Rapid Treatment of Subungal Onychomycosis Using Controlled Micro Nail Penetration and Terbinafine Solution

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ABSTRACT

Onychomycosis continues to be a common and intractable problem in adults, often responding poorly to topical treatment due to limited drug penetration of the nail plate. Improving penetration has been attempted previously by chemical and physical means with some success. The authors present three cases of toenail onychomycosis treated topical terbinafine 1% solution using controlled micro-penetration of the nail using a novel intelligent nail drill system which is able to drill nail plate without penetrating the delicate nail bed beneath. The cases illustrate how the device has been successfully employed to deliver the antifungal drug directly and rapidly to the site of infection with minimal side effects or complications, whilst maintaining the nail integrity.

INTRODUCTION

Onychomycosis continues to be a common and intractable problem in adults, often responding poorly to drug treatment. Toenails are most frequently affected by the infection, particularly the hallux. Studies suggest its prevalence to be around 29% across Europe, showing an increase in prevalence with age and in countries with longer winters. The causative agents are typically the dermatophyte species of fungi which spread from plantar skin over many months to invade the nails through a distal and lateral subungual route producing the characteristic discolouration of the nail plate. Over many months, complete invasion of the nail may lead to total dystrophy. Onychomycosis is often trivialised as a cosmetic condition but studies have confirmed its effect on the patient’s well-being and quality of life. Moreover, the presence of fungus on the foot is a risk factor for the development of lower limb cellulitis – a particular risk for patients with peripheral vascular disease and diabetes who have an increased propensity for the disease.

Management of the condition to date has proved challenging. Oral systemic agents such as terbinafine and itraconazole have shown good mycological cure rates when taken over a number of months. However, potential side effects, drug interactions and reluctance from some patients to oral medications remains a limitation. Exploring new techniques, the use of lasers has been suggested and reported as a less invasive and safer technology to destroy the subungal infection by rapid heating of the infected area. However, results have suggested that it has little evidence to date to support their widespread use in onychomycosis.

Topical treatments, applied directly to the nail plate, have also been used widely but consistently have been shown to be less effective than the systemic drug regimes. The nail plate is naturally a barrier to drug penetration, effectively shielding the subungal area so the underlying infection remains protected. In addition, patients are expected to apply the medicament to the nail for many months. Studies of topical medicament usage have shown that compliance decreases the longer the treatment continues, which may result in a treatment failure.

Measures designed to enhance topical drug delivery have been trialled with some success. Chemical penetration enhancers have been developed and incorporated into many topical drugs to boost delivery of the active ingredient through the nail. Combination therapy – utilising a dual approach using concurrent topical and oral antifungals medications – has also been shown to improve overall cure rates. Topically, nail reduction by mechanical thinning of the nail has shown to modestly improve the clinical response to antifungal agents. Recently, researchers have employed the use of fractional lasers to penetrate the full thickness of nail plate to create a porous structure, thus allowing the easier passage of any applied antifungal. Fractional lasers concentrate power to a very small area, thus reducing the risks of thermal damage to peripheral tissue. This work is ongoing, with potential promise, but the expense of such systems is still prohibitive for general podiatric use. In addition, as with most “hot” lasers, pain appears to be a commonly reported side effect of the treatment with a risk of damage to the delicate subungual tissues.
CASE REPORT

Three patients with laboratory and clinically confirmed onychomycosis who elected for topical therapy were offered the additional treatment with the device. Nails were treated pre-operatively with chlorhexidine spray and then multiple holes were drilled through the nail plate into the infected areas of the nail plate, a few millimetres apart, with some overlapping the diseased area onto uninfected areas of the nail. The number of holes required being proportional to the amount of nail infected. Patients were then instructed to use a 1% terbinafine spray for eight weeks (Lamisil® AT 1% Spray; Novartis UK Ltd) on the drilled nail and to leave it on for a few minutes to allow the solution to drain through the holes. Patients were asked to continue this once daily and were reviewed on a regular basis to

In 2013, a new device was introduced to market in the United Kingdom, with the potential to overcome a number of these issues. The Clearanail® device (Medical Device Treatment Ltd., Brighton, UK) is based on a simple nail drill design with a unit and hand piece (Figure 1a) fitted with a single use 0.4 mm carbide micro cutter (Figure 1b). Using a micro cutter, the drill when applied vertically to the nail and activated, bores a hole directly into the nail plate but safely stops once it is through the nail plate before damaging the underlying soft tissue of the nail bed. The result is a nail plate which can be successfully perforated with multiple holes. By rendering the nail more permeable, it can be hypothesised that chemicals and drugs would have a more rapid journey to the nail bed allowing a faster, antifungal effect at the heart of the dermatophyte infection (Figures 2a and 2b). Once the nail surface is cleared of debris the holes are barely visible to the patient.

FIGURE 1. (A) Clearanail Device and handpiece. (B) Microcutter.

FIGURE 2. (A) Mycotic nail (before drilling). (B) Mycotic nail (after drilling).
FIGURE 3. (A) Patient A at week 1. (B) Patient A at week 8. (C) Patient A at week 18.

