

Role of Some Trace Elements in Pathogenesis and Severity of Acne Vulgaris in Iraqi Male Patients

Basil O Saleh^{1*}, Zainab NH Anbar² and Ali Y. Majid³

¹Clinical Biochemistry, Department of Biochemistry, College of Medicine, University of Baghdad, Iraq

²Clinical Biochemistry, Biochemistry Department, Baghdad College of Pharmacy, Iraq

³Poisoning Consultation Center, Baghdad Teaching Hospital, Iraq

Abstract

Background: Recently on the dermatological fields, the serum levels and the roles of Zn, Cu and Mg have been studied especially in acne vulgaris, but the results were controversial.

Objective: The aim of the present study is to investigate a relationship between the severity of acne and the serum levels of zinc (Zn), copper (Cu) and magnesium (Mg) in Iraqi males.

Subjects and Methods: This case controlled study was conducted in the Department of Biochemistry, College of Medicine, Baghdad University, in the Dermatology and Venereology and in the Poisoning Consultation Center of Baghdad Teaching Hospital between May 2009 to January 2010.

Forty-five male patients with acne vulgaris, their ages ranged from 18-30 [21.82 ± 3.77 , as (mean \pm SD)] years and 45 healthy male subjects as controls, their ages ranged from 18-30 (22.18 ± 3.85) years were included in this study. Patients were subdivided into three groups according to the severity of their acne; mild acne group (n=15), moderate (n=15) and severe acne group (n=15). Investigations included serum estimation of Zn, Cu and Mg in both patient and control groups.

Results: The (mean \pm SD) values of serum levels of Zn, Cu and Mg did not differ significantly between the patient [all severities combined] and control groups. However, serum Zn level was significantly decreased in severe acne group compared with controls (P=0.0001), mild-(P=0.0001) and moderate-(P=0.003) acne groups (P<0.05). Serum Mg concentration was significantly lower in severe acne group compared with mild acne group (P<0.011). With regard to serum Cu levels, there was no significant difference between patient groups themselves as well as between patient and control groups.

Conclusion: This study revealed a significant association between serum levels of each of Zn and Mg with the severity of acne.

Keywords: Acne vulgaris; Zinc; Copper; Magnesium

Introduction

Acne vulgaris is the most common cutaneous disorder manifested by comedones, papules, pustules and cysts. The etiology of acne appears to be multifactorial, involving follicular hyperkeratinization, hormonal function, proliferation of Propionibacterium acnes, increased sebum production and inflammation. Despite a significant body of scientific literature, the sequence of events leading to the production of acne lesions is not well understood [1]. Specific dietary agents and certain supplements are known to enhance the health and appearance of the skin by improving immune function at the skin level and providing therapeutic bioactive agents that assist in the treatment of many skin conditions, such as psoriasis, eczema and acne [2,3]. It has become increasingly clear that nutritional factors such as vitamins and minerals are involved in the pathogenesis of acne [4]. Previous studies over the last three decades have shown that zinc (Zn) levels are lower in acne patients than healthy subjects and that oral and topical combination of zinc may be of therapeutic value [5,6]. Pohit et al. in 1985 suggest that people with acne have lower-than-normal levels of Zn in their bodies [7]. This fact alone does not prove that taking zinc supplements will help acne, but several small double-blind studies involving a total of more than 300 people have found generally positive results [8]. The results of El-Saaiee et al. in 1983 revealed differences in the copper and iron content of the sera between 30 individuals complaining of moderate acne vulgaris type II and healthy individuals, although they

were statistically not significant. The Zn content showed no changes compared to the control group [9].

Recently, Nasiri et al. in 2009 indicated that serum zinc levels in 30 Iranian acne patients were lower than that of 35 healthy controls; however, this difference was not significant (P=0.32) [10].

Many studies including an epidemiological Iraqi study had showed that acne vulgaris in general was more common in males than females (74.24%) versus (61.9%) [11-13]. On literature review, we found several studies, of which [14], conducted on female patients with acne to investigate the pathogenesis of this disease, however, few involved male acne patients. Therefore, the aim of the present study is to assess the serum concentrations of zinc, copper, and magnesium in male Iraqi patients with acne vulgaris and to clarify their correlation with the severity of acne.

