

## Insight about Lines of Treatment of Onychomycosis: Review Article

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### ABSTRACT

**Background:** Fungal infections of the nail bed are known as onychomycosis. Nail plate hypertrophy, onycholysis, and nail discoloration are all symptoms. Nail plate, nail matrix, and nail bed are all parts of the nail unit that might be impacted.

**Objective:** Review of literature about lines of treatment of onychomycosis.

**Methods:** We searched Science Direct, Google Scholar as well as PubMed for relevant articles on Onychomycosis and Lines of treatment. Only the most recent or thorough study was taken into account between December 2015 and April 2023. The authors also evaluated the value of resources culled from other works in the same genre. Documents written in languages other than English have been ignored due to lack of translation funds. Unpublished works, oral presentations, conference abstracts, and dissertations were generally agreed upon not to qualify as scientific research.

**Conclusion:** Because the fungus lives so deeply within the nail plate, treatment for onychomycosis can take a long time, patients often don't stick with it, and the condition often returns. Possible treatments include surgical avulsion, laser therapy, photodynamic therapy, and both topical and oral antifungal medications (e.g., very thick and chronic fungal nail).

**Keywords:** Onychomycosis, Treatment.

### INTRODUCTION

Onychomycosis is a fungal infection of the nail unit that causes nail discoloration, onycholysis, and nail plate thickness (dermatophytes, non-dermatophyte moulds, and yeasts). All of the three components of the nail, the plate, the matrix, and the nail bed, are interconnected and vulnerable to damage. Nail fungus derives from the Greek (onyx) for nail and (mykes) for fungus (onychomycosis). At least half of all nail illnesses can be traced back to onychomycosis, the most common nail ailment <sup>(1)</sup>.

It is advised and cost-effective to confirm a clinical diagnosis of onychomycosis in the lab before beginning treatment. Over the past few years, fresh diagnostic tools and therapeutic approaches have evolved, making onychomycosis easier to spot and cure than ever before. The target audience for this message is anyone interested in staying abreast of the latest developments in diagnosing and managing onychomycosis <sup>(2)</sup>.

According to recent published epidemiological studies, onychomycosis has a global frequency of about 5.5% in the general population. The disorder is seen far more frequently in older people than in younger ones, and its incidence rises with age. In North America, it is estimated that 0.4% of children have it, while the number rises to as high as 35% of those over the age of 65 <sup>(3)</sup>.

Onychomycosis is caused by dermatophytes, non-dermatophytic moulds, or yeasts coming into touch with the nail. Due to defective cell-mediated immunity, the nail unit is easily infected by fungi. Fungi produce proteolytic, keratinolytic, and lipolytic enzymes, which break down the keratin in the nail plate and make room for the fungus to invade <sup>(4)</sup>.

Fungal infections may be more common in people whose immune systems are weakened in some way.

Different clinical subgroups of onychomycosis are generated due to the place and pattern of fungal invasion. Fungi can avoid standard antifungal treatments by forming biofilms, which also contributes to antifungal resistance. Onychomycosis causes a staining of the nail, usually white or yellowish-brown. Color changes, including violet, green, and even black, have been observed on the nail plate. Other clinical symptoms include thickening of the nail plate, subungual hyperkeratosis, and onycholysis (nail separation from the nail bed) (onychchauxis) <sup>(5)</sup>.

### Treatment

To avoid a misdiagnosis, it may be prudent to have a lab confirm onychomycosis prior to starting treatment. Potentially harmful drug interactions between systemic antifungal drugs, therapeutic failure, and patient discomfort from excessive treatment are all possible outcomes of an incorrect diagnosis. The patient may also have to pay for it out of their own pocket. Many doctors still treat onychomycosis by trial-and-error methods <sup>(4)</sup>.

Because the fungus lives so deeply within the nail plate, treatment for onychomycosis can take a long time, patients often don't stick with it, and the condition often returns. Surgical avulsion, laser therapy, as well as photodynamic therapy <sup>(6)</sup>.

#### • Oral antifungal agents

When it comes for treating onychomycosis, oral antifungal therapy is preferred over topical antifungal therapy for both children and adults due to its shorter treatment courses and greater cure rates. Oral antifungal medications have a lesser risk of causing side effects in youngsters <sup>(7)</sup>.

Fungicidal terbinafine is an antifungal medication in the allylamine class. However, terbinafine has fewer potential drug interactions and side effects than other fungistatic medications like itraconazole and fluconazole. At present, oral terbinafine (for 25 kg body weight, 125 mg once day; for 25 to 35 kg body weight, 187.5 mg once daily; > 35 kg body weight, 250 mg once daily) is the drug of choice for the treatment of onychomycosis <sup>(8)</sup>.

