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Title Page

Biotin for the Treatment of Nail Disease: What is the Evidence?

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Abstract

Biotin is a B vitamin that is necessary for several metabolic pathways in humans. As a result of *in vitro* and animal studies on hooves and claws, it was explored as a treatment for several nail disorders. This review will describe the pharmacology, mechanism of action, and studies using of biotin to treat brittle nails, triangular worn down nails, trachyonychia, and habit tic nail deformity.

Introduction

Biotin a water-soluble B vitamin that is derived in humans from food sources, including cereals, walnuts, peanuts, milk, and egg yolks, or synthesis by intestinal bacteria. It was first discovered during an experiment in which rats that consumed a diet rich in raw egg whites developed a constellation of symptoms including hair loss, dermatitis, and neuromuscular dysfunction. “Protective Factor X,” which was later recognized as biotin, was curative.¹ In addition, it was found that raw egg whites contain the glycoprotein, avidin.^{2,3} Avidin binds to biotin and thus blocks its absorption.

The chemical structure of biotin is bicyclic compound and there are 8 possible stereoisomers. Only the d-(+)-biotin stereoisomer is found in nature and enzymatically active.⁴ Key information on biotin is shown in Table 1 and the chemical structure is shown in Figure 1. Biotin has been studied *in vitro* in keratinocyte cell lines, in animal

hooves and claws, and 4 human nails conditions, namely, brittle nails, triangular worn down nails, trachyonychia, and habit tic deformity.

Pharmacology and Mechanism of Action

When biotin is administered orally, even at high doses, it is completely absorbed. In addition, urinary excretion of intravenous and oral dosing of biotin is equivalent, signifying that when biotin is given orally, there is 100% bioavailability.⁵ After ingestion, biotin is absorbed by the intestine and is taken up by the liver. It also has the ability to cross the blood-brain barrier.⁶ In normal adults and children, it is cleared by the kidney.⁷ Biotin can also be transported across the placenta,⁸⁻¹⁰ and through breastmilk.^{11,12} A topical ointment containing biotin was shown to be readily absorbed in both normal and atopic skin.¹³

Biotin is an important component of a number of metabolic pathways in humans. It serves as an essential cofactor for five different mammalian carboxylase enzymes that are involved in fatty acid synthesis, gluconeogenesis, and amino acid catabolism.¹⁴⁻¹⁶ In addition, at high doses, biotin has also been shown to inhibit the cytokines (interleukin-1 β and interleukin-2) and proliferation of peripheral blood mononuclear cells in healthy adults.¹⁷

Rationale for Use of Biotin to Treat Human Nails

Several observations in animals and cells lines led to the hypothesis that biotin could be used to treat human nails. For example, biotin deficiency in swine results in hooves that are brittle, weak, and necrotic and biotin supplementation reverses these

changes. This vitamin also improves the strength and hardness of pig claws and equine hoofs even in animals that are not biotin deficient.¹⁸⁻²¹ In addition, human nails share similarity with animal hooves and claws, in that they are all composed of keratin.²² In humans, insufficient biotin affects multiple organ systems resulting in dermatitis, seizures, vomiting, hypotonia, ataxia, and developmental delay.^{23,24} Biotin deficiency is exceedingly rare and may be inherited or acquired. Acquired forms may occur in cases of severe malnutrition, total parenteral nutrition without biotin supplementation, long-term anticonvulsant or antibiotic therapy, and ingestion of raw egg whites. Inherited conditions include biotinidase deficiency and multiple carboxylase deficiency. Oral supplementation improves these symptoms and if initiated early is often life saving.²⁵ Oral and intravenous biotin has also been shown to have a beneficial effect on atopic dermatitis and cutaneous psoriasis.^{26,27} In addition, in a keratinocyte cell line, pharmacological biotin concentrations caused upregulation of cytokeratins. It also stimulated epidermal cell differentiation and helped to maintain epidermal cell growth.²⁸

Biotin and Brittle Nails

Brittle nails are characterized by signs of nail plate fragility and splitting. This condition affects 20% of the population with women affected more often than men. It is not merely a cosmetic problem as patients may have sensitivity and have problems performing daily living activities.²⁹ Brittle nails are clinically diagnosed by onychorrhexis (longitudinal fissures) and onychoschizia (nail peeling) (Figure 1).³⁰ Pathogenesis is likely due to faulty intercellular adhesion of corneocytes, as well as

pathologic nail formation. Treatment includes avoidance of irritants, limiting water immersion, and emollients.²⁹