***Corresponding author:** Dr. Basil O Saleh, Assistant Professor, (Clinical Biochemistry) Department of Biochemistry, College of Medicine, and University of Baghdad, Iraq, Tel: 07904407625; E-mail: Basil_omsal@yahoo.com

Received January 14, 2013; **Accepted** January 27, 2013; **Published** January 30, 2013

Citation: Saleh BO, Anbar ZNH, Majid AY (2013) Role of Some Trace Elements in Pathogenesis and Severity of Acne Vulgaris in Iraqi Male Patients. J Clin Exp Dermatol Res 4: 169. doi:10.4172/2155-9554.1000169

Copyright: © 2013 Saleh BO, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Subjects and Methods

This case controlled study was carried out in the Department of Biochemistry, College of Medicine, in the Dermatology and Venerology and in the Poisoning Consultation Center of Baghdad Teaching Hospital, Iraq, from May 2009 to January 2010. The study involved 45 male patients with acne vulgaris, aged range between 18-30 (mean \pm SD; 21.82 \pm 3.77 years). Patients were divided into three groups according to the severity of their acne. A mild acne group that included 15 patients a moderate acne group of 15 patients and severe acne group of 15 patients. Scoring the severity of acne was according to the following rule:

Mild acne

In which the count of papules is less than 10 and the count of pustules is less than 20.

Moderate acne

In which the count of papules ranges from 10 to 30 and the count of pustules ranges from 20 to 40.

Severe acne

In which the count of papules is more than 30 and the count of pustules is more than 40 [15]. Exclusion criteria were intake of oral zinc, magnesium, or copper supplements or multivitamins containing such elements three months before the study, and the presence of any metabolic disease that affected serum elements levels. Control group consisted of 45 healthy males without acne, and were matched for age 18-30 years (mean \pm SD; 22.18 \pm 3.85 years), and body mass index (mean \pm SD; 23.04 \pm 1.38 Kg/m²).

Five milliliters of peripheral venous blood was collected from each patient and control male in plain test tubes, left to clot, then centrifuged at 2500 rpm for 10 minute. The separated serum stored at -20°C until the time of mineral assay.

Serum zinc, copper, and magnesium were determined using flame atomic absorption spectrophotometer (AA-646 Shimadzu, Japan). Samples were diluted 1:10 with n- butanol solution as diluents [16]. Levels of serum Zn, Cu, and Mg were calculated after application of absorbancies on suitable calibration curve for each element made from standard solutions.

SPSS version 6 for window was used for all statistical analysis.

Statistical significance was assessed by ANOVA and student t-tests. The linear regression test was applied for the correlation between different parameters, and the significance of the r-value was checked using t-test. P-values of less than 0.05 were considered significant.

Results

Table 1 shows the clinical [age and BMI values as mean (\pm SD)] and biochemical data for healthy male subjects and male patients with acne. The results showed that the mean (\pm SD) value of serum Zn levels of acne patients (97.33 \pm 17.50 mg/dl) was lower than that of controls (102.42 \pm 18.10 mg/dl), but the difference did not reach the significant level. Similarly, the mean (\pm SD) values of serum Cu and Mg levels did not differ significantly between acne male patients and controls (Table 1).

The mean (\pm SD) values of serum Zn, Cu, and Mg concentrations in patients with -mild, -moderate, and -severe acne types and male controls group are shown in Table 2 and Figures 1 and 2. These results revealed that mean value of serum Zn levels of severe acne (79.67 \pm 7.19 mg/dl) was significantly lower than that of healthy males (102.42 \pm 18.10 mg/dl, P=0.0001), mild acne- (116.67 \pm 12.34 mg/dl, P=0.0001), and moderate acne- types (95.67 \pm 4.58 mg/dl, P=0.003). Moreover, patients with moderate type of acne had significantly lower levels of serum Zn mean (\pm SD) value than that of mild acne type (P= 0.0001). The mean (\pm SD) value of serum Cu levels did not differ significantly between the acne group types and controls as well as between the acne patient groups themselves. With regard to serum Mg serum level, the mean (\pm SD) value of serum Mg levels was significantly decreased in severe type of acne patients (1.13 \pm 0.20 mg/dl) when compared with that of mild acne type (1.29 \pm 0.18 mg/dl, P=0.011). However, the mean values of serum Zn, Cu, and Mg concentrations of acne patients did not differ significantly with respect to their BMI values. Furthermore, the results of the present study revealed no significant correlation between the serum levels of the studied elements (Zn, Cu, and Mg) and the values of BMI and age of patient and control groups (p>0.05).

