Assessment of serum Desnutrin levels in patients with acne vulgaris

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By

Mohamed Abd El Hamid Habib

M.B, B.Ch.

Faculty of Medicine – Ain shams university

Under Supervision of

Professor/ Hanan Mohammed Saleh

Professor of Dermatology, Venereology and Andrology

Faculty of Medicine – Ain shams university

Doctor/ Manal Ahmed Sharara

Lecturer of Dermatology, Venereology and Andrology

Faculty of Medicine – Ain shams university

Faculty of Medicine

Ain Shams University

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ABSTRACT

Background: Acne vulgaris is a common chronic skin disease involving blockage and/or inflammation of pilosebaceous units (hair follicles and their accompanying sebaceous gland). Desnutrin is the major triglyceride lipase in the adipose tissue of mice and excessive secretion from adipocytes results in decreased triacylglycerol storage and increased lipolysis, fatty acid oxidation and thermogenesis.

Objective: The aim of this study is to evaluate serum level of Desnutrin in acne vulgaris patients and correlate it with disease severity.

Patients and Methods: This study was performed on 40 patients with active acne lesions and 40 healthy subjects with no previous history of acne and no active acne lesions as controls. The control group was composed of age, gender, and Body mass index (BMI) matched individuals. All the patients were recruited from the outpatient clinic of Dermatology & Venereology Department, Ain Shams University hospitals, from March 2016 till August 2016.Serum desnutrin assessment was done by ELISA kit using Sandwich-ELISA as a method. The Micro elisa stripplate has been pre-coated with a Horse Radish Peroxidase antibody specific to desnutrin. The optical density was measured spectrophotometrically.

Results: There was a **significantly lower** level of serum desnutrin among cases compared to that of control group, while the fasting blood glucose level was **significantly higher** among cases compared to that of control group. The collective data from both study groups showed a **significant negative correlation** between the mean serum fasting blood glucose level and desnutrin level. There was **no significant correlation** between the severity of acne and serum desnutrin level.

Conclusion: The level of serum desnutrin can affect the occurrence and the progression but not the severity of acne among susceptible individuals. The level of fasting blood glucose is also of value regarding the occurrence of acne and has a negative effect on the level of desnutrin.

Keywords: Acne, Serum desnutrin, severity, fasting blood glucose, lipid profile.

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Table of Contents

List of abbreviations

IGF-1	Insulin-like growth factor-1
IGFBP-1	Insulin-like growth factor-1-binding protein
PNPLA2	Patatin-like phospholipase domain-containing protein 2
ATGL	Adipose triglyceride lipase
Ipla2	Independent phospholipase A2
VCAM-1	Vascular cell adhesion molecule-1
ICAM-1	Intercellular adhesion molecule-1
HLA–DR	Human leukocyte antigen
P acnes	Propionibacterium acnes
DHEA-S	Dehydroepiandrosterone sulfate
RAR	Retinoic acid receptor
RXR	Retinoids X receptor
RAMBAs	Retinoic acid metabolism blocking agents
BP	Benzoyl Peroxide
OCs	Oral contraceptives
FDA	Food and Drug Administration
EE	Ethinyl estradiol
CBC	Complete blood count
AAD	American Academy of Dermatology
COC	Combined oral contraceptives
WHO	World Health Organization
TAG	Triacylglycerol
mRNA	Messenger ribonucleic acid
cAMP	Cyclic adenosine monophosphate
AMP	Adenosine monophosphate
HSL	Hormone-sensitive lipase
WAT	White adipose tissue
UCP-1	Uncoupling protein 1
FA	Fatty acid
aP2	Adipocyte Protein 2
NEFA	Non-essential fatty acid
BMI	Body mass index
PKU	Phenylketonuria
LDL	Low density lipoprotein
VLDL	Very low-density lipoprotein
HDL	High density lipoprotein
ELISA	Enzyme linked immunosorbent assay
HRP	Horseradish Peroxidase

SD	Standard deviation
ANOVA	Analysis of Variance
NS	Non-significant
HS	Highly significant
FBG	Fasting blood glucose
HOMA-IR	Homeostasis Model Assessment of Insulin Resistance

List of Tables

List of Figures

Introduction

Acne vulgaris is a common chronic skin disease involving blockage and/or inflammation of pilosebaceous units (hair follicles and their accompanying sebaceous gland). Acne can present as noninflammatory lesions, inflammatory lesions, or a mixture of both, affecting mostly the face but also the back and chest **(Dawson et al., 2013).**

Acne vulgaris has a multifactorial pathogenesis, of which the key factor is genetics**.** Acne develops as a result of an interplay of the following four factors: (1) follicular epidermal hyperproliferation with subsequent plugging of the follicle, (2) excess sebum production, (3) the presence and activity of the commensal bacteria Propionibacterium acnes, and (4) inflammation **(Thiboutot et al., 2009).**

Androgens and insulin contribute to an increase in sebum production in the pathogenesis of acne vulgaris. In addition, a correlation between insulin-like growth factor-1 (IGF-1) and facial sebum levels has been shown **(Vora et al., 2008).**

High glycemic load diets may result in increased androgen activity and IGF-1, thereby promoting the development of acne. There was significant improvement of acne severity in patients who adhered to a low glycemic load diet resulted in significant reductions in weight, body mass index, free androgen index, increased IGF-binding protein (IGFBP)-1 serum levels with reduced bioavailability of free IGF-1 and improved insulin sensitivity. Serum IGFBP-1 and IGFBP-3 increased from baseline in the low glycemic load group **(Smith et al., 2007).**

