The effectiveness of laser treatments for onychomycosis in adults in the community: a systematic review thesis

Thesis submitted in fulfillment of the requirements of the Master of Clinical Science,
School of Translational Health Science,
Faculty of Health Sciences,
The University of Adelaide

Heather J Glaser, BA (Lib Stud), BPod
Declaration of authenticity and acknowledgement of authorship

I, Heather J Glaser, certify that this work contains no material which has been accepted for the award of any other degree or diploma in my name, in any university or other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text. In addition, I certify that no part of this work will, in the future, be used in a submission in my name, for any other degree or diploma in any university or other tertiary institution without the prior approval of the University of Adelaide and where applicable, any partner institution responsible for the joint-award of this degree.

I give consent to this copy of my thesis, when deposited in the University Library, to be made available for loan and photocopying, subject to the provisions of the Copyright Act 1968.

I also give my permission for the digital version of my thesis to be made available on the web, via the University's digital research repository, the Library Search and also through web search engines, unless permission has been granted by the University to restrict access for a period of time.

Heather J Glaser Date
Table of contents

THE EFFECTIVENESS OF LASER TREATMENTS FOR ONYCHOMYCOSIS IN ADULTS IN THE COMMUNITY: A SYSTEMATIC REVIEW THESIS

DECLARATION OF AUTHENTICITY AND ACKNOWLEDGEMENT OF AUTHORSHIP

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

ABSTRACT

ACKNOWLEDGEMENTS

CHAPTER 1: INTRODUCTION

1.1 Context of the Review

1.1.1 Onychomycosis

1.1.2 Dermatophytes, saprophytes, distribution and incidence

1.1.2.1 Types of onychomycosis

1.1.2.2 Demographics, social and economic impact

1.1.2.3 Microbiological identification techniques

1.1.2.3.1 Direct microscopy

1.1.2.3.2 Mycological culture

1.1.2.3.3 Confounding factors for identification

1.1.2.3.4 Sampling techniques

1.1.2.3.5 Sample types

1.1.2.3.6 Cumulative evidence

1.1.2.3.7 Emerging technology

1.1.2.3.8 Defining recurrence and cure

1.1.2.3.9 Sample types

1.1.3.2 Topical pharmaceutical treatments

1.1.3.1 Pharmacokinetics of topical treatments

1.1.4 Effectiveness of topical treatments

1.1.4.1 Oral systemic pharmaceutical treatments

1.1.4.2 Pharmacokinetics of oral treatments

1.1.4.3 Effectiveness of oral systemic pharmaceutical treatments

1.1.4.4 Laser technology and potential medical applications

1.1.4.5 Laser technology and potential medical applications

1.1.4.6 Types of lasers

1.1.4.6.1 Gas

1.1.4.6.2 Solid- State

1.1.4.6.3 Diode

1.1.4.7 Potential laser treatment parameters for onychomycosis

1.1.4.8 Laser research for onychomycosis

1.2 Why this systematic review was undertaken

1.3 Statement of the review question

1.4 Overview of the science of evidence synthesis

1.4.1 Narrative synthesis

1.4.2 Method of synthesis

1.4.3 What constitutes best evidence

1.4.4 Different forms of evidence

1.5 Methodological basis of the chosen approach to synthesis

1.6 Definition of terms

CHAPTER 2: THE SYSTEMATIC REVIEW PROTOCOL

23
List of tables

TABLE 3:1 SUMMARY OF INTERVENTIONS FOR ONE COHORT STUDY AND FIVE CASE SERIES USING ND:YAG 1064 NM................................................................. 34

TABLE 3:2 SUMMARY OF INTERVENTIONS FOR COHORT STUDY BY NICOLOPOULOS ET AL. 163 .... 35

TABLE 3:3 CRITICAL APPRAISAL SCORES FOR COMPARABLE COHORT/CASE CONTROL STUDIES 36

TABLE 3:4 CRITICAL APPRAISAL SCORES FOR FIVE INCLUDED DESCRIPTIVE/CASE SERIES STUDIES ........................................................................................................... 37

TABLE 3:5 CRITICAL APPRAISAL SCORES FOR TWO EXCLUDED DESCRIPTIVE/CASE SERIES...... 38

TABLE 3:6 SUMMARY OF OUTCOMES FOR COHORT STUDIES BY ZHANG ET AL. 164 AND NICOLOPOULOS ET AL. 163 ........................................................................................................... 39

