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

(Thesis)
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By
Sameh Kamel Fawzy Tawfiek
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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
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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

17β-HSD	17β hydroxy steroid dehydrogenase
5α - DHT	5α – 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
CTACK	*Cutaneous T-cell attracting chemokine*
CW	Continuous wave
DCD	Dynamic cooling device
DCs	Dendritic cells
DHEA	Dehyroepiandrosterone
DHEAS	Dehyroepiandrosterone 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- α	Growth-related oncogene-α
GSTP	Glutathione –S- Transferase pi
GSTT	Glutathione –S- Transferase theta
GSTZ	Glutathione –S- Transferase zeta
HPLC	High-performance liquid chromatography
IFN	Interferon
IL	Interleukin

IP-10	*Interferon-inducible protein -10*
J/cm^2	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
MCP	*Monocyte chemotactic protein*
MGSA	Melanoma growth-stimulating activity
MIP-1	*Macrophage inflammatory protein-1*
MMP	Matrix metalloproteinase
mRNA	messenger Ribonucleic acid
NAP-2	*Neutrophil activating peptide-2*
NF-κB	Nuclear factor kappa; light chain-enhancer of activated B cells
NK	Natural killer
No.	Number
P	Probability value
P. acnes	*Propionibacterium acnes*
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
RANTES	Regulated upon activation, normal T-cell expressed and secreted
RARs	*Retinoic acid receptors*
SAPHO syndrome	Synovitis, acne, pustulosis, hyperostosis and osteitis syndrome
SCC	Squamous cell carcinoma
SCM	Single- C Motif
SD	Standard deviation
SDF-1	*Stromal-derived factor-1*
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

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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/cm2), 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).***

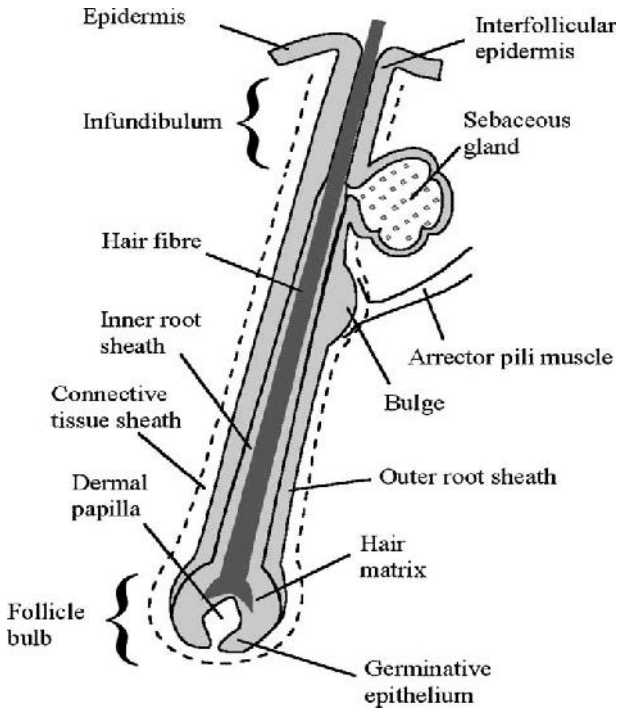

Fig. (1): Schematic representation of the pilosebaceous unit showing the hair follicle and sebaceous gland, as well as epithelial compartments, the outer and inner root sheaths, germinative epithelium and matrix; mesenchymally derived compartments, the dermal papilla and connective tissue sheath ***(Schaller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