COMPARATIVE STUDY BETWEEN FRACTIONAL CO₂ LASER VERSUS INTRALESIONAL STEROIDS IN TREATMEANT OF ALOPECIA AREATA

Thesis
Submitted for Partial Fulfillment of Master Degree in

Dermatology, Venerology and Andrology

Presented by: Sara Mohammed Khalifa Elframawy

M.B. B,Ch. Faculty of Medicine Ain Shams University

Under the Supervision of:

Prof. Dr. Mohamed Abdel-Rahim Mahmoud Abdallah

Professor of Dermatology, Venerology and Andrology Faculty of Medicine Ain Shams University

Dr.Rania Mahmoud El Husseiny

Lecturer of Dermatology, Venerology and Andrology Faculty of Medicine Ain Shams University

Faculty of Medicine
Ain Shams University



2018



ACKNOWLEDGEMENT

First of all thanks to ALLAH for his care and generosity throughout my life.

I would like to express my sincere gratitude and deep appreciation to **Prof. Dr. Mohamed Abdel-Rahim Mahmoud Abdallah** Professor of Dermatology, Venereology and Andrology, Faculty of Medicine, Ain Shams University, for his continuous scientific guidance and strict supervision.

My appreciation and deep thanks are extended to **Dr. Rania**Mahmoud El Husseiny, lecturer of Dermatology, Venereology and Andrology, Faculty of Medicine, Ain Shams University, for her scientific guidance, helpful cooperation and effective advice throughout the entire work.

Sara Mohammed

Contents

List of Tables	• • • • • •
List of Figures	
List of Abbreviations	
Introduction	1
CHAPTER 1	4
Alopecia Areata	4
Defenition and Epidemiology	4
Pathogenesis	4
Clinical presentation and classification	10
Histopathology	14
Diagnosis and differential diagnosis	16
Course and Prognosis	20
Management	21
CHAPTER 2	28
Fractional CO ₂ Laser	28
Indications for Fractional Laser treatment	30
Mechanism of action of fractional ablative CO ₂ laser	in
treatment of AA	
Clinical and histological healing course	33
Contraindications for Fractional lasers	34
Complications of Fractional lasers	34
Chapter 3	36
Intralesional Cs	
Method of administration	37
Mode of action	38
Adverse effects	40
Patients And Methods	43
Patients	43
Materials	44
Study design and treatment	45
Evaluation of treatment response	46
Statistics	49
RESULTS	51
DISCUSSION	77
Conclusion	81
RECOMENDATION	82
SUMMARY	83
REFERENCES	
ARABIC SUMMARY	1

List of Tables

<u>Table 1:</u> Classification of Alopecia Areata
<u>Table 2:</u> Differential diagnosis of Alopecia Areata
<u>Table 3:</u> Complications of fractional laser resurfacing
<u>Table 4:</u> Mean Improvement Score by Physician47
<u>Table 5:</u> The demographic and clinical characteristics of patients52
<u>Table 6:</u> The demographic and clinical characteristics of all treated patient 53
<u>Table 7:</u> Comparison between treatment of AA with FCO ₂ laser and ILCs according to MISP, patient satisfaction and hair density
<u>Table 8:</u> Clinical results obtained for all treated 20 patients
<u>Table 9:</u> Comparison between treatment of AA with FCO ₂ laser and ILCs according to MISP in percentage
<u>Table 10:</u> Comparison between MISP, patient satisfaction and hair density seen 1month and 3 months after the last session of ILCs68
<u>Table 11:</u> Comparison between the results seen 1month and 3 months after the last session of ILCs according to MISP in percentage70
<u>Table 12:</u> Comparison between MISP, patient satisfaction and hair density seen 1month and 3 months after the last session with FCO ₂ laser71
<u>Table 13:</u> Comparison between the results seen 1month and 3 months after the last session of FCO ₂ laser according to MISP in percentage73
<u>Table 14:</u> Correlations between patient sex and MISP, patient satisfaction and hair density with FCO ₂ laser and ILCs
<u>Table 15:</u> Correlations between history of prior episode and MISP, patient satisfaction and hair density with FCO ₂ laser and ILCs75
<u>Table 16</u> : Correlations between the family history and MISP, patient satisfaction and hair density with FCO ₂ laser and ILCs
<u>Table 17:</u> Correlations between each of patient's age and duration of alopecia with the MISP patient satisfaction and hair density with FCO ₂ laser and ILCs

