

**Evaluation of Serum Cutaneous T-cell  
Attracting Chemokine (CTACK) after Pulsed  
Dye Laser for Inflammatory Acne**

(Thesis)

Submitted for the partial fulfillment of the Master Degree  
in Dermatology, Venereology and Andrology

By

**Sameh Kamel Fawzy Tawfik**

MB.BCh. 2006

Under Supervision of

**Prof. Dr. May Hussein El Samahy**

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

**Dr. Enas Attia Saad El Din Attia**

Assistant Professor of Dermatology, Venereology and  
Andrology

Faculty of Medicine, Ain Shams University

**Dr. Yasser Abdallah Abd El Aziz**

Assistant Professor of Plastic Surgery  
Faculty of Medicine, Ain Shams University

Faculty of Medicine  
Ain Shams University  
2013

## *Acknowledgements*

First of all, thanks to **Allah**, the most merciful, for helping me complete this work.

I wish to express my deepest gratitude and respect to my honored professor, **Prof. Dr. May Hussein El Samahy**, Professor of Dermatology, Venereology, and Andrology, Ain Shams University, for her valuable guidance and supervision throughout this work.

I would like also to express my deepest gratitude and respect to **Dr. Enas Attia Saad El Din Attia**, Assistant Professor of Dermatology, Venereology, and Andrology, Ain Shams University for her kind support and constant guidance and supervision throughout this work.

Special thanks go to **Dr. Yasser Abdallah Abd El Aziz**, Assistant Professor of Plastic Surgery, Ain Shams University for his sincere efforts and fruitful encouragement.

I would like also to thank **Dr. Sherine El Bendary**, Assistant Professor of Microbiology, Ain Shams University for her kind support and supervision of the laboratory part of this work.

I would like to thank all members of the Dermatology and Venereology Department at Kobry Elkobba Armed Forces Hospital for their help and cooperation.

Finally, I would like to thank my family and friends for their constant support, help and guidance throughout my work. I could not have done it without them.

*Sameh kamel fawzy*

## Introduction

Acne vulgaris is a chronic inflammatory disorder of sebaceous follicles, found primarily on the face and upper trunk (chest and back), characterized by the formation of comedones, erythematous papules and pustules and less frequently by nodules or pseudocysts. It is a pleomorphic disorder with multifactorial pathogenesis (**Oberemok and Shalita, 2002**). *Propionibacterium acnes* (*P. acnes*) are gram-positive, anaerobic diphtheroids that are part of the normal skin flora (**Kang et al., 2005**). They play an important role in the pathogenesis of acne vulgaris by triggering pro-inflammatory mediators (**Graham et al., 2004**).

Acne is the most common skin disease, estimated to affect approximately 80% of individuals at some point between the ages of 11 and 30 years. Although not life-threatening, acne can adversely impact psychosocial development, and may cause significant emotional problems, depression, and even suicide (**Aktan et al., 2000**). Colonization with *P. acnes* is closely associated with the development of antibiotic resistance and is related to acne treatment failure (**Eady et al., 1993**).

*P. acnes* are porphyrin containing organisms that are killed by exposure to specific wavelengths of light (**Ashkenazi et al., 2003**). The photosensitivity of the bacterium accounts for the improvement noticed by most individuals with acne after exposure to sun light and has encouraged the development of artificial visible light sources as treatment for this disease (**Stillman and Green, 2000**).

Lasers differ from non-laser light sources in that they emit minimally divergent coherent light that can be focused to a small area of tissue to provide very high irradiances.

Pulsed dye lasers (PDLs) emit visible light that is mainly absorbed by oxyhaemoglobins so high irradiation energy densities (fluences) are used to treat vascular lesions such as port wine stains (*Bernstein, 2006*). Non ablative PDLs are increasingly used in cosmetology practice to improve the appearance of fine wrinkles and are found to be effective in the treatment of atrophic acne scarring (*Patel and Clement, 2002*). In addition, experiences in several clinics suggests that patients receiving low- fluence PDL treatment have coincidental striking and long standing improvements in inflammatory acne after a sole treatment of the face (*Seaton et al., 2003*). PDL appears to be a useful therapeutic option for inflammatory acne patients who are recalcitrant to standard treatment and poor candidates for systemic retinoids (*Riddle et al., 2009*).

