



Tazarotene as Topical Treatment of Onychomycosis: Does It Really Work?

Thesis

*Submitted for Partial Fulfillment of the Master Degree in
Dermatology and Venereology*

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2018

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قالوا

سببنا انك لا تعلم لنا
إلا ما علمتنا إنك أنت
العليم العظيم

صدق الله العظيم

سورة البقرة الآية: ٣٢

Acknowledgment

*First of all, all gratitude is due to **God** almighty for blessing this work, until it has reached its end, as a part of his generous help, throughout my life.*

*Really I can hardly find the words to express my gratitude to **Prof. Dr. Rania Adel Lotfy**, Professor of Dermatology, Andrology and Venereology, Faculty of Medicine, Ain Shams University, for his supervision, continuous help, encouragement throughout this work and tremendous effort he has done in the meticulous revision of the whole work. It is a great honor to work under his guidance and supervision.*

*I would like also to express my sincere appreciation and gratitude to **Asst. Prof. Marwa Saad Fathi**, Asst. Prof of Medical Microbiology & Immunology, Faculty of Medicine, Ain Shams University, for her continuous directions and support throughout the whole work.*

*Really I can hardly find the words to express my gratitude to **Dr. Marwa Yassin Ahmed Soltan**, Lecturer of Dermatology, Andrology and Venereology, Faculty of Medicine - Ain Shams University, for her continuous directions and meticulous revision throughout the whole work. I really appreciate their patience and support. **Dr. Amira Esmail Abd Elhamid** Lecturer of Medical Microbiology & Immunology, Faculty of Medicine, Ain Shams University.*

*My deepest thanks are also to **Dr. Ibrahim Nassim Elatabany**, for valuable suggestions and instructions throughout this work.*

*Last but not least, I dedicate this work to **my family**, whom without their sincere emotional support, pushing me forward this work would not have ever been completed.*

Zeyad Swidan

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List of Abbreviations

Abb.	Full term
<i>AIDS</i>	<i>Acquired immune deficiency syndrome</i>
<i>APC</i>	<i>Antigen presenting cells</i>
<i>CMI</i>	<i>Cell-mediated immunity</i>
<i>CO</i>	<i>Candida onychomycosis</i>
<i>DLSO</i>	<i>Distal and lateral subungual onychomycosis</i>
<i>DM</i>	<i>Dermatophytes</i>
<i>DSO</i>	<i>Distal subungual onychomycosis</i>
<i>EO</i>	<i>Endonyx onychomycosis</i>
<i>FDA</i>	<i>Food and Drug Administration</i>
<i>HIV</i>	<i>Human immunodeficiency virus</i>
<i>LNF</i>	<i>Lateral nail folds</i>
<i>MAL</i>	<i>Methyl aminolevulinate</i>
<i>MHC</i>	<i>Major histocompatibility</i>
<i>NDM</i>	<i>Non-dermatophyte molds</i>
<i>NK</i>	<i>Natural killer</i>
<i>ODB</i>	<i>Hyponychium, onychodermal band</i>
<i>PDT</i>	<i>Photodynamic therapy</i>
<i>PNF</i>	<i>Proximal nail fold</i>
<i>PSO</i>	<i>Proximal subungual onychomycosis</i>
<i>PVD</i>	<i>Peripheral vascular disease</i>
<i>SWO</i>	<i>Superficial white onychomycosis</i>
<i>TDO</i>	<i>Total dystrophic onychomycosis</i>
<i>TNL</i>	<i>Terbinafine nail lacquer</i>
<i>US</i>	<i>United States</i>

ABSTRACT

Background: Onychomycosis is a fungal infection of the fingernails or toenails that causes discoloration, thickening, and separation from the nail bed. The causative organisms could be dermatophytes, yeasts or non-dermatophytic fungi. Dermatophytes especially of genus *Trichophyton* account for most of the cases, other pathogens like *Candida* and non dermatophytic molds are more frequent in countries with hot and humid climate.

Purpose: To evaluate the efficacy of tazarotene as a single topical treatment modality for onychomycosis.

Patients and Methods: The present study is a clinical interventional study, conducted on 80 patients with finger(s) and/or toe(s) nail onychomycosis (OM). These patients were recruited from the outpatient clinic of dermatology department at Ain Shams University Hospitals, during the period from January 2016 till October 2017.

Results: Our study included eighty patients with clinical and mycological-confirmed onychomycosis. All patients were recruited from the Dermatology Outpatient Clinic at Ain Shams University Hospitals during the period between January 2016 to October 2017. All patients were informed about the study and an informed consent was obtained; however, ten patients withdrew their consent and subsequently they were completely eliminated from the study.

