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# Clinics in Dermatology

*Nails and the Clinician*

Guest Editor: Aditya K. Gupta, MD, PhD, FRCP (C)



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## Improved efficacy in onychomycosis therapy

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**Abstract** The success rate of onychomycosis treatment is limited by several factors, including the access of the therapeutic agent to the fungal mass, the presence of conidia, and the susceptibility of the different infectious agents to the antifungals. Different strategies used to improve efficacy of the currently available antifungal treatments, their rationale, and the published evidence of their beneficial effects are reviewed. An improved efficacy was demonstrated for some of these strategies, such as combined oral and topical antifungal therapies, whereas most of them lack clear and direct evidence of an increase in therapeutic success. © 2013 Elsevier Inc. All rights reserved.

### Introduction

Despite the good therapeutic responses obtained with an appropriate treatment of onychomycosis, treatment failures or recurrences are frequent. To improve the short- and long-term efficacy outcomes, different treatment strategies have been developed. These strategies could be divided into five categories: (1) treatments based on the biological cycle of the fungus, (2) modified dosing regimens, (3) combination therapy, (4) technology to improve drug delivery, and (5) adjunct/prophylactic care.

### Treatments based on the biological cycle of the fungus

Fungi exist under at least two forms: dormant conidia and growing hyphae. Under appropriate conditions, such as humidity and the presence of nutrients, the conidia could germinate and lead to the invasive hyphae phase. In turn, the

filamentous fungus can produce conidia through asexual reproduction.<sup>1</sup> Consequently, both hyphae and conidia are present in infected nails, and they have shown differential susceptibility to antifungals.<sup>2,3</sup> Conidia have been shown to be less susceptible to the antifungal action of itraconazole and terbinafine than hyphae for dermatophytes<sup>4,5</sup> and nondermatophyte molds.<sup>6</sup>

Different strategies can be used to induce the germination of conidia and make the infectious agent more susceptible to the antifungal therapies. For example, it is believed that nail lacquers have the potential to induce the germination of conidia by reducing transonychial water loss.<sup>1</sup> Germination can also be induced by placing a piece of Sabouraud's agar on the nail plate during topical therapy (boosted antifungal topical treatment [BATT]) or oral therapy (boosted oral antifungal treatment [BOAT]). In an open study treating 13 participants with a history of treatment failure or recurrence of dermatophyte onychomycosis, 5% amorolfine nail laquer was applied one weekly for 6 months. As an adjunct, participants applied sabourad agar with chloramphenicol and cycloheximide to the nail plate with sticking plaster for 24 hours every second day, for one week per month for two months. At the end of the 6 months, 85% of the participants were mycologically cured.<sup>7</sup> In another open study, 10 participants with onychomycosis in

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