

Serum Zinc Levels in Patients with Acne Vulgaris and Its Relation to The Severity of Disease

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ABSTRACT

Background: acne vulgaris is a chronic inflammatory disease of the skin that affects the individuals of all ages, especially adolescents. An association between serum zinc levels and acne vulgaris have been reported in some studies.

Objective: the aim of our study was to estimate serum zinc level in patients with acne vulgaris and healthy subjects and its association with severity of disease.

Patients and Methods: this study was conducted on 60 patients (subdivided into 4 groups according to severity of disease according to Global Acne Grading System) and 60 normal individuals as a control group.

Results: there was highly significantly statistical difference between all patients and control groups as regard serum zinc level (mean of serum zinc level in patients and control groups were 49.85 ± 19.61 and 63.46 ± 22.95 respectively, $p < 0.001$).

Conclusion: it is concluded that zinc deficiency in acne patients could be one of the causes of acne and also that zinc levels may not be related to the severity.

Keywords: Acne vulgaris; Zinc; Global Acne Grading System (GAGS); Inflammation; Propionibacterium acnes; Pilosebaceous unit; Sebaceous glands; Comedones; Retinol binding protein (RBP); Interleukin 6 (IL-6); Tumor necrosis factor alpha (TNF α).

INTRODUCTION

Acne vulgaris (AV) is a disease of the pilosebaceous unit that lead to non-inflammatory lesions (open and closed comedones), inflammatory lesions (papules, pustules, and nodules) and may cause scarring in some patients. AV is an extremely common condition with a lifetime prevalence of approximately 85% and occurs mostly during adolescence ⁽¹⁾.

Areas of the body with hormonally sensitive sebaceous glands, such as face, neck, chest, upper back, and upper arms are the most sites that affected by acne vulgaris ⁽²⁾.

Pathogenic processes which cause acne lesions are: alteration of follicular keratinization that leads to comedones, increased and altered sebum production under androgen control, follicular colonization by Propionibacterium acnes (P. acnes) and complex inflammatory mechanisms ⁽³⁾.

Acne lesions is divided into: primary lesions, characteristic for active acne, secondary lesions, which represent the sequelae of disease. Primary acne lesions are further subdivided into non-inflammatory lesions (comedones) and inflammatory lesions (papules, pustules, nodules and cysts). Secondary lesions which follow primary lesions comprise post-inflammatory erythema, hyperpigmentation and scarring ⁽⁴⁾.

Zinc, a divalent cation, is an essential element for humans and a component of more than 300 metalloenzymes and over 2000 transcription factors that

are important for regulation of lipid, protein and nucleic acid metabolism, and gene transcription ⁽⁵⁾.

Although the exact mechanism by which zinc can improve acne vulgaris is not fully understood, recent knowledge suggests various mechanisms. For instance, zinc inhibits P. acnes proliferation, maintain immunologic response by preserving macrophage and neutrophil function and stimulates natural killer cells and complement activity ⁽⁶⁾.

Moreover, zinc inhibits interleukin 6 (IL-6) and tumor necrosis factor alpha (TNF α) production and modulates expression of integrins, mainly intracellular adhesion molecule- (ICAM-) 1 and leucocyte function associated antigen ⁽⁷⁾.

This study was performed to evaluate the relation between low serum zinc levels and acne vulgaris and its relation to severity of disease.

SUBJECTS AND METHODS

Subjects:

This study was conducted in collaboration between the Clinical Pathology and Dermatology and Venerology Departments at Al-Hussien University Hospital, Faculty of Medicine, Al-Azhar University.

The study was approved by the Ethics Board of Al-Azhar University.

All patients were collected from Dermatology outpatient Clinic at Al-Husseini University Hospital over

a period from 15th January 2019 to 20th March 2019, with appropriate consent to participate in this study after explanation how much it is helpful in diagnosis and treatment and also explaining to the patients that it is just a blood sample collection. Those subjects were divided into 2 groups: (patients group) and (control group). The patients group was subdivided into 4 subgroups according to Global Acne Grading Score (GAGS): as follows:

Subgroup 1A: comprising 18 patients suffering from mild degree (form) of acne vulgaris. They were 4 males and 14 females. Their ages ranged between 15 and 22 years.

Subgroup 1B: comprising 21 patients suffering from moderate degree of acne vulgaris. They were 5 males and 16 females. Their ages ranged between 17 and 25 years.

Subgroup 1C: comprising 13 patients suffering from severe degree of acne vulgaris. They were 3 males and 10 females. Their ages ranged between 15 and 27 years.

Subgroup 1D: comprising 8 patients suffering from very severe degree of acne vulgaris. They were 3 males and 5 females. Their ages ranged between 19 and 28 years.

Group 2 (control group): comprising 60 apparently healthy individuals (age and sex matched).

Inclusion criteria:

Acne cases who had not taken any treatment for acne vulgaris during the last 6 months before the study.

Exclusion criteria:

- Any disfiguring facial condition other than acne vulgaris.
- History of active malignancy.
- Under immunosuppressive treatment.
- Pregnancy.
- Alcoholism.

SAMPLES AND METHODS

Full history and clinical examination; including assessment of acne vulgaris severity according to Global Acne Grading System (GAGS).

Eight ml venous blood were withdrawn from all participants of the study and divided into two portions: the first portion (two ml) was put in EDTA tube for CBC which was done using cell dyne Ruby automated cell counter. The second portion (six ml) was put in plain tube and left to clot for 30 minutes then serum was separated and divided into two aliquots, one for routine biochemical tests performed by a Biolis 50i Superior (Tokyo Boeki) while the other aliquot was stored freezed at - 20°C for estimation of serum Zinc level by photospectrometry technique using a commercially available (colorimetric) kit supplied by Centronic GmbH, Germany.