In one study, 71 patients with brittle nails were treated with oral biotin 2.5 mg daily to determine the effect on nail hardness. Forty five patients out of the initial group were analyzed and 41 (91%) showed improvement in firmness and hardness of the fingernails following a 5.5 +/- 2.3 month course.³¹ From this initial study, 22 patients with 23 brittle nails were enrolled in a second study to determine the effect of biotin on thickness and onychoschizia using scanning electron microscopy. Ten nails from healthy patients were used as controls. Scanning electron microscopy showed that nail thickness increased by 25% after biotin therapy and onychoschizia resolved in about half of the patients. It should be noted that it was not determined whether the patients were biotin deficient.³²

In another study, a detailed questionnaire was sent to 46 patients with complaints of splitting and dry nails, who had onychorrhexis and/or onychoschizia on clinical exam, and were offered 2.5 mg of daily biotin as treatment. Responses were obtained from 35 of these patients. The median was 57 years old (range 21-74) and patients reported that they had the condition for 2 months to 30 years. With treatment duration of 1.5 to 7 months, 22/35 (63%) had improvement in their nails in 1 to 4 months (average 2 months). There were no adverse effects in the group except for one patient who had gastrointestinal distress requiring discontinuation of biotin.³³

Triangular Worn Down Nails

Triangular worn down nails are a subset of brittle nails that are characterized by a triangular area of nail plate thinning extending from the mid-nail plate to the distal margin. Wedge-shaped nicking and mild erythema of the distal can also be seen. The dominant hand is most often affected, particularly the 2nd, 3rd and 4th, fingernails. In most patients it is associated with self-induced mechanical trauma such as rubbing the nail with the digits or a cloth. Women present more often than men and occupations involving frequent manipulation of the digits are overrepresented (clerks, tailors, healthcare professionals). In one study, the mean age at presentation was 43 (range 32-56) and average duration of symptoms was 22 months (range 4 months-3years). Hematological and biochemical studies including iron, ferritin, and zinc are normal in these patients, but biotin levels were not assessed.³⁴

In a report on 9 patients with triangular worn down nails, subjects were instructed to avoid mechanical trauma, clip the nails short, take oral biotin 5 mg/daily, and apply a urea ointment once or twice a day. At 6 months, clinical improvement was seen in 6/9 patients and completely normal nails were seen in 3/9 patients. One year after the baseline visits, all 9 patients were cured, but recurrences occurred in 3 patients soon after.³⁴

Biotin for Trachyonychia

Trachyonychia describes roughness of the nail plate.³⁵ It can affect any number of nails and each nail can vary in severity. There are both shiny and opaque types.³⁶ The opaque type is generally more severe and with a “sandpaper” like feel and appearance.

There is longitudinal ridging and the cuticle is hyperkeratotic. In the shiny type, the nails have small geometric pits forming longitudinal ridges, but retain their shine. The pathogenesis is likely due to severe chronic defective nail matrix keratinization for the opaque type and mild intermittent inflammation in the shiny type.³⁷ Trachyonychia is most common in the pediatric population and is associated with psoriasis, lichen planus, and alopecia areata, but most cases are idiopathic.^{38,39} Treatment options include observation, topical steroids, intralesional matrix kenalog injections, systemic corticosteroids, cyclosporine and retinoids.⁴⁰

In a small case series, a 6-year-old girl with trachyonychia (shiny) present for 3.5 years, and an 8 year old with trachyonychia (opaque) present for 3 years, were treated with 2.5 mg of oral biotin daily for 180 days. The patients had no personal or family histories of atopic dermatitis, lichen planus, psoriasis, or alopecia areata. A clinical examination of the nails was performed by 2 independent investigators at baseline, at 90 and 180 days of treatment, and at 180 days following the end of therapy. Longitudinal ridging decreased in both patients after 90 days of therapy. After 180 days of biotin therapy, and at 180 days post-therapy, there was diminished longitudinal ridging, thinning, and distal notching in both girls. There were no adverse effects.⁴¹

Biotin for Habit-tic Deformity of the Nail

Habit tic deformity of the nail is usually due to repeatedly manipulating and rubbing the cuticle and proximal nail fold with another digit. Patients may be unaware of this behavior, however in many cases, they become more conscious when probed. Clinically, there is a midline furrow longitudinally, with numerous parallel transverse

ridges.⁴² While any nail may be affected, the thumbnails are most commonly involved. Treatment options include occlusive dressings, cyanoacrylate adhesives, cognitive behavioral therapy, as well as psychotropic medications with varying successes.⁴³