Headaches altered sense of taste, dermatitis, nausea, vomiting, abdominal discomfort, diarrhoea, medication interactions, and, less frequently, possible adverse reactions include sadness, a lowered immune system (neutropenia), liver problems, and Stevens-Johnson syndrome. The effectiveness of continuous terbinafine treatment for toenail onychomycosis is comparable to that of pulse terbinafine treatment, however some studies have demonstrated that the continuous method is preferable <sup>(7,9)</sup>.

Itraconazole is given orally at a dosage of 5mg/kg to children under 20 kg, 100 mg/day to children 20-40 kg, 200 mg/day to children 40 kg and higher, and 200 mg/day to adults for 3-6 months. Patients with onychomycosis caused by moulds or yeasts other than those in the dermatophyte family who are intolerant of or have no reaction to oral terbinafine may want to try this alternative treatment <sup>(5)</sup>.

Headaches, upset stomach, upper respiratory infections, high triglyceride levels, liver problems, and heart problems are all possible side effects <sup>(4)</sup>.

Although the European Union has approved oral fluconazole for the treatment of onychomycosis, the FDA in the United States has not done so <sup>(10)</sup>.

Oral fluconazole (three to six milligrams per kilogram once weekly; adults, one hundred fifty milligrams once weekly) is used to treat onychomycosis off-label in the United States, Canada, and Australia. Patients who have had responses to terbinafine or itraconazole that were intolerable may find that this drug is beneficial for them <sup>(8)</sup>.

Orally administered griseofulvin (Gris-peg, Grifulvin V) is less effective, has more adverse events, and requires longer periods of treatment, but is unavailable in many countries. Oral griseofulvin for onychomycosis treatment is not commonly suggested due to these side effects. Oral ketoconazole (Nizoral) is also not recommended for treating onychomycosis because it has been linked to catastrophic side effects like liver poisoning <sup>(3)</sup>.

In severe cases of onychomycosis, such as when more than half of a nail is infected, when the infection has spread to many nails, when it has spread into the nail matrix, or when dermatophytoma is present, oral antifungal medications are advised <sup>(11)</sup>.

The success rate of treatment improves when oral antifungals are combined with topical antifungals. Sequential or simultaneous application of combination therapy is possible. Each patient needs a treatment plan that is specifically designed for them. Onychomycosis,

especially if it is chronic, may require multiple treatment cycles <sup>(10)</sup>.

#### ● Topical antifungal agents

Nail polishes and soaking solutions can be used as part of a topical antifungal treatment plan. Nails are more receptive to antifungal treatments when they are applied topically in an aqueous medium. The medicine is delivered transungually by applying a topical antifungal agent to the nail's dorsal surface <sup>(12)</sup>.

Concurrent use of nail polish with topical antifungal medications (such as efinaconazole) does not reduce the effectiveness of either treatment, although it may cause cosmetic changes to the nail polish that are less than ideal over time. Nail polish applications should be spaced out to avoid this <sup>(13)</sup>.

The most common adverse reactions to topical antifungal medicines include periungual erythema and burning at the treatment site. When compared to oral medication, topical therapy may be less effective, necessitating longer treatment periods (usually 48 weeks or more), perhaps due to low nail plate penetration. The impermeability of the nail is a result of the keratin network's strong hydrogen bonding and disulfide bonds <sup>(14)</sup>.

Mild to moderate onychomycosis may be treated with topical monotherapy if the infection affects fewer than three nails and does not extend into the matrix. Considering the superficial nature of white superficial onychomycosis, topical antifungal therapy is often adequate <sup>(10)</sup>.

When oral antifungal medicines are ineffective or dangerous, topical antifungal therapy can be a useful alternative. Because of the synergistic antifungal action of topical and oral antifungal medications, they can be administered together to improve the success rate of treatment. Topical antifungal medication is more likely to be successful in treating children than adults due to the faster nail growth rate and thinner nail plate in children <sup>(9)</sup>.

#### ● Photodynamic therapy

In photodynamic therapy, a photosensitizer is "turned on" by light of a certain wavelength. The photosensitizer gains energy through the process of photoactivation. Tissue oxygen and the released energy react to create harmful reactive oxygen species and free radicals. The fungal cells absorb the photosensitizer, making them more susceptible to apoptosis and necrosis than the surrounding healthy tissue <sup>(15)</sup>.

The use of photosensitizers has led to the development of methylene blue, 5 porphyrins, aluminium-phthalocyanine chloride, -Aminolevulinic Acid (5-ALA), Methyl Aminolevulinic Acid (MAL), toluidine blue, and rose bengal. Case reports and uncontrolled studies are the main sources of information about photodynamic treatment <sup>(16)</sup>. Mild discomfort, erythema, burning, edoema, and blistering were reported and were generally well tolerated <sup>(17)</sup>.

### • Miscellaneous

Nail abrasion, cutting, avulsion, and debridement are procedures that may be used to facilitate the topical penetration of antifungal medications and reduce the fungal burden, depending on the severity of the illness. White superficial onychomycosis is treated by scraping away the infected skin and then using a topical antifungal treatment <sup>(18)</sup>.