Conclusion: The antifungal activity of Tazarotene is of moderate potency and is comparable to some of the commercially available topical antifungal. Owing to its modest efficacy, we cannot support its use as a single treatment in cases of OM.

Keywords: *Distal Subungual Onychomycosis - Endonyx onychomycosis - Candida Onychomycosis*

1. INTRODUCTION

Onychomycosis is a fungal infection of the fingernails or toenails that causes discoloration, thickening, and separation from the nail bed. The causative organisms could be dermatophytes, yeasts or non-dermatophytic fungi (**Westerberg and Voyack, 2013**). Dermatophytes especially of genus *Trichophyton* account for most of the cases (**Kaur et al., 2008**), other pathogens like *Candida* and non dermatophytic molds are more frequent in countries with hot and humid climate (**Chi et al., 2005**).

Accurate diagnosis is crucial for successful treatment of onychomycosis as the clinical picture of onychomycosis may mimic other conditions like nail psoriasis and chronic nail trauma (**Ameen et al., 2014**). Thus, laboratory identification of fungal elements is essential for diagnosis of onychomycosis. Direct microscopic examination after potassium hydroxide (KOH) preparation could reveal the presence of hyphae, pseudohyphae, or spores in positive cases, however, fungal culture is needed for identification of the specific species of pathogens (**Markinson et al., 2015**).

Treatment of onychomycosis is not easily accomplished because nails are made of keratin, which is non-vascular and impermeable to many agents resulting in poor drug delivery to nails and subsequently the treatment time may be prolonged (**Westerberg and Voyack, 2013**). Topical agents used for the

treatment of onychomycosis have the advantage of few contraindications and lack of drug-drug interactions. However, the hard keratin and compact structure of the dorsal nail plate act as a barrier to topical drug diffusion into and through the nail plate and thus, these agents are of limited efficacy when used alone. Topical therapy with ciclopirox has a failure rate exceeding 60% (*Kaur et al., 2008; Romero-Cerecero et al., 2008; Ameen et al., 2014*). Systemic antifungals are considered -to date- as the gold standard effective treatment with the highest clinical and mycotic cure rates but they have the risk of multiple drug interactions, systemic side effects and intolerability in some patients with systemic diseases (*Shemer, 2012; Piraccini and Gianni, 2013*).

Lasers like Nd: YAG and photodynamic therapies showed some success for treatment (*Piraccini and Gianni, 2013*).

Campione et al. (2015) investigated topically applied tazarotene for onychomycosis based on its immunomodulating properties and anti-inflammatory activity (*Epstein and Stein Gold, 2013*) and found that daily topical application of tazarotene 0.1% gel for 12 weeks was effective for clinical and mycotic cure in microbiological confirmed onychomycotic toenails. The anti-mycotic effectiveness of tazarotene was further confirmed through in vitro studies as the authors showed that the disk diffusion assay after 48 hours of incubation with tazarotene solution showed a central area of inhibition in all examined fungal cultures. They supposed that

the beneficial effects of tazarotene on ungual hyperkeratosis together with the activity of tazarotene against inflammation through immunomodulation might induce the blocking of fungal keratinolytic proteases which may explain the efficacy of tazarotene. However, the small sample size (12 patients) and lack of placebo control group constitute limitations for such results which should be further re-evaluated.

2. AIM OF THE WORK

The aim of this study is to evaluate the efficacy of tazarotene as a single topical treatment modality for onychomycosis.

Chapter 1

3.1. NAIL APPARATUS

The human nail can be considered to have many mechanical and social functions. The most prominent functions are fine manipulation, scratching, physical protection of the extremity and a vehicle for cosmetics and aesthetic manipulation (*De-Berker et al., 2007*).

Nails are keratinous horny plates that form protective coverings of the distal phalanges of the fingers and toes (*Daniel et al., 2004*). The nail is the permanent product of the nail matrix. Its normal appearance and growth depend on the integrity of several components such as the surrounding tissues (*De-Berker et al., 2007*).

The nail helps to increase the sensory perception in the pulp and helps in picking up small objects. Nail loss or deformity is not only unaesthetic in appearance but can be functionally incapacitating. A proper knowledge and understanding of nail anatomy is essential for a proper management of various conditions affecting it (*Bajantri and Bharathi, 2011*).

3.1.1. Overview of the nail physiology:

The growth rate of nails is highly variable among individuals, with average values of 3 mm per month for fingernails and 1mm per month for toenails. A normal