In a small case series, 2 patients with habit tic nail deformities were treated with a multivitamin containing vitamin c (250 mg), folate (200 mcg), biotin (6000 mcg), zinc (25mg), soluble keratin (500 mg), para-aminobenzoic acid (75 mg) and lemon bioflavonoid complex (75 mg) (Dermavite; MediNiche, Saint Louis, Mo).⁴⁴ Both patients, however, denied manipulating their nails. The first patient was a 33-year-old woman with transverse ridging of her left thumbnail for 1.5 years. Her medical history was significant for SLE, which had been inactive for many years. She was treated with daily multivitamins for 5 months with resolution of the nail deformity. She also continued the therapy for 1 year and with no recurrence of the onychodystrophy. The 2nd patient was a 39-year-old man with no past medical history with transverse ridging of the bilateral thumbnails for 1 year. The onychodystrophy resolved after 4 months of treatment with a daily multivitamins but recurred when the therapy was discontinued for 6 months. Oral biotin 2.5 mg daily for 6 months, failed to correct the nail deformity, but reintroduction of the multivitamin led to resolution.⁴⁵

Discussion

Biotin is a vitamin that is essential for a number of metabolic pathways in humans. A number of observations contributed to the hypothesis that biotin could be used to treat nail disease. For example, it was shown that *in vitro*, biotin stimulates epidermal cell differentiation and aids in maintaining epidermal cell growth.²⁸ Secondly,

augmenting animal feed with this vitamin resulted in improved hoof strength and hardness.¹⁸⁻²¹ Finally, biotin deficiency in humans affects multiple organ systems.^{23,24}

To date, oral biotin at a dose of 2.5 mg daily has been used to treat brittle nails in three studies.³¹⁻³³ There is some data to suggest that it improves firmness, hardness, and thickness of brittle nails. However, it should be noted all studies were small and 2 of the studies lacked a control group. Biotin was also been explored for the treatment of 9 patients with triangular worn down nails.³⁴ While all patients had clinical improvement or cure of their nail condition with 5 mg/daily after 6 months and 100% had cure after 1 year of therapy, these patients were also using a urea ointment. Therefore, it is not clear whether the biotin, urea, or the combination had the beneficial effect. Oral biotin (2.5 mg/daily) was associated with a beneficial effect on trachyonychia in two children with both the opaque and shiny types.⁴¹ While these results are encouraging, previous studies have shown that trachyonychia may improve over time without treatment, so it is unclear whether the clinical improvement can be attributed to the biotin. There is also a report of using a multivitamin containing 6000 mg of biotin in two patients with habit tic nail deformity.⁴⁵ Interestingly, the onychodystrophy resolved in both cases with the multivitamin, but not in one patient who took biotin 2.5 mg/daily only. It is possible that biotin in combination with other vitamins are necessary for treatment. Alternatively, it is possible that higher doses are necessary to improve the onychodystrophy.

Nail toxicity, including leukonychia, melanonychia, onycholysis, Beau's lines, onychomadesis, and onychorrhexis, is common in patients undergoing chemotherapy. Supplementation with oral biotin has also been suggested for these changes to prevent

nail changes, however, there have been no trials or case reports to support this recommendation.^{46,47}

Conclusions

Biotin is a vitamin that has been used to treat several nail conditions including brittle nails, triangular worn down nails, trachyonychia, and habit tic deformity with promising results. It has an excellent safety profile. Further larger clinical trials with controls are necessary to determine efficacy and optimal dosing.

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Table 1: Key Information on biotin

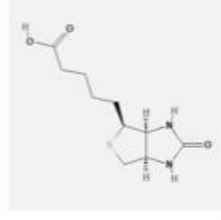
Chemical Names	Biotin; D-biotin; Vitamin H; Coenzyme R; Vitamin B7
Molecular Formula	C ₁₀ H ₁₆ N ₂ O ₃ S
Molecular Weight	244.309 g/mol

Table 2: Case Reports and Clinical Trials with Biotin to Treat Nail Disorders

Indication	Level of Evidence	Number of Patients
Brittle nails	1. Clinical trial ³¹	71
	2. Clinical trial ³²	22
	3. Survey based study ³³	35
Triangular worn down nails	Case series ³⁴	9
Trachyonychia	Case series ⁴¹	2
Habit-tic Nail deformity	Case series ⁴⁵	2

Figure 1: Chemical structure of biotin.

Figure 2: Brittle nails. The right fingernails with onychorrhexis and onychoschizia.



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