List of Figures

Figure 1: Hair growth cycle patterns in alopecia areata
Figure 2: Multifactorial etiology of Alopecia Areata
Figure 3: Model for pathogenesis of alopecia areata
Figure 4: Breakdown of immune privilege in alopecia areata
Figure 5: Role of Immune Privilege in Alopecia Areata
Figure 6: Characteristic "exclamation mark" hairs of alopecia areata10
Figure 7: Clinical variants of AA
Figure 8: The Histopathological features of AA
Figure 9: Assessment of hair using the Folliscope® and phototrichogram The density of the hair on the scalp (hair/cm2) and average caliber of the hair fibers (mm) can be calculated automatically
Figure 10: Dermoscopic features of alopecia areata
Figure 11: Treatment algorithm for AA involving the scalp
Figure 12: Demonstration of effects of ablative, non-ablative and fractional lasers
Figure 13: (a) Schematic picture of FP depicting MTZs surrounded by unharmed tissue. (b) Clinical picture depicting MTZs surrounded by unharmed tissue
<u>Figure 14:</u> Histological pattern seen after treatment with 20 mJ CO ₂ AFP 34
<u>Figure 15:</u> mechanism of action of corticosteroids
<u>Figure 16:</u> Glucocorticoid activation of anti-inflammatory gene expression42
<u>Figure 17:</u> Corticosteroid suppression of activated inflammatory genes42
Figure 18: Fire-Xel Bison Fractional CO ₂ laser machine
Figure 19: Intralesional corticosteroid injection
<u>Figure 20:</u> Patients overall rates of satisfaction

<u>Figure 21:</u> (Folliscope) microscopic camera connected to the laptop48
Figure 22: The software which analyses the images
<u>Figure 23:</u> Sex distribution among the studied group
<u>Figure 24:</u> The distribution of treated AA patches among patients52
Figure 25: A32 yr. old male with 2patches of AA showing excellent improvement in FCO ₂ laser treated patch while minimal improvement with ILCs treated patch with spreading of AA
Figure 26: Folliscopic pictures of AA patches in 32 yrs. old male (hair density x100) treated with FCO ₂ laser and ILCs
Figure 27: A 36 yr. old male with 2 patches of AA showing complete improvement in FCO ₂ laser treated patch while minimal improvement with ILCs treated patch that deteriorated later
Figure 28: Folliscopic pictures of AA patches in 36 yrs. old male (hair density x100) treated with FCO ₂ laser and ILCs
Figure 29: A 19 yr. old male with 2 patches of AA showing excellent improvement in FCO ₂ laser treated patch while moderate improvement with ILCs treated patch.
<u>Figure 30:</u> Folliscopic pictures of AA patches in 19 yrs. old male (hair density x100) treated with FCO ₂ laser and ILCs60
Figure 31: A 41 yr. old male with 2 patches of AA showing excellent improvement in FCO2 laser treated patch while minimal improvement with ILCs treated patch
<u>Figure 32:</u> Folliscopic pictures of AA patches in 41 yrs. old male (hair density x100) treated with FCO ₂ laser and ILCs
Figure 33: A 35 yr. old female with 2patches of AA showing marked improvement in FCO ₂ treated patch while moderate improvement with ILCs treated patch.
<u>Figure 34:</u> Folliscopic pictures of AA patches in 35 yrs. old female (hair density x100) treated with FCO ₂ laser and ILCs64
Figure 35: Comparison between treatment of AA with FCO ₂ laser and ILCs according to MISP in percentage

<u>Figure 36:</u> Comparison between treatment of AA with FCO ₂ laser and ILCs 3 months after the last session according to patient satisfaction66
Figure 37: Comparison between treatment of AA with FCO ₂ laser and ILCs according to folliscopic results of hair density 3 months after the last session.
Figure 38: Comparison between MISP seen 1 month and 3 months after the last session of ILCs
Figure 39: Comparison between patient satisfaction seen 1 month and 3 months after the last session of ILCs
Figure 40: Comparison between hair density (folliscope) seen 1 month and 3 months after the last session of ILCs
Figure 41: Comparison between the results seen 1month and 3 months after the last session of ILCs according to MISP in percentage70
Figure 42: Comparison between MISP seen 1 month and 3 months after the last session of FCO ₂
Figure 43: Comparison between patient satisfaction seen 1 month and 3 months after the last session of FCO ₂
Figure 44: Comparison between hair density (folliscope) 1 month and 3 months after the last session of FCO ₂
Figure 45: Comparison between the results seen 1month and 3 months after the last session of FCO ₂ according to MISP in percentage
<u>Figure 46:</u> Correlation between patient sex and MISP with ILCs74

