after discontinuing calcipotriol. |
| Tzung et al. (2008) [76] | Randomized, investigator-blind, controlled trial | Topical calcipotriol | Topical 0.005% plus 0.05% betamethasone dipropionate ointment once daily; 0.005% calcipotriol ointment twice daily | 40 patients | Mean age 53.2±19.1 years; 7 female patients and 25 male patients | Fingernails | At 12 weeks, total nail psoriasis severity index score had a statistically significant reduction in both treatment arms ($p < 0.045$). There was no difference between treatment arms using either investigator's global assessment ($p = 0.071$) or nail psoriasis severity index ($p = 0.649$). No adverse events were reported. |

**Table 6** (continued)

| Study | Design | Therapy | Dosage | Sample size | Patient demographics (age/sex) | Nail involvement | Outcomes |
|---|---|---|---|---|---|---|---|
| Kole et al. (2014) [77] | Randomized, double-blinded trial | Topical calcitriol | Calcitriol ointment 3 μg/g twice daily; topical betamethasone dipropionate 64 μg/g twice daily | 10 patients | Mean age 57 years (36–74); sex NR | Fingernails and toenails | At 20 weeks, average physician global assessment scale decreased from 2.5 at baseline to 1.25 in the calcitriol group, and 2.375 at baseline to 2.2 in the betamethasone group ($p$ = 0.075 between groups). At 24 weeks, there was a 38 and 35% reduction in nail thickness in the calcitriol and betamethasone groups, respectively ($p$ = 0.42 between groups). |
| Usmani and Wilson (2006) [78] | Case report | Topical calcitriol | Calcipotriol cream 50 μg/g twice daily, reduced to calcitriol ointment 3 μg/g after several days | 1 patient | 38/F | Fingernails | Improved new nail growth and resolved discoloration after 2 months. Further clinical improvement noted at 6 months. Recurrence occurred 3-months post-therapy with onycholysis, subungual hyperkeratosis, and nail pitting. |
| Márquez Balbás et al. (2009) [79] | Case series | Topical tacalcitol | Tacalcitol ointment 4 μg/g nightly | 15 patients | Age NR; 7 female patients and 8 male patients | Fingernails | Clinical improvement observed at 3 months ($p$ = 0.001, compared to baseline), 6 months ($p$ = 0.001, compared to baseline), and at 6-months post-therapy ($p$ = 0.004, compared to 3 months therapy). Greatest reduction in subungual hyperkeratosis and onycholysis, followed by oil drop discoloration and nail pitting. At 6 months, all 10 patients with baseline pain reported resolution of pain. No adverse events reported. |

turnover [35]. It has been hypothesized that systemic retinoids may serve a therapeutic adjuvant role in the treatment of onychomycosis [35].

In a clinical trial of 135 onychomycosis patients, patients were subdivided into three arms, including itraconazole pulse therapy (400 mg/day for 1 week/month), oral acitretin (25 mg/day), or combined pulsed itraconazole/acitretin (itraconazole 400 mg/day for 1 week/month and oral acitretin 25 mg/day) for 3 months. Mycological and complete cures were achieved in 51.1 and 20% of the itraconazole group, 28.9 and 28.9% of the acitretin group, and 80.0 and 53.3% in the combined itraconazole/acitretin group (mycological cure $p \leq 0.05$ and clinical cure $p = 0.007$), respectively. Cheilitis was reported in 44.4% (20/45) of the oral acitretin group and 57.7% (26/45) of the combined itraconazole/acitretin therapy group [35].

Habit-tic nail deformity occurs due to repeated, habitual self-induced mechanical trauma of the cuticle and proximal nail fold using another digit [43]. The thumbnails are most frequently involved. Clinical examination is significant for a longitudinal midline furrow with numerous parallel transverse ridges [44]. Treatment includes occlusive dressings, cyanoacrylate adhesives, cognitive behavioral therapy, and psychotropic medications [45].

Evidence for the management of habit-tic nail deformity with oral multivitamins is limited to a single case series ($n$ = 2) (Table 4). Both patients denied a history of trauma or self-manipulation. Both patients had complete resolution of transverse ridging after treatment with an oral multivitamin for 5 and 4 months, respectively [46].