Nail avulsion surgery is unpleasant and can lead to permanent scarring. **Bristow *et al.*** <sup>(19)</sup> revealed a novel nail drill technique that permits micro-penetration with pinpoint accuracy and no damage to the nail bed. Using this device, the authors say they were able to effectively provide a topical antifungal medicine to the site of infection in a short amount of time and with little side effects, all without harming the nail. **Chiu *et al.*** <sup>(20)</sup> applied a dermaroller (Infinitive Beauty, Birmingham, UK) to the nail bed to create microscopic pores.

Drugs that break down the keratin in the nail, called keratolytics. They can be used to treat nail fungus more quickly. Nam presented a novel approach to curing onychomycosis. The primary ingredients of the invention are water (45-60%), urea (5%-10%), fumaric acid (5%-10%), 1, 3-butylene glycol (5%-10%), a gel-forming polymer (5%-10%), and a cross-linking agent (5%-10%). The keratolytic and moisture-retaining qualities of the preparation make it useful for treating onychomycosis. Topical urea may help with thick, dystrophic nails that break easily during clipping (40% ointment or cream) <sup>(3)</sup>.

Topical use of urea to the treated area prior to therapy may increase nail softening and therapy success. K101 nail solution (Emtrix, Nalox, Naloc) contains the following ingredients: urea, propylene glycol, and lactic acid. Onychomycosis can be cleared up faster with combination therapy using oral terbinafine or itraconazole and topical K101 nail solution, according to a retrospective study <sup>(21)</sup>.

Animal studies have shown that iontophoresis can help topical antifungal medications penetrate the nail plate and reach the fungus underneath. Tingling is a possible side effect of the current application. More research is needed to prove the safety and efficacy of iontophoresis as a treatment for onychomycosis, but it shows promise <sup>(3)</sup>.

### • Lasers

Recently, lasers have shown a lot of promise in treating onychomycosis, a fungal infection of the toenails. Most lasers use the selective photothermolysis concept, in which laser energy is absorbed exclusively by the fungal mycelia, causing a rapid rise in temperature within the mycelia and, eventually, fungal cell death. There shouldn't be any unintentional effects on other systems because the treatment is so targeted <sup>(3)</sup>.

To effectively treat toenail fungus, a laser needs to have a wavelength between 750 and 1300 nm, a pulse

duration less than the fungus' "thermal relaxation period," and a spatially homogenous beam to prevent "hot patches." <sup>(13)</sup>.

Long pulsed neodymium-doped yttrium aluminium garnet (Nd: YAG) lasers, diode lasers, and fractional carbon dioxide (CO<sub>2</sub>) lasers are only a few of the lasers that have been used to treat onychomycosis. Researchers found that laser treatments for onychomycosis were only moderately effective in meeting cosmetic goals, and did not even come close to matching the efficacy of currently available topical and oral antifungal drugs <sup>(22)</sup>.

Safe but pricey laser therapies may be an option for patients when systemic antifungal medicines cannot be used, or as part of a combination therapy to perhaps increase the likelihood of effective fungus clearance <sup>(23)</sup>.

### • Prevention

Patients should be advised to keep their feet dry and cold, to wear absorbent socks, and to keep their toenails short because fungi thrive in warm, moist environments. Treat your tinea pedis if you have it. Those with fungal nail infections like onychomycosis or tinea pedis should also get their loved ones treated <sup>(2)</sup>.

High-risk patients are advised in some studies to maintain topical antifungal therapy on a weekly or bimonthly basis for up to two years after treatment has ended. It is possible to treat non-leather running shoes by either washing them in hot water or using a device that produces ultraviolet C <sup>(24)</sup>.

### • Prognosis

When medical care is provided, the prognosis is typically good. Onychomycosis caused by non-dermatophyte moulds, dermatophytoma, and the formation of yellow streaks along the nail's lateral margin are all associated with a poor response to treatment (in particular, *Fusarium* species). Additional risk factors include noncompliance, advanced disease, nail matrix involvement, subungual hyperkeratosis bigger than 2 mm, the two-foot-one-hand syndrome, and immunodeficiency <sup>(3)</sup>.

The lacklustre treatment response may also be attributed to the topical antifungal medication's inability to penetrate the nail plate and the chronic nature of fungal infection. Recurrence rates have been reported to range from 10% to 53%. Most relapses occur within three years after a patient's last treatment. The recurrence could be due to a relapse or reinfection <sup>(3)</sup>.

### CONCLUSION

Because the fungus lives so deeply within the nail plate, treatment for onychomycosis can take a long time, patients often don't stick with it, and the condition often returns. Surgical avulsion, laser therapy, photodynamic therapy, with topical as well as oral antifungal therapies are some of the treatment possibilities.

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