Early inflammatory acne lesions are characterized by the infiltration of the pilosebaceous duct with CD4+T-helper-1 cells that are reactive to *P. acnes* (*Norris and Cunliffe, 1988*). Cutaneous T-cell attracting chemokine (CTACK) is a member of the CC chemokine family and a functional ligand for CC chemokine receptor 10. It is selectively expressed in skin and attracts CC chemokine receptor 10-expressing skin-homing memory T cells. The epidermal keratinocyte is a main source of CTACK, suggesting its involvement of various skin diseases as atopic dermatitis, psoriasis (*Kakinuma and Saeki, 2003*), and mycosis fungoides (*Fugita et al., 2006*), and possibly, inflammatory acne vulgaris.

## **Aim of the work**

The aim of this study is to evaluate the efficacy and tolerability of low-fluence PDL treatment in patients with facial inflammatory acne with assessment of serum CTACK level before and after therapy, in comparison to normal controls.

## List of Abbreviations

17 -HSD	17 hydroxy steroid dehydrogenase
5 - DHT	5 – dihydroxy testosterone
ALA	Aminolevulinic acid
BCA	B-cell activating chemokine
CLA	Cutaneous lymphocyte associated antigen
CREST syndrome	Calcinosis, Raynaud’s phenomenon, esophageal dysmotility, sclerodactyly, and telangiectasia syndrome
<i>CTACK</i>	<i>Cutaneous T-cell attracting chemokine</i>
CW	Continuous wave
DCD	Dynamic cooling device
DCs	Dendritic cells
DHEA	Dehydroepiandrosterone
DHEAS	Dehydroepiandrosterone sulfate
ELR motif	Elliptical rough motif
EMLA	Eutectic Mixture of Local Anaesthesia
ENA-78	Epithelial-neutrophil activating peptide 78
FDA	Food and Drug Administration
FPDL	Flash lamp pulsed dye laser
GITRL	Glucocorticoid-induced TNF receptor-related protein ligand
GM-CSF	Macrophage-colony stimulating factor
GRO-	Growth-related oncogene-
GSTP	Glutathione –S- Transferase pi
GSTT	Glutathione –S- Transferase theta
GSTZ	Glutathione –S- Transferase zeta
HPLC	High-performance liquid chromatography
IFN	Interferon
IL	Interleukin

<i>IP-10</i>	<i>Interferon-inducible protein -10</i>
J/cm <sup>2</sup>	Joules per square centimeter
Lab	Laboratory
LASER	Light amplification by the stimulated emission of radiation
LH	Luteinizing hormone
LTB4	Leukotriene B4
LTPDL	Long tunable pulsed dye laser
MAL	Methyl aminolevulinic acid
<i>MCP</i>	<i>Monocyte chemotactic protein</i>
MGSA	Melanoma growth-stimulating activity
<i>MIP-1</i>	<i>Macrophage inflammatory protein-1</i>
MMP	Matrix metalloproteinase
mRNA	messenger Ribonucleic acid
<i>NAP-2</i>	<i>Neutrophil activating peptide-2</i>
NF- B	Nuclear factor kappa; light chain-enhancer of activated B cells
NK	Natural killer
No.	Number
P	Probability value
<i>P. acnes</i>	<i>Propionibacterium acnes</i>
PASI	Psoriasis area and severity index
PDL	Pulsed dye laser
PF4	Platelet factor 4
PPARs	Peroxisome Hyper-Proliferator Activated Receptors
PRRs	Pattern recognition receptors
PRT	Pulse repetition time
PSU	The pilosebaceous unit
PWS	Port wine stain

r	Correlation coefficient factor
Q	Quality
<i>RANTES</i>	Regulated upon activation, normal T-cell expressed and secreted
<i>RARs</i>	<i>Retinoic acid receptors</i>
SAPHO syndrome	Synovitis, acne, pustulosis, hyperostosis and osteitis syndrome
SCC	Squamous cell carcinoma
SCM	Single- C Motif
SD	Standard deviation
<i>SDF-1</i>	<i>Stromal-derived factor-1</i>
SP	Selective Photothermolysis
SPSS	Statistical Package for Scientific Studies
TARC	Thymus activation-regulated chemokine
TLR	Toll- like receptor
TNF	Tumor necrosis factor
TRT	Thermal relaxation time
UV	Ultraviolet
UVR	Ultraviolet radiation
$X^2$	Chi-Square test



## Contents

	<b>Page</b>
<b>List of Abbreviations .....</b>	i – iii
<b>List of Tables.....</b>	iv
<b>List of Figures .....</b>	v – vii
<b>Introduction.....</b>	1
<b>Review of Literature</b>	
<b>Chapter 1: Acne Vulgaris</b>	5
<b>Chapter 2: Pulsed Dye Laser</b>	35
<b>Chapter 3 : Chemokines in Acne</b>	58
<b>Subjects and Methods.....</b>	80
<b>Results.....</b>	92
<b>Discussion .....</b>	109
<b>Summary and Conclusion.....</b>	120
<b>References.....</b>	125
<b>Arabic Summary.....</b>	.....