Human papilloma virus is responsible for development of verruca and is the most common nail viral infection. Verruca typically involves the nail fold and less commonly the nail bed. Proximal nail fold verruca may result in longitudinal ridging and nail plate dystrophy, whereas nail bed verruca may cause onycholysis [47]. Periungual and subungual verruca are challenging to treat. Local destruction is associated with high recurrence rate and may also cause scarring and permanent onychodystrophy [48].

Vitamin D plays a role in the proliferation and differentiation of keratinocytes and is thought to stimulate cell-mediated immunity. It regulates epidermal cell proliferation/differentiation and modulates cytokine production [48].

In a prospective observational study, 63 patients with clinically diagnosed palmoplantar and periungual warts, refractory to standard treatment modalities, were treated with intralesional vitamin D3 injections [49]. Of the 14/

63 patients with periungual warts, 92.9% (13/14) had complete clearance, 7.1% (1/14) had moderate response (50 to <100% reduction in number of warts), and 0% (0/14) had mild response (<50% reduction in number of warts). Mean number of injection sessions (2-week intervals) until complete clearance was 3.05 ± 0.83. In a case series of 2 patients with periungual warts, 1/2 had complete resolution (100% regression) and 1/2 had partial resolution (>50% regression) after 3-week interval injections until complete resolution or for a maximum of 4 total sessions [50] (Table 5).

Tretinoin is a vitamin A derivative that interrupts epithelial cell differentiation and HPV replication in verruca [52]. It promotes cornified cell detachment and enhances shedding. It also increases turnover of loosely adherent corneocytes via increased mitotic activity [53]. In a retrospective observational study of 36 patients treated with superficial X-ray therapy or a combination regimen of superficial X-ray therapy (28 days) with topical tretinoin (occluded for 8 h/day for 20 days), clinical cure was achieved in 75 and 92.7% of patients, respectively ($p < 0.046$) [51].

Nail involvement is estimated to occur in 40% of patients with cutaneous psoriasis, with lifetime prevalence of 80–90% [54]. In addition, 5–10% of patients have isolated nail psoriasis, with no or limited skin involvement. Clinical findings include nail pitting, onycholysis, subungual hyperkeratosis, and splinter hemorrhages, all of which may contribute to pain, limited functionality, and poor cosmetic appearance [55, 56]. Treatment is dichotomized into 3 or fewer nails involved or greater than 3 nails involved and includes intralesional steroid injections, topical steroids, topical vitamin D analogs, systemics, and biologics (Table 6) [57]. As nail psoriasis is a chronic condition requiring long-term treatment, effective and safe treatment options are needed [58–61].

Vitamin A for nail psoriasis treatment is available as tazarotene, a topical vitamin A derivative, and oral synthetic retinoids. Mechanism of action is decreased epidermal hyperproliferation, normalization of cellular differentiation, and inflammatory control [69, 80].

Use of topical tazarotene for nail psoriasis has been studied in several trials. In a randomized controlled trial of 31 patients treated with topical tazarotene, there was greater reduction in onycholysis in occluded nails ($p \leq 0.05$ at weeks 4 and 12) and greater reduction in onycholysis in nonoccluded nails ($p \leq 0.05$ at week 24) compared to vehicle gel [62]. In a trial of 46 patients randomized to topical tazarotene or clobetasol propionate, there was improvement in both groups ($p < 0.001$) in pitting, onycholysis, and hyperkeratosis after 12 weeks ($p > 0.05$ between groups). At 24 weeks, the group treated with tazarotene showed greater reduction in hyperkeratosis compared to the group treated with clobetasol ($p < 0.001$) [63]. In an open, prospective study of 25 patients treated with topical tazarotene, 76% (19/25) of patients had reduction in onycholysis, hyperkeratosis, oil spots, and pitting ($p < 0.0001$) at 12 weeks [64]. Of note, Piraccini et al. [67] reported pyogenic granuloma formulation in a case series of 2 patients with nail psoriasis treated with topical tazarotene.

