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Rapid clearance of sub-ungual onychomycosis by controlled micro penetration and topical terbinafine solution using the Clearanail® device

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INTRODUCTION

Introduction

Onychomycosis continues to be a common and intractable problem, often responding poorly to drug treatment. Toenails are most frequently affected by the infection [1] – particularly the hallux [2]. Studies suggest its prevalence to be around 29% across Europe [3], showing an increase in prevalence with age [4] 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 sub-ungual route producing the characteristic discolouration of the nail plate [5]. Over many months, complete invasion of the nail may lead total dystrophy. Onychomycosis is often trivialised as a cosmetic condition but studies have confirmed its effect on the patient's wellbeing and quality of life [6-8]. Moreover, the presence of fungus on the foot is a risk factor for the development of lower limb cellulitis [9] – a particular risk for patients with peripheral vascular disease and diabetes who have an increased propensity for the disease [10].

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 [11]. 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 sub-ungual infection by rapid heating of the infected area. However, results from a recent systematic review have suggested that it has little evidence to date to support their widespread use in onychomycosis [12].

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 [13], effectively shielding the sub-ungual 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 [14] 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 [15].

Topically, nail reduction by mechanical thinning of the nail has shown to modestly improve the clinical response to antifungal agents [16]. Most 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 [17]. 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 sub-ungual tissues.

In 2013, a new device was invented and patented in the UK, 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 and is fitted with a single use 0.4mm carbide micro cutter. 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 expected 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 (see figure 1).

FIG.1a

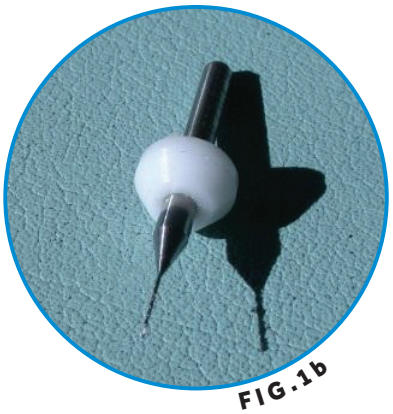

FIG.1b

Case Reports

Patients with laboratory and clinically confirmed onychomycosis who elected for topical therapy were offered the additional treatment with the Clearanail® 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 (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 assess progress. Photographs were taken at week 1 and subsequently at review for visual comparison (figures 2-6).