Statistical analysis

All results were analyzed using Statistical package for social science (SPSS V.15, IBM Corp. U.S.A). Descriptive statistics as: mean and standard deviation were used. Chi square test was used for comparison of sex. *Mann-Whitney test* and *Kruskal-Wallis test* were used to compare means of parametric data of different groups. Independent-samples t-test of significance was used when comparing between two means. For all analysis, a two-tailed test was used and p <0.05 was considered statistically significant.

RESULTS

As regard to zinc level, there was statistically highly significant difference (P-value < 0.001) between patients and controls, table (1).

There was no statistical significant difference (p-value >0.05) between patients subgroups as regard zinc level, table (2).

Table (1): Comparison between patients and control as regard zinc:

	Patients		Controls		t-test
	Mean	±SD	Mean	±SD	P-value
Zinc(µg/dl)	49.85	19.61	63.46	22.95	0.0007

Table (2): Comparison between patients' subgroups as regard zinc:

	G 1A		G 1B		G 1C		G 1D		P-value
	Mean	SD	Mean	SD	Mean	SD	mean	SD	
Zinc(µg/dl)	50.38	20.5	52.57	24.08	46.46	17.09	47	7.36	0.8186

DISCUSSION

The importance of zinc in human health and especially on the health and integrity of the skin has been revealed in recent years ⁽⁸⁾.

Zinc deficiency (ZnD) is reported in some skin disorders including inflammatory diseases (atopic dermatitis, oral lichen planus, Behcet's disease, and autoimmune bullous diseases (pemphigus vulgaris and bullous pemphigoid) ⁽⁹⁾.

P. acnes is considered to play a crucial role in pathogenesis of acne vulgaris. Zinc has anti-inflammatory action in acne through inhibition of polymorphonuclear cell chemotaxis, growth of *P. acnes* and activation of natural killer (NK) cells ⁽²⁾.

Both zinc and vitamin A are important for normal skin growth. Zinc deficiency can lead to increased androgenic production, which affects the activity of sebaceous glands ⁽¹⁰⁾.

Zinc supplementation induces a significant increase in the expression of all markers included in innate immunity. Some studies have shown that Toll-like receptor-(TLR-) 2 expression, a receptor of the innate immune system, was increased in acne lesions and could play a crucial role in acne pathogenesis. One of the anti-inflammatory mechanisms of zinc salts in acne is inhibition of TLR2 surface expression by keratinocytes ⁽¹¹⁾.

In the current study an attempt was done to clarify the relation between serum zinc level and acne vulgaris and its relation the severity of the disease and in turn understanding its predictable beneficial effects in treatment of acne vulgaris.

The results of this study were concordant with that of **Amer et al.** ⁽¹²⁾, who compared the serum zinc levels in 50 patients with acne vulgaris and 38 control subjects and found statistically significant lower zinc levels in acne patients compared to the control group.

Moreover, a study conducted by **Michaëlsson et al.** ⁽¹³⁾, the serum zinc levels and retinol binding protein (RBP) were determined in 173 patients with acne and compared with those of a control group. They reported that the mean serum zinc level in male patients with severe acne was significantly lower than that of the healthy group.

In addition, the study of **Kaymak et al.** ⁽¹⁴⁾, included 47 patients with acne vulgaris and 40 healthy control subjects. There was statistically significant difference between acne patients and control group as regard to serum zinc level. The study also showed no relation between the zinc level and the severity of acne or disease duration.

Furthermore, **Ozuguz et al.** ⁽⁶⁾, evaluated serum vitamins A and E and zinc levels in 94 acne patients and 56 age- and sex-matched healthy volunteers as control group. All

patients were classified according to GAGS and grouped as mild, moderate, severe, and very severe. There was a negative correlation between acne severity and vitamin E and zinc levels.

Similarly, the results of **El-Dibany and Elhassi** ⁽¹⁵⁾, illustrated that there was a highly significant difference between means of serum zinc of acne patients and their controls (P value = 0.0001). The study showed no correlation between serum zinc level and severity of acne and the results were statistically not significant (P value = 0.522).

On the other hand, **Cochran et al.** ⁽¹⁶⁾, evaluated the efficacy of topical zinc therapy in 30 patients with mild to moderate acne vulgaris. Over a 12-week period, there was no difference noted between placebo- and zinc-treated participants in regard to either the number or the type of acne lesions. Serum zinc levels were not significantly elevated between the two regimens before, during, or after treatment. They suggested that topical zinc therapy alone is not beneficial in the treatment of acne vulgaris

Similarly, **Mogaddam et al.** ⁽²⁾, reported that there was no significant difference in serum zinc levels between acne patients and healthy subjects. While there was a significant correlation between serum zinc levels with severity and type of acne lesions.

Moreover, **Erpolat et al.** ⁽¹⁷⁾, made a study, which included 43 patients with acne vulgaris and 37 healthy control subjects. The severity of acne was classified according to Global Acne Grading System. The serum zinc level in acne patients were 81.48 ± 14.21 µg/dl and 83.69 ± 12.43 µg/dl in healthy subjects. There was no relation between serum zinc levels and acne and they suggested further studies.

The differences between our results and other investigators could be attributed to the differences in number of cases in various studies, association of other epidemiological factors affecting zinc and differences in the cutoff value of zinc deficiency.

CONCLUSION

It is concluded that zinc deficiency in the studied acne patients could be one of the causes of acne. The findings of the present study revealed no relation between low serum zinc levels and the severity of acne vulgaris.

RECOMMENDATION

Follow up studies should be considered in order to determine the level of zinc in patients with acne vulgaris, thereby zinc supplementation could be beneficial in prevention and treatment of acne patients.

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