## List of Figures

Figure	Title	Page
<b>Figure (1)</b>	Schematic representation of the pilosebaceous unit.	6
<b>Figure (2)</b>	Different types of pilosebaceous unit.	7
<b>Figure (3)</b>	Modern aspects of acne pathogenesis.	10
<b>Figure (4)</b>	Illustration of microcomedo.	11
<b>Figure (5)</b>	<i>Whiteheads</i> (closed comedones): stays beneath the skin, slightly raised, light coloured lesion; and <i>Blackheads</i> (open comedones): a whitehead becomes a blackhead when it enlarges until a dark plug protrudes through the skin surface.	11
<b>Figure (6)</b>	Pathway of androgen biosynthesis.	13
<b>Figure (7)</b>	Events in the evolution of an inflammatory acne lesion.	17
<b>Figure (8)</b>	Acne lesions and acne pathogenesis.	21
<b>Figure (9)</b>	Spontaneous emission.	35
<b>Figure (10)</b>	Monochromaticity of laser waves.	36
<b>Figure (11)</b>	Collimation of laser waves.	36
<b>Figure (12)</b>	The wavelength of PDL (577-595 nm) corresponds to the yellow light in the visible spectrum of light, being able to penetrate deeper and target dermal blood vessels.	48
<b>Figure (13)</b>	The electromagnetic spectrum.	49
<b>Figure (14)</b>	Hemoglobin absorption curve.	50
<b>Figure (15)</b>	V- Beam Platinum, 595 nm, Candela Laser.	84
<b>Figure (16)</b>	Gender distribution among the studied groups.	92
<b>Figure (17)</b>	Age distribution among the studied groups.	93
<b>Figure (18)</b>	Skin phototype distribution among the studied groups.	94

<b>Figure (19)</b>	Patient no. 2: pretreatment photo (left) with mild acne on cheeks, and post-treatment photo (right); improvement of acne lesions was excellent (score 4).	97
<b>Figure (20)</b>	Patient no. 5: pretreatment photos (left) with moderate acne on cheeks, and post-treatment photos (right); improvement of acne lesions was good (score 3).	98
<b>Figure (21)</b>	Patient no. 7: pretreatment photo (left) with mild acne on cheeks, and post-treatment photo (right); improvement of acne lesions was good (score 3) with improvement of acne scars as well.	99
<b>Figure (22)</b>	Patient no. 8: pretreatment photo (right) with moderate acne on cheeks, and post-treatment photo (left); improvement of acne lesions was fair (score 2).	99
<b>Figure (23)</b>	Patient no. 10: pretreatment photo (left) with mild acne on cheeks, and post-treatment photo (right); improvement of acne lesions was excellent (score 4). Improvement of non-inflammatory acne lesions (arrows) was less than inflammatory lesions.	100
<b>Figure (24)</b>	Improvement score distribution among the studied cases.	101
<b>Figure (25)</b>	Level of Satisfaction among the studied cases.	101
<b>Figure (26)</b>	Comparison between CTACK before treatment among cases versus controls.	103
<b>Figure (27)</b>	Comparison between CTACK before and after treatment among cases.	103
<b>Figure (28)</b>	Correlation between CATCK levels before and after treatment among the studied cases.	104

<b>Figure (29)</b>	CATCK levels in both genders of the studied cases.	105
<b>Figure (30)</b>	CATCK levels in patients with different skin phototypes.	106
<b>Figure (31)</b>	Relation between CATCK level and improvement score among the studied cases.	107