Patient 1

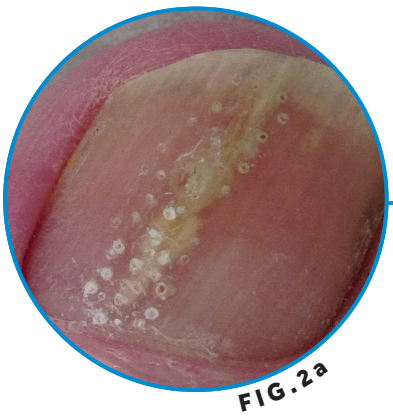

FIG.2a

WEEK 0 → WEEK 2

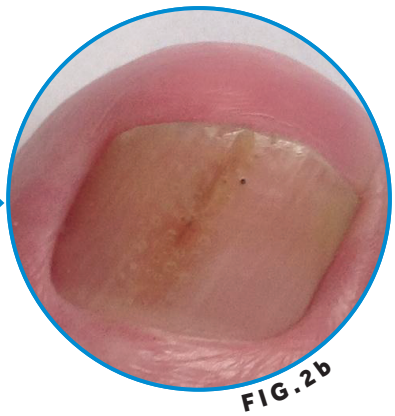

FIG.2b

Patient 2

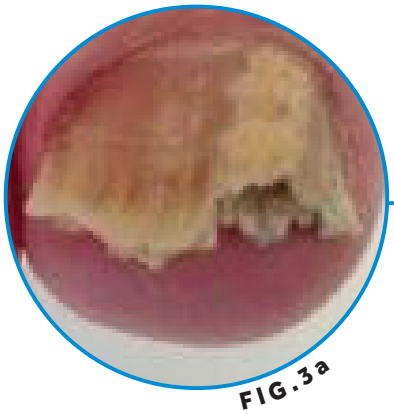

FIG.3a

WEEK 0 → WEEK 2

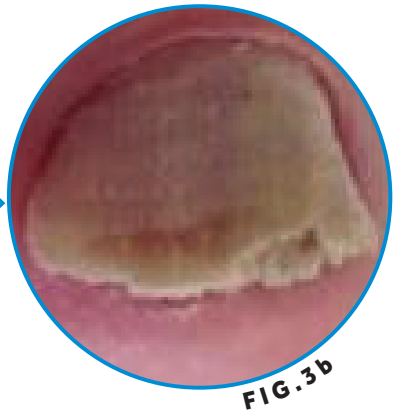

FIG.3b

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Patient 3

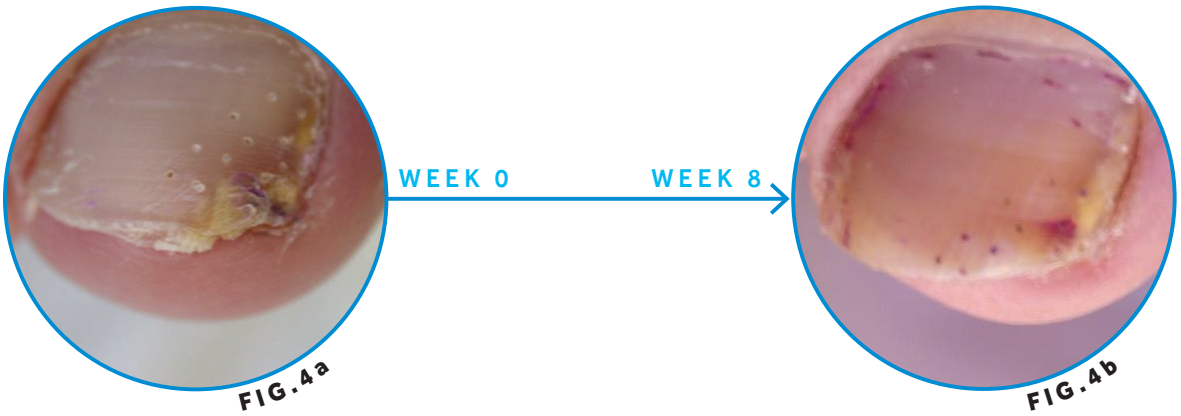

FIG.4a FIG.4b

Patient 4

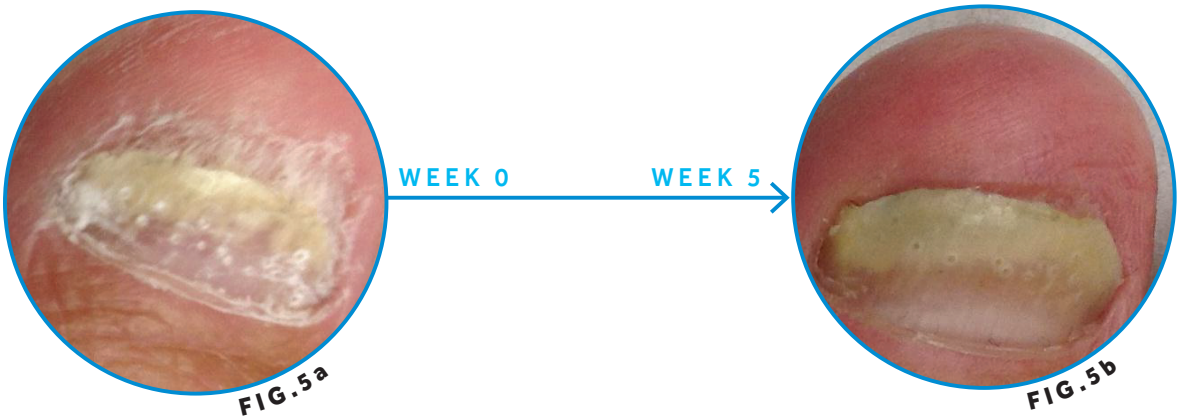

FIG.5a FIG.5b

Patient 5

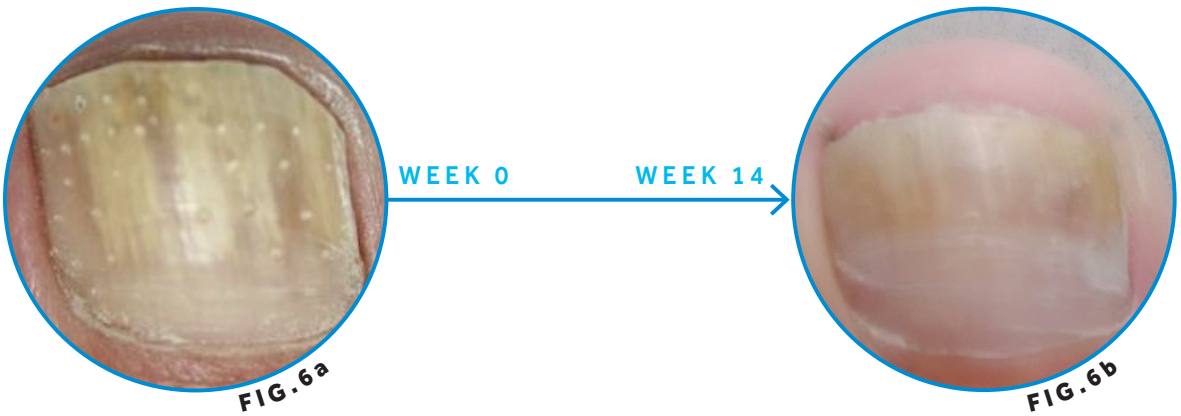

FIG.6a FIG.6b

Discussion

This paper represents the first 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 [18] describe how dermatophyte infection of the nail is frequently complicated by a sub-ungual 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. In addition, lateral spread of the solution 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.