List of Abbreviations

Abbreviation	Description
AA	Alopecia Areata
ADTA	Acute diffuse and total alopecia
AFP	Ablative fractional photothermolysis
AT	Alopecia Totalis
AU	Alopecia Universalis
BD	Becton Dickinson
CCCA	Central centrifugal cicatricial alopecia
CO2	Carbon Dioxide
DNCB	Dinitrochlorobenzene
FP	Fractional photothermolysis
HLA	Human leukocyte antigen
ILCs	Intralesional Corticosteroids
LASER	Light Amplification by Stimulated
	Emission of Radiation
LLLT	Low-level laser therapy
MEND	microscopic epidermal necrotic debris
MHC	Major histocompatibility complex
MISP	Mean Improvement Score by Physician
MTZ	Micro thermal Treatment Zones
PDGF	Platelet-derived growth factor
PMNs	Polymorphonuclear cells
PRP	Platelet Rich Plasma
PUVA	Psoralen plus UVA
SALT	Severity of Alopecia Tool score
TE	Telogen effluvium
VAS	visual analogue scale

INTRODUCTION

Alopecia Areata (AA) is a common non-scarring alopecia which affects 0.1-0.2% of the population and accounts for 0.7-3% of all cases seen in dermatology practice (*Alkhalifah*, 2013; Sinclair, 2014).

AA affects all races and both genders (male and female) equally although it is thought that there may be a male predominance in the adult population (*Kyriakis et al.*, 2009).

This inflammatory disease affects hair follicles and can also affect the nails in up to 66% of patients. Genetic predisposition, autoimmunity, and environmental factors play an important role in the etiopathogenesis of AA (*Kutner and Friedman*, 2013).

Alopecia areata is characterized by sudden appearance of round or oval, non-scarring, flat, single or multiple areas of alopecia, which may coalesce forming large patches of alopecia (*Estefan et al.*, 2015b).

Patchy type is the most common form of AA, other types of AA include classic forms (AA in unifocal patch, AA in multifocal patches, ophiasic AA, Alopecia Totalis (AT) and Alopecia Universalis (AU)) in addition to atypical forms (sisaifo or inverse ophiasis, reticular AA and diffuse AA) (*Pratt et al.*, 2017).

Atopy and autoimmune thyroiditis are the most common associated medical conditions. Peribulbar and intrabulbar lymphocytic inflammatory infiltrate resembling "swarm of bees" is characteristic on histopathology (*Seetharam*, 2013).

Trichoscopy and phototrichogram using a folliscope are recent methods which are very useful in diagnosis and assessment of treatment for AA. They are non-invasive, easy

Introduction

and painless methods that enable objective assessment of the disease activity (Brzezinska-Wcislo et al., 2014).

There are different modalities for treatment of alopecia areata including corticosteroids, minoxidil, anthralin, topical immunotherapy, phototherapy, prostaglandin analogues, sulfasalazine, mesotherapy, platelet rich plasma (PRP) and fractional CO₂ laser (*Farhangian et al.*, 2015).

Corticosteroids, because of their anti-inflammatory activity, have been considered the main line of treatment for AA. Topical steroids are preferred as a first choice in the treatment of AA. ILCs have been used since 1958 in the treatment of AA. It is the most effective treatment in patients with limited AA and a shorter duration of disease, with success rates of 60-75%. However, Patients with extensive AA or AT and longer duration of the disease (> 1 year) showed poor response .Systemic corticosteroids have been used in daily, weekly, and monthly pulses with good outcome in patchy AA and less favorable outcome in ophiasis, AT, and AU (*Kar et al.*, 2005; *Kassim et al.*, 2014; *Gupta et al.*, 2017).

Fractional photothermolysis is a newly introduced laser technique. Its action depends on the production of a unique thermal damage pattern called 'microthermal treatment zones (MTZ)' and characteristically spares the tissue surrounding each MTZ. It keeps the strarum corneum intact and induces 'fractional' microscopic thermal columns to the dermis, which leads to a healing process that includes inflammatory cells, such as lymphocytes (*Manstein et al.*, 2004).