FIGURE 4. (A) Patient B at week 1 (after drilling). (B) Patient B at week 12. (C) Patient B at week 24.
assess progress. Photographs were taken at week 1 and subsequently at review for visual comparison (Figures 2-5). Patients were advised not to use any varnishes, paints, or lacquers during the treatment period.

Finally, during the treatment period, patients were asked to treat any co-existing tinea pedis with terbinafine Hydrochloride 1% cream to prevent relapse or reinfection during nail treatment.

**DISCUSSION**

This paper represents the first published case reports of patients treated using this novel mechanical modality. The early response seen in the small number of cases has been extremely encouraging. Firstly, by the speed of change in the visual appearance of the nail plate within a matter of weeks, rather than months, which is rarely observed with simple topical applications.

Studies have shown that active fungal infection in a nail is found at the advancing edge of the infection as it travels towards the lunula, away from the free edge. Therefore, for any treatment to be successful it is required to reach this active fungal fringe. Roberts and Evans describe how dermatophyte infection of the nail is frequently complicated by a subungual mass of dermatophyte hyphae which are not attached to the nail bed or underside of the nail plate but remain shielded by the overlying nail plate. They hypothesised that resistance to treatment, in part, is facilitated by this protected fungal enclave.

By introducing holes into the overlying plate, an antifungal solution can readily reach the point of infection directly, with little or no reduction in its effectiveness, which may account for its rapidity in its action in these reported cases. As hypothesised by Gupta et al the presence of the air gap facilitates the passage of low tension anti-fungal solutions such as terbinafine 1% solution. In addition, lateral spread of the medicament under the nail is achieved as the patient stands and pressure is placed on the digit, and downward counter pressure from the nail plate across the nail bed spreads the antifungal agent further. Holes within the nail plate remained patent for the duration of treatment, eventually growing out with the advancing nail. Once a successful cure was achieved, patients were given detailed advice about preventing and treating any recurrent tinea pedis as it was highly likely in these patients to recur and potentially lead to nail reinfection.

The concept of making the nail more permeable to topical agents is not a new one. Many experimental chemical agents have been trialled to assess their ability to render the human nail more permeable and work in the 1980’s experimented using the CO₂ laser to create holes in the nail plate to permit easier passage of medicaments to the nail bed. The concept of drilling small holes in the nail – termed “nail trephination” – was first

**FIGURE 5.** (A) Patient C at week 1. (B) Patient at week 8 (nail plate has collapsed revealing air space). (C) Patient at week 24.
developed in the USA and has been used to treat subungual haematoma. The mechanical technique described here has a number of advantages over chemical and laser technologies. Firstly, the cost of the device; retailing at £2000 GBP the device is significantly cheaper than laser technologies and therefore potentially more accessible to clinical practitioners. Secondly, the device has demonstrated to be safe for the patient and practitioner alike. The rotation speed of the drill means little dust is produced, only producing a burr of nail debris during its operation rather like drilling metal. In addition, the technology employed in the device permits nail plate drilling but prevents the drill bit from penetrating the softer nail bed underneath. The system detects the difference in nail plate and nail bed through sensing the power delivered to rotate the drill bit. As nail keratin is harder than epidermis, more power is required by the drill but, as soon as softer underlying structures are reached, the power demand of the cutter diminishes, triggering the drill to stop, and safely withdraw.

Patients occasionally reported a slight pricking sensation during treatment when the drill was penetrating the healthy nail at the edge of the infected area of the nails, but no post-operative bruising or bleeding was noted in any of the patients. Consequently, there are no significant contra-indications for this technique with the vast majority of patient with subungual onychomycosis being suitable candidates for this this treatment. To prevent cross-infection, micro cutter bits are disposed of after each patient, costing around £15 GBP per cutter. With the patients using on average per nail 15 mLs of terbinfine 1% spray costing £14 GBP, the treatment itself was very cost effective.

Whilst these initial cases highlight a potential new modality for treating onychomycosis, it should be treated with caution. The numbers of cases treated here is small and longer term follow-up is required to confirm its effectiveness incorporating microbiological surveillance to ensure a full clinical cure. However, most patients attend practices seeking visual improvement in their nails, and therefore this device, based on early observations, potentially offers an alternative to current therapies with minimal contraindications.

In addition, drilling of the nail plate produced a fine nail debris at the site of penetration (Figure 1b). This subsequently could be harvested for microbiological analysis allowing the operator to yield nail samples safely from the advancing proximal edge of the infection, which previously has been technically difficult, with damaging the nail structure but further work is ongoing to fully assess its utility.

**CONCLUSION**

The use of a novel micro-cutter device has been demonstrated to facilitate and enhance the delivery of antifungal drugs to the nail bed in patients with onychomycosis. The system in these initial cases has been demonstrated to be effective and safe, with no adverse events reported by patients. Further work is ongoing to fully assess its potential.

**DISCLOSURES**

Medical Device Development Ltd. supplied the equipment on loan to the authors. The authors declare they have received no funding from the manufacturers or its partners in the preparation of this paper.

**REFERENCES**