Desnutrin is a patatin-like domain-containing protein, desnutrin (PNPLA2), is also known as human adipose triglyceride lipase (ATGL) and ipla2. Desnutrin is highly expressed in adipose tissue and produced at

low levels in other tissues. Desnutrin secretion is stimulated by fasting and glucocorticoids **(Villena et al., 2004).**

Desnutrin is the major triglyceride lipase in the adipose tissue of mice and excessive secretion from adipocytes results in decreased triacylglycerol storage and increased lipolysis, fatty acid oxidation and thermogenesis. It has been reported that these effects result in high energy expenditure and resistance to diet-related obesity development **(Ahmadian et al., 2009).**

Patients with acne vulgaris are more likely to experience an increase in serum glucose levels. This was found to probably cause suppression in serum Desnutrin levels and its function **(Betul et al, 2014).**

Aim of the work

The aim of this work is to evaluate serum level of Desnutrin in acne vulgaris patients and correlate it with disease severity.

Acne

Acne vulgaris is a common chronic skin disease involving blockage and/or inflammation of pilosebaceous units (hair follicles and their accompanying sebaceous gland). Acne can present as noninflammatory lesions, inflammatory lesions, or a mixture of both, affecting mostly the face but also the back and chest. ***(Dawson, 2013).***

Although acne vulgaris is neither life threatening nor physically debilitating, acne can severely affect social and psychologic functioning. ***(Abdel-Hafez et al., 2009).***

I. Epidemiology:

Persons of some races are affected more than others. Cystic acne is prevalent in the Mediterranean region from Spain to Iran. Moderate-to-severe acne affects around 20% of young people and severity correlates with pubertal maturity. The heritability of acne is almost 80% in first-degree relatives. ***(Smith, 2007).***

Race:

Acne is common in North American whites. African Americans have a higher prevalence of pomade acne, likely stemming from the use of hair pomades. Ethnicities with darker skin are also more prone to post inflammatory hyperpigmentation. ***(Davis and Callender, 2010).***

Sex:

During adolescence, acne vulgaris is more common in males than in females. In adulthood, acne vulgaris is more common in women than in men. ***(Shaw and White, 2001).***

Age:

Acne or acneform lesions, such as in neonatal cephalic pustulosis, may be present in the first few weeks and months of life, when a newborn is still under the influence of maternal hormones and when the androgen-producing portion of the adrenal gland is disproportionately large. This

neonatal acne tends to resolve spontaneously. However, some neonates may require therapy (e.g., topical retinoids). ***(Eichenfield et al., 2013).***

Adolescent acne usually begins with the onset of puberty, when the gonads begin to produce and release more androgen hormone. Acne is not limited to adolescence. Twelve percent of women and 5% of men at aged 25 years have acne. By age 45 years, 5% of both men and women still have acne. ***(Schlosser, 2012).***

II. Pathophysiology:

The pathogenesis of acne vulgaris is multifactorial. The key factor is genetics. ***(Zouboulis et al., 2002).***

Family history of acne was also significantly associated with an increased risk. The evidence of a major genetic influence on acne should stimulate the search for potential genes that may lead to new therapeutic approaches. ***(Bataille et al., 2002).***

Acne develops as a result of interplay of the following four factors. ***(Thiboutot et al., 2009)***:

- Release of inflammatory mediators into the skin.
- Follicular hyperkeratinization with subsequent plugging of the follicle.
- *Propionibacterium acnes* follicular colonization.
- Excess sebum production. ***(Thiboutot et al., 2009).***

Inflammatory response:

Research has shown that inflammatory responses actually occur before hyperkeratinization. Cytokines produced by CD4+ T cells and macrophages activate local endothelial cells to up-regulate inflammatory mediators such as vascular cell adhesion molecule-1 (VCAM-1), intercellular adhesion molecule-1 (ICAM-1), and human leukocyte

antigen (HLA)–DR in the vessels around the pilosebaceous follicle. ***(Jeremy et al., 2003).***

Follicular hyperkeratinization:

Follicular hyperkeratinization is a key element in the pathogenesis of acne and a main target of retinoid activity. Hyperkeratinization occurs when the cells of the follicle become cohesive and do not shed normally onto the skin's surface. Follicular hyperkeratinization involves increased keratinocyte proliferation and decreased desquamation, leading to sebum- and keratin-filled microcomedones. The result is subsequent lesions characteristic of acne. ***(Thiboutot, 2009).***

Propionibacterium acnes (P acnes):

Propionibacterium acnes is an anaerobic organism present in acne lesions. The presence of P acnes promotes inflammation through a variety of mechanisms. P acnes stimulates inflammation by producing proinflammatory mediators that diffuse through the follicle wall. Studies have shown that P acnes activates the toll-like receptor 2 on monocytes and neutrophils. ***(Kim et al., 2002).*** Activation of the toll-like receptor 2 leads to the production of multiple proinflammatory cytokines, including interleukins 12 and 8 and tumor necrosis factor. Hypersensitivity to P acnes may also explain why some individuals develop inflammatory acne vulgaris while others do not. ***(Lai and Gallo, 2009).***

Excess sebum:

Excess sebum is another key factor in the development of acne vulgaris. Sebum production and excretion are regulated by a number of different hormones and mediators. In particular, androgen hormones promote sebum production and release. The degree of comedonal acne in prepubertal girls correlates with circulating levels of the adrenal androgen dehydroepiandrosterone sulfate (DHEA-S). ***(Makrantonaki et al., 2011).***

Numerous other mediators and receptors, including growth hormone and insulin like growth factor, as well as peroxisome