There are many dermatological applications for fractional CO_2 laser e.g. improves scars, fine lines, dyspigmentation, striae and wrinkles (*Goel et al.*, 2011).

Recently, Fractional CO₂ laser can be applied in treatment of AA. Ho Yoo and colleagues found that fractional

Introduction

photothermolysis induces complete hair growth after 6 months in a patient with patchy alopecia of the scalp (*Yoo et al.*, 2010).

So the aim of our study is to assess the efficacy of fractional CO_2 laser in comparison to intralesional steroid injection in treatment of alopecia areata.

I. ALOPECIA AREATA

Definition and Epidemiology:

Alopecia areata (AA) is a common non cicatricial, autoimmune, inflammatory disease, which is characterized by hair loss on the scalp and or body, It accounts for 0.7% to 3.8% of dermatology clinics visits (*Wasserman et al., 2007*).

AA affects both genders (male and female) equally (*Kyriakis et al.*, 2009). The most commonly affected age group are the children where they constitute about 20% of AA patients (*Nanda et al.*, 2002).

Pathogenesis:

Hair growth depends on 3 phases of hair cycle, anagen (active growth phase), catagen (involution phase), and telogen (resting phase). Normally, hair sheds out after the resting phase when the new hair anagen growth starts (exogen). In alopecia, hair loss happens even before the anagen phase starts leaving the hair follicle empty (kenogen). So, AA is in general a disease of hair cycling and is considered to be a state of kenogen (Fig. 1) (Seetharam, 2013).

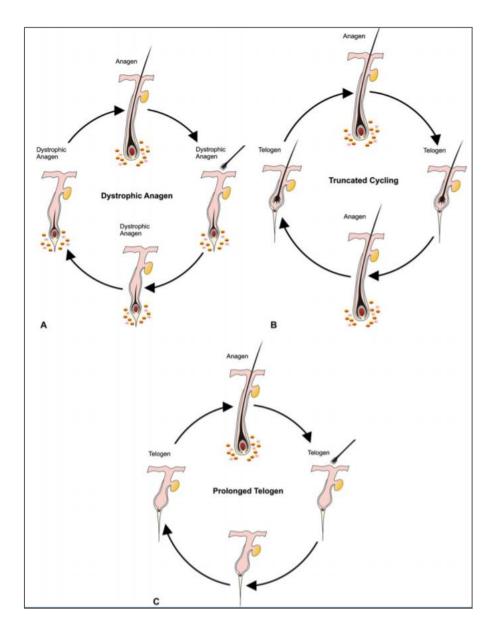


Figure 1: Hair growth cycle patterns in alopecia areata. **A**, Hair follicles held in dystrophic anagen by mild inflammatory insult unable to produce significant hair fiber. **B**, Anagen growth phases truncated by moderate inflammatory insult resulting in rapid cycling and brief hair fiber growth. **C**, Hair follicles enter prolonged telogen dormancy with development of chronic alopecia areata (*Alkhalifah et al.*, *2010a*).

AA has a multifactorial etiology; it is most likely an organ-specific autoimmune disease. Gene association studies confirm a genetic predisposition. Environmental triggers have been postulated, but none have been confirmed and this means that alopecia areata have a multifactorial etiology (Fig. 2) (*Perera et al.*, 2015).

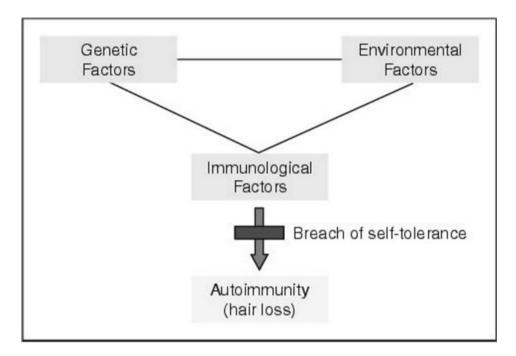


Figure 2: Multifactorial etiology of Alopecia Areata (Alexis et al., 2004).

Autoimmunity is thought to play an important role in the development of AA. It is regarded as a tissue-specific immune disease of hair follicles, mediated by T-helper (Th1) cell response (Fig. 3) (*Kuwano et al.*, 2007).