In an open, prospective study of 36 nail psoriasis patients treated with oral acitretin 0.2–0.3 mg/kg daily, average fingernail psoriasis severity index score decreased from 31.5 to 18.6 (41% mean percent reduction, no $p$ value reported), and 25% (9/36) of patients had clinical resolution at 6 months. One patient developed multiple pyogenic granulomas 2 months after therapy [68]. In a prospective, controlled observational study of 41 patients treated with oral acitretin 0.6–0.8 mg/kg daily, nail bed and matrix thickness decreased after 6 months, as measured by ultrasound ($p = 0.046$, $p = 0.031$, respectively) after 6 months [71].

Vitamin D3 analogs, which have antiproliferative and immunomodulatory effects, have also been studied for the treatment of nail psoriasis [81]. Two vitamin D analogs are currently available for the treatment of psoriasis in the USA: calcitriol and calcipotriol (calcipotriene).

In a double-blind trial, 58 nail psoriasis patients were randomized to calcipotriol ointment or betamethasone dipropionate and salicylic acid ointment, with no difference between groups in reduction in subungual hyperkeratosis. For fingernails, subungual hyperkeratosis decreased by 49.2 and 51.7% in the calcipotriol group and betamethasone and salicylic acid group at 5 months, respectively ($p < 0.001$ from baseline). For toenails, subungual hyperkeratosis decreased by 40.7 and 51.9% in the calcipotriol group and betamethasone and salicylic acid group at 5 months, respectively ($p < 0.001$ from baseline) [58]. In another trial, 40 nail psoriasis patients were randomized to treatment with 0.005% calcipotriol plus, 0.05% betamethasone dipropionate ointment once daily or 0.005% calcipotriol ointment twice daily. At 12 weeks, the nail psoriasis severity index score was reduced in both treatment arms ($p < 0.045$), with no difference between treatment arms ($p = 0.649$) [76].

While it is appealing to treat nail diseases with topical and oral vitamin/vitamin derivatives, there is only robust evidence for use of vitamin D3 analogs and retinoids for

nail psoriasis treatment. There is a paucity of high-quality studies assessing therapeutic benefit and safety of vitamin/vitamin derivatives for the management of other nail conditions (YNS, BNS, onychomycosis, habit-tic nail deformity, periungual/subungual verruca).

Nail psoriasis had the highest evidence for treatment with vitamin derivatives, with topical vitamin D analogs and topical retinoids included in established treatment algorithms [57]. Although combination regimens of topical vitamin D analogs and steroids are typically first line, there is evidence to support equivalent efficacy of topical vitamin D monotherapy. In a randomized controlled trial of 40 patients, Tzung et al. [76] found that topical vitamin D monotherapy was equally effective as a topical vitamin D and steroid combination regimen for the treatment of nail psoriasis. In a double-blind randomized trial of 58 patients, Tosti et al. [58] found that topical vitamin D monotherapy was as efficacious as a topical steroid and salicylic acid regimen for nail psoriasis treatment. Although there is sufficient evidence to support topical tazarotene for nail psoriasis treatment, physicians should caution patients of potential side effects, including periungual skin irritation, proximal nail fold erythema, and proximal nail fold peeling. Evidence for oral acitretin is currently limited, and further trials with standard therapy control arms are needed. More studies are needed to investigate pyogenic granuloma formation associated with topical tazarotene and oral acitretin, which was reported in multiple cases [67, 68].

The strongest evidence for YNS treatment is for oral vitamin E with pulse-dose antifungals, which was only supported by one small clinical trial and several case reports. Topical or oral vitamin E monotherapy for YNS was limited to case reports and one small retrospective cohort study. Oral vitamin E for YNS was prescribed at doses ranging from 536 mg/day (800 IU/day) to 804 mg/day (1,200 IU/day). Although adverse events were not reported, high oral vitamin E intake has known coagulopathic risk due to vitamin K antagonism, hypoprothrombinemic effect, cytochrome p-450 interaction, and antiplatelet activity [82]. Toxicity may occur at doses greater than 1,000 mg/day [83]. However, there are case reports of coagulopathies in patients with oral vitamin E intake below this threshold and with only marginally elevated serum vitamin E levels [82, 84]. Therefore, the use of vitamin E should be avoided in older patients, those taking drugs that may increase risk of bleeding, such as oral anticoagulants and NSAIDs, and those with preexisting hypertension [82, 84]. Topical vitamin E has a more benign side effect profile; however, evidence is limited to case reports.