TABLE 3:7 SUMMARY OF TWO CASE SERIES STUDIES HOCHMAN 165 AND KIMURA ET AL. 166 USING SHORT PULSED ND:YAG 1064 NM LASER ................................................................................................. 41

TABLE 3:8 SUMMARY OF THREE CASE SERIES STUDIES BY KOLODCHENKO 167 KOZAREV 168 AND KOZAREV 2011 168 USING LONG PULSED ND:YAG 1064NM LASER ........................................................... 43
List of figures

FIGURE 1: FLOW DIAGRAM OF SEARCH RESULTS AND SUBSEQUENT PROCESS OF REVIEW........ 32
Abstract
Background
There is growing public interest in the application of laser therapy to common nail conditions such as onychomycosis, where traditional pharmaceutical options are long-term, expensive, messy and often unsuccessful, and suited to a limited demographic. Recent reviews highlighting the potential of laser therapies to offer effective, convenient, short duration treatment regimens have not demonstrated the effectiveness of different laser types and treatment modalities creating the need for further detailed research. This systematic review identifies, critically appraises, synthesises and presents the best available evidence for the effectiveness of laser treatments on onychomycosis of the nails in adults living in the community. The specific review question was: can laser treatment of onychomycotic nails produce outcomes comparable to the current ‘gold standard’ treatment of oral terbinafine over a minimum 12 week treatment period, for adults living in the community?

Methods
A three step search strategy for published and unpublished studies in English language, in the date range 1/1/1985 to 30/6/2013 resulted in nine studies being critically appraised by two independent reviewers using the Joanna Briggs Institute Meta Analysis of Statistics, Assessment and Review Instrument (MAStARI). Seven papers were included for data extraction and synthesis. The primary outcome was cure or clinical response defined by at least 3mm of clear nail growth in a three to 12 month period, or negative microscopy (periodic acid-Schiff [PAS] or potassium hydroxide [KOH] and negative mycological culture [mycological cure]). Complete cure was defined as totally clear nail with negative culture and microscopy (PAS or KOH).

Main Findings
There was a weak association that neodymium-doped yttrium aluminum garnet Nd:YAG 1064nm laser for the treatment of onychomycosis in adults could produce clear nail growth and a mycological cure in a 12 week period. Although there is a plethora of laser therapy options currently on the market, evidence is either of poor quality and a measurable effect cannot be identified, or is absent, to the point that it is not possible to objectively evaluate claims of benefit. Practitioners should be aware of there are significant gaps in the evidence, and that current evidence only supports Nd:YAG 1064nm laser therapy.

Interpretation
Before a new intervention is implemented, there should be clear evidence of benefit in direct head-to-head comparative studies against a known gold standard intervention. This systematic review found no such evidence related to most forms of laser therapy, and also an absence of evidence for many claims associated with laser therapy. While Nd:YAG 1064nm laser for the treatment of onychomycosis in adults is supported, multi center, randomised studies with good controls and adequate power that directly compare laser therapy against oral terbinafine are needed in order to determine the therapeutic effectiveness of laser therapy.

The objectives, inclusion criteria and methods of analysis for this review were specified in advance and documented in a protocol,\(^1\) registration number CRD42013006731 in PROSPERO.\(^2\)

Initial keywords used were: laser, light therapy, mycoses, onychomycosis, and \textit{Trichophyton rubrum}. 
Acknowledgements

I would not have been able to undertake and complete my thesis without the help and support of a number of significant people who I would like to acknowledge and thank.

Firstly I would like to thank Emeritus Professor Alan Pearson for accepting my application into the Master of Clinical Science program.

I would also like to thank Dr Paul Harvey and Ms Kathy Barrett for their support of my application.

My journey through the program has been guided by two wonderful individuals, my supervisors, Associate Professor Dr Craig Lockwood and Dr Karolina Lisy. Their time, patience, and kind words of encouragement have sustained me.

Thank you to research librarian Ms Maureen Bell, Endnote wizard Ms Lucy Luzolo and all JBI staff for their assistance.

My dream of undertaking postgraduate study would not have been realised without the enduring support and encouragement of my fabulous husband, Alexander.