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 [19]. The concept of drilling small holes in the nail – termed "nail trephination" was first developed in the USA and has been used to treat sub-ungual haematoma [20]. The mechanical technique described here has a number of advantages over chemical and laser technologies. Firstly, the cost of the device; retailing at £2000 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 the 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. Earlier studies of a similar technique have confirmed the procedure is well tolerated by patients with no pain or bleeding [20].

One patient reported a slight pricking sensation during treatment with one or two holes but no post-operative bruising or bleeding was noted. Consequently, there are no significant contra-indications for this technique with the vast majority of patient with sub-ungual onychomycosis being suitable candidates for this this treatment. Work with this device is ongoing with a randomised controlled trial being proposed for the future to assess its true potential. To prevent cross-infection, micro cutter bits are disposable. The unit itself comes complete with 20 drill bits and additional ones can be purchased.

Whilst these initial cases highlight a potential new modality for treating onychomycosis, it should be treated with cautiousness. The presented cases represent the earliest patients treated and the treatment is currently continuing. 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.

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 demonstrated to be effective and safe, with no adverse events reported by patients. Further work is ongoing to fully assess its potential.

REFERENCES

References

1. Zaikovska, O., M. Pilmane, and J. Kisis, Morphopathological aspects of healthy nails and nails affected by onychomycosis. Mycoses, 2014. 57(9): p. 531-536.
2. Andre, J. and G. Achten, Onychomycosis. Int J Dermatol, 1987. 26(8): p. 481-90.
3. Burzykowski, G., et al., High prevalence of foot diseases in Europe: results of the Achilles project. Mycoses, 2003. 46: p. 496-505.
4. Szepietowski, J.C., et al., Evaluation of quality of life in patients with toenail onychomycosis by Polish version of an international onychomycosis-specific questionnaire. Journal of the European Academy of Dermatology and Venereology, 2007. 21(4): p. 491-496.
5. Baran, R., et al., A text atlas of Nail Disorders:Techniques in investigation and diagnosis. 3rd ed. 2003, London: Martin Dunitz.
6. Lubeck, D., et al., Quality of life of persons with onychomycosis. Quality of life research, 1993. 2: p. 341-348.
7. Elewski, B.E., Onychomycosis. Treatment, quality of life, and economic issues. Am J Clin Dermatol, 2000. 1(1): p. 19-26.
8. Elewski, B., The effect of toenail onychomycosis on patient quality of life. International Journal of Dermatology, 1997. 36(10): p. 754-756.
9. Bristow, I.R. and M.C. Spruce, Fungal foot infection, cellulitis and diabetes: a review Diabet Med, 2009. 26(5): p. 548-551.
10. Gupta, A., et al., Prevalence and epidemiology of toenail onychomycosis in diabetic subjects: a multicentre survey. Brit J Dermatol, 1998. 139: p. 665-671.
11. Gupta, A.K., J. Ryder, and A.M. Johnson, Cumulative meta-analysis of systemic antifungal agents for the treatment of onychomycosis. Brit J Dermatol, 2004. 150: p. 537-544.
12. Bristow, I., The effectiveness of lasers in the treatment of onychomycosis: a systematic review (in press). Journal of foot and ankle research, 2014.
13. Gupchup, G.V. and J.I. Zatz, Structural characteristics and permeability properties of the human nail : A review. Vol. 50. 1999, New York, NY, ETATS-UNIS: Society of Cosmetic Chemists.
14. Carroll, C.L., et al., Adherence to topical therapy decreases during the course of an 8-week psoriasis clinical trial: Commonly used methods of measuring adherence to topical therapy overestimate actual use. Journal of the American Academy of Dermatology, 2004. 51(2): p. 212-216.
15. Bristow, I.R. and R. Baran, Topical and oral combination therapy for toenail onychomycosis: an updated review. J Am Podiatr Med Assoc, 2006. 96(2): p. 116-9.
16. Malay, D.S., et al., Efficacy of debridement alone versus debridement combined with topical antifungal nail lacquer for the treatment of pedal onychomycosis: a randomized, controlled trial. J Foot Ankle Surg, 2009. 48(3): p. 294-308.
17. Morais, O.O., et al., The use of the Er:YAG 2940nm laser associated with amorolfine lacquer in the treatment of onychomycosis. An Bras Dermatol, 2013. 88(5): p. 847-9.
18. Roberts, D.T. and E.G.V. Evans, Sub-ungual dermatophytoma complicating dermatophyte onychomycosis. British Journal of Dermatology, 1998. 138: p. 189-190.
19. Borovoy, M. and M. Tracy, Noninvasive CO 2 laser fenestration improves treatment of onychomycosis. Clin Laser Mon, 1992. 10(8): p. 123-4.
20. Ciocon, D., et al., How Low Should You Go: Novel Device for Nail Trephination. Dermatologic Surgery, 2006. 32(6)

Authors Declaration of Interests
Medical Device Treatment 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 and have no competing interests.

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