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Breaking the Fungal Biofilm with Q-Switched Nd: Yag Laser and Black Peel: Species-Blind Non-pharmacological Eradication of Azole-Resistant Onychomycosis

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ABSTRACT

Background: Onychomycosis (ONM), hitherto an easily manageable problem, more commonly seen in elderly patients has unfortunately transformed into an extremely-difficult-to-treat nail disorder, especially due to the widespread azole resistance. Not only has the azole resistance become a reason of treatment failure with itraconazole or ITRA (the usual drug of choice), the azole-induced cross-resistance to oral terbinafine and topical amorolofine has rendered ONM caused by dermatophytes, yeasts as well as molds to multi-drug-resistant (MDR) ONM, refractory to all forms of pharmacological interventions. The problem is reaching epidemic proportions in South Asian Countries. The use of ITRA further becomes impossible in the elderly who are not only on polypharmacy (owing to plethora of drug-interactions of ITRA), but also stemming from its absolute contraindication in patients with any disease that has impaired or has the potential to compromise the patient's cardiac function. Dermatologists across the Asia-Pacific are finding it difficult to treat all forms of ONM, especially because most have been rendered azole-resistant due to unscrupulous use of ITRA with respect to wrong dosage, duration and dietary-intake instructions due to wrong prescription by non-specialists and/or self-use by the patients.

INTRODUCTION

Onychomycosis accounts for 30% of all dermatophyte infections and accounts for 18%–40% of all nail disorders this is general data as available. Its prevalence is much higher in specific populations such as in diabetes mellitus, the elderly, and the immunosuppressed.

Onychomycosis can be nondermatophytic (1%) and dermatophytes (99%) The dermatophytes trichophyton rubrum and trichophyton mentagrophytes are the most common causative pathogens responsible for up to 90% of all cases. Among the non-dermatophytes, the yeast Candida Albicans, Candida tropicalis, and aspergillus, and other molds may be responsible however now Mixed infections are being increasingly encountered.

Toe Nail Onychomycosis

In recent times, both fractional ablative lasers and QS lasers have been successfully used as innovative treatment modalities for toenail onychomycosis. The laser has been used as a stand-alone therapy as well as in combination with topical and/or oral antifungals. The 1024 nm long-pulsed Nd: YAG laser has been found highly efficacious in this regard.

The Helios III QSNY laser utilizes the principle of multi-layered bulk heating of the fungus-infected nail plate and matrix, thereby providing fungicidal effect as well as enhancing the subsequent penetration of topical antifungal lacquers. The procedure is painful. For laser treatment of onychomycosis of toenails, the fractional and zoom hand-pieces are used. This approach is useful for patients who are intolerant or otherwise non-candidates for oral Toenails are far more likely to be involved than fingernails.

In addition to the cosmetic concerns of the patients, onychomycosis is a serious medical problem that can be the source of recurring fungal infections of surrounding tissues.

Also, it may predispose patients to secondary bacterial infections leading to localized paronychia and perhaps worse and deeper infections such as erysipelas-cellulitis, diabetic foot,tc., especially in the high-risk groups such as diabetics

Clinically it can cause varying degrees of pain or discomfort (especially in walking) and problems in cutting nails.

The rationale of using lasers:-

- Suboptimal penetration of topicals
- Inadequate drug levels achieved by systemic drugs
- BIOFILM formation-induced PHARMACOLOGICAL RESISTANCE
- ITRACONAZOLE MENACE - indiscriminate and injudicious use of itraconazole being produced by propaganda companies prescribed by all kinds of quacks in improper dosages and periods which has led to the emergence of MULTI-DRUG RESISTANT "super onychomycosis" on which no conventional therapy works.

Patients typically report after having taken itraconazole 200 mg bd for 4-6 months, with persistent disease and visible matrix damage.

Lasers In Onychomycosis – Basic Rationale

Temperatures over 45°C (fluence of >16 J/cm2) can result in pain and necrosis in humans, whereas fungicidal temperatures occur at 50°C. Fungal cells and dermal cells differ in membrane conductivity and water content. As these dermal structures have higher thermal conductivity, heat can be easily dissipated. Fungal cells, however, do not have this property and can, therefore, be targeted. The mycelium surrounded by the chitin wall is slow to dissipate heat between successive pulses, resulting in a buildup of temperature within the mycelium, unlike the surrounding tissue where heat is conducted away by tissue and water.

Nd: YAG Lasers for ONM:-

- MOA – Selective photothermolysis
- Fungal chromophores for Nd: YAG lasers – xanthomegnin, melanin
- Chromophores absorb enough heat - shifted to the fungal tissue - elevation of the tissue temperature - damage of the fungi.
- Nd: YAG lasers can effectively reach the depth of the nail bed, the site of the fungus colony.
- The surface temperature is controlled on 43~51 °C, which is curative for ONM

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Focus: Physical therapies, especially **Q switched Nd: YAG** and **fractional lasers** have been anecdotally reported to provide gratifying results in ONM. However, their success in eradication of proven MDR onychomycosis is lacking. In my lecture, I shall be discussing the mechanism of action, methodology, success rates, and mild precautions required while treating MDR ONM with lasers, especially Q-switched Nd:YAG laser. I would crystallize the concepts on exploiting the latter's property of selective photothermolysis against the fungal chromophore of xanthomegnin (532 nm) or melanin (1064 nm), and thermal disruption of biofilms to result in a cost-effective, species-blind high-efficacy, and geriatric-safe approach to eradication of azole-resistant and MDR onychomycosis.

For colleagues who don't have access to this otherwise easily available and affordable device, I shall dwell upon our team's novel innovation of successful repurposing of the Black Peel, a cosmetic peel for acne and pigmentation consisting black acetic acid, salicylic acid, tetrahydrojasmonic acid, bio sulphur, and potassium iodide for successful treatment of ONM, in combination wth topical ciclopirox nail lacquer. The innovative use of chemical peel for ONM, although requires multiple sessions, it offers an excellent option in resource- and cost-limited settings.

Conclusion: Q-switched laser and special chemical peels offer a drug-free, extremely safe, convenient, and efficacious option of successfully treating azole-resistant and MDR onychomycosis. The knowledge and acquisition of these skills have become essential for any practicing specialist in today's era oof rampant drug-resistant pathogenic dermatophytic, candida and mold infections.