There is weak evidence to support treatment with oral biotin for brittle nail syndrome, given paucity of studies supporting therapeutic benefit and, moreover, interference with laboratory values, including troponins, thyroid stimulating hormone, N-terminal pro-brain natriuretic peptide, and parathyroid hormone [85, 86]. Despite a Food and Drug Administration (FDA) warning on biotin's potential for significant interference with laboratory tests [87], in a study examining consumer perception of biotin on Amazon, there was limited consumer awareness of the FDA warning [88]. In a survey study of 149 physicians, 43.9% of physicians recommended biotin, primarily for nail and hair disorders, and 45.9% of physicians did not ask patients to discontinue biotin prior to laboratory testing [89]. In an assessment of biotin supplementation among 447 patients in an urban outpatient dermatology clinic, 33.7% (152/447) of patients indicated current or past use, of which 28.8% had been recommended biotin by a primary care physician or dermatologist, and of which only 6.6% of users were aware of the FDA warning [90].

Effective alternative therapies for onychomycosis may be needed given poor medicaid coverage for onychomycosis treatment [91] and the patient "fear factor" regarding terbinafine-associated hepatoxicity [92]. There was moderate evidence for onychomycosis treatment with topical vitamin E, topical tazarotene, and oral acitretin in several clinical trials. Alessandrini et al.'s [30] study on topical vitamin E yielded promising results with an almost 80% complete cure rate reported following 6 months of treatment. Nasr et al.'s [35] study on oral acitretin similarly yielded promising results with 80.0% mycological cure rate with combination itraconazole/oral acitretin, compared to 28.9 and 51.1% with itraconazole and acitretin alone, respectively ($p \leq 0.05$). Acitretin may have innate antifungal activity, and/or it may have a beneficial effect on onychomycosis treatment by accelerating nail growth. Larger controlled studies are needed to confirm these findings, and currently there are better-studied FDA-approved oral and topical alternatives.

Evidence for periungual verruca treatment with intralesional vitamin D3 included one clinical trial with a small sample size and several case reports. The highest quality study for treatment of verruca with intralesional vitamin D injections was Priya et al.'s [49] clinical trial; however, only about 20% of patients had periungual verruca. In addition, Raghukumar et al.'s [50] study included only about 3% patients with periungual verruca, of which 50% show complete response rate. Adverse events specific to these patients were not reported in

either study. More clinical trials examining safety and efficacy of periungual and subungual verruca are necessary to draw firm conclusions.

## Conclusion

There is limited evidence for treatment of nail disorders with oral, topical, and intralesional vitamins/vitamin derivatives. Given the rarity of YNS, randomized clinical trials are challenging to perform. Therefore, given the limited treatment options for YNS, treatment topical vitamin E may be reasonable, given that it has a benign side effect profile. Oral vitamin E may be a reasonable YNS treatment option except in older patients, those taking drugs that may increase the risk of bleeding, and those with pre-existing hypertension. We recommend against prescribing oral biotin for BNS, given potential laboratory interactions and lack of high-quality studies proving efficacy. Topical vitamin E may be effective for onychomycosis treatment, however clinical trials are needed to evaluate the efficacy and side effect profile. Topical tazarotene and vitamin D analogs have proven efficacy and may safely be prescribed for nail psoriasis, but pyogenic granuloma formation is a known risk with topical tazarotene. Intralesional vitamin D3 appears to be safe and efficacious for verruca treatment, however further studies dedicated to periungual and subungual verruca are needed.

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## Author Contributions

Kaya Curtis prepared methodology, acquired and interpreted data for the work, wrote the original manuscript draft, prepared tables, gave the final consent for the version to be published, and agreed to be accountable for all aspects of the work. Dr. Shari Lipner conceptualized the work, prepared methodology, acquired and interpreted data for the work, reviewed and edited the manuscript, gave final consent for the version to be published, and agreed to be accountable for all aspects of the work.

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