## List of Tables

<b>Table</b>	<b>Subject</b>	<b>Page</b>
<b>Table (1)</b>	Inflammatory factors involved in Acne.	17
<b>Table (2)</b>	Characteristic features of non-inflammatory and inflammatory lesions in acne.	20
<b>Table (3)</b>	Chemokine receptors, corresponding human loci, and human ligands	63-65
<b>Table (4)</b>	Improvement scores of acne lesions	85
<b>Table (5)</b>	Comparing cases to controls revealed statistically matched gender distribution among both groups.	92
<b>Table (6)</b>	Comparing cases to controls revealed statistically matched age distribution among both groups.	93
<b>Table (7)</b>	Skin phototype distribution in cases compared to controls.	93
<b>Table (8)</b>	Clinical data of the patients.	94
<b>Table (9)</b>	Comparison between pre-treatment and post-treatment CTACK among cases, as well as in cases versus controls.	102
<b>Table (10)</b>	Comparison between CATCK levels among both genders of the studied cases.	104
<b>Table (11)</b>	Comparing CATCK levels in patients with different skin phototypes.	105
<b>Table (12)</b>	Correlation between CATCK levels and age among the studied cases.	106
<b>Table (13)</b>	Relation between CATCK level and improvement score among the studied cases.	107

# **Chapter 1**

## **Acne Vulgaris**

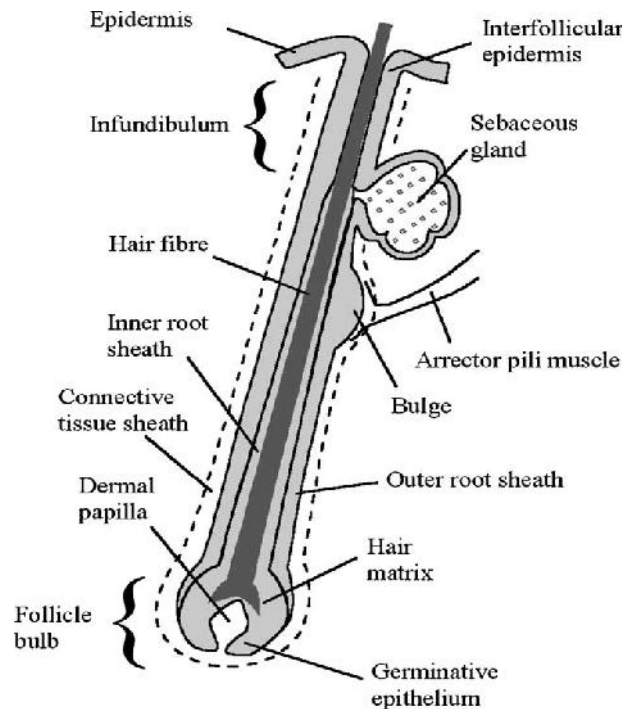
Acne vulgaris is a chronic inflammatory disorder of sebaceous follicles, found primarily on the face and upper trunk (chest and back), characterized by the formation of comedones, erythematous papules and pustules and less frequently by nodules or pseudocysts (*Williams et al., 2012*). Acne is the most common skin disease, estimated to affect approximately 80% of individuals at some point between the ages of 11 and 30 years. Although not life-threatening, acne can adversely impact psychosocial development, and may cause significant emotional problems, social withdrawal, depression, and even suicide (*James, 2005*).

### **- Etiopathogenesis of acne vulgaris:**

The pilosebaceous follicles are mostly found on the face (900 glands/cm<sup>2</sup>), behind the ears and on the upper portion of the chest and the back; the sites for predilection of acne. The follicle consists of 4 parts: the keratinized follicular infundibulum, the hair, the cauliflower-like convoluted sebaceous gland, and the sebaceous duct which connects the gland with the infundibulum (*Goodman, 2001*).

The pilosebaceous unit (PSU) is the site of acne (**Fig. 1**). In acne-prone skin, the PSU is composed of large, multi-lobulated sebaceous glands, a rudimentary hair and a wide follicular canal lined with stratified squamous epithelium in sebaceous follicle (**Fig. 2**). During the regular turnover process of the skin, desquamated cells are extruded from the follicular canal towards the infundibulum (the funnel shaped opening at the top of the follicle), pushed by the sebum secreted from the sebaceous glands. Normal development, growth and differentiation of the PSU require

the interaction of androgens with numerous other biological factors, including growth factors and thyroid hormones (Deplewski and Rosenfield, 2000; Schaller and Plewig, 2003).



**Fig. (1):** Schematic representation of the pilosebaceous unit showing the hair follicle and sebaceous gland, as well as epithelial compartments, the outer and inner root sheaths, germinative epithelium and matrix; mesenchymally derived compartments, the dermal papilla and connective tissue sheath (Schaller and Plewig, 2003).