Discussion

The present study showed that serum Zn level was lower in acne patients than in healthy male controls, but the difference was not significant. This finding is consistent with that observed by Nasiri et al. in 2009 [10] who found insignificant decrease of serum Zn in their Iranian people compared with healthy controls. However, the present

Parameters	Controls (n=45)	Acne patients(n=45)	P-value
Age(year)	22.18 \pm 3.85	21.82 \pm 3.77	NS
BMI(Kg/m ²)	23.04 \pm 1.38	22.76 \pm 1.28	NS
Zn(mg/dl)	102.42 \pm 18.10	97.33 \pm 17.50	NS
Cu(mg/dl)	97.56 \pm 14.48	98.89 \pm 18.98	NS
Mg(mg/dl)	1.14 \pm 0.17	1.21 \pm 0.19	NS

Table 1: Clinical and biochemical data for healthy male controls and patients with acne vulgaris.

Parameters	Controls (n=45)	Mild acne(n=15)	Moderate acne(n=15)	Severe acne(n=15)
Zn(mg/dl)	102.42 \pm 18.10	116.67 \pm 12.34 NS	95.67 \pm 4.58 NS	79.67 \pm 7.19 ¹
Cu(mg/dl)	97.56 \pm 14.48	102.67 \pm 22.82 NS	98.67 \pm 18.85 NS	95.33 \pm 15.06 NS
Mg(mg/dl)	1.14 \pm 0.17	1.29 \pm 0.18 NS	1.20 \pm 0.18 NS	1.13 \pm 0.20 ²

BMI: Body Mass Index

NS: t-test no significant difference between - mild, - moderate acne types and controls

¹t-test significant differences for Zn between each of controls (P=0.0001), mild- (0.0001), and moderate acne (P=0.003) with severe acne type.

²t-test significant difference for Mg between mild acne type and severe acne type (P=0.011)

Table 2: Mean (\pm SD) values of Serum Zinc, Copper, and Magnesium Concentrations in Healthy Male Controls and Patients with Mild-, Moderate,- and Severe Acne Vulgaris.

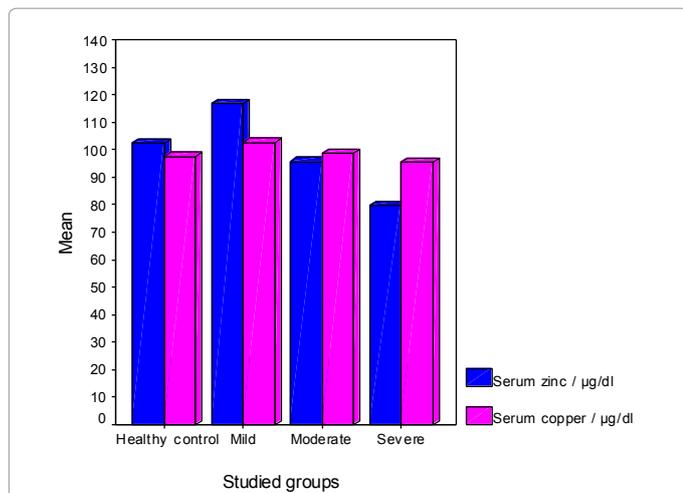


Figure 1: Serum Concentrations of Zinc (µg/dl), Copper (µg/dl) in healthy control, Mild-, Moderate-, and Severe acne patients groups.

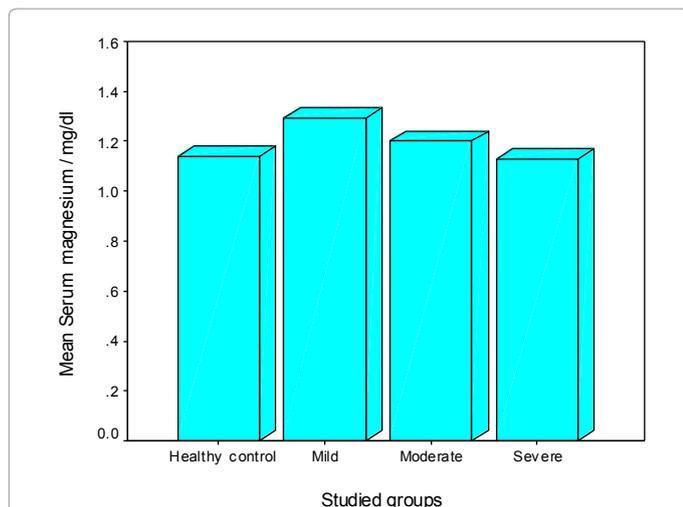


Figure 2: Serum concentration of Magnesium (mg/dl) in Healthy Control, Mild-, Moderate-, and Severe acne patients groups.

study has shown that serum Zn levels of the severe type of acne were significantly lower than that of healthy controls, mild, and moderate types of acne. These data are in agreement with that reported by Michaelsson et al. and Amer et al. [17,18] who showed that serum Zn level was significantly reduced in severe acne male patients compared with controls. These authors suggested that low levels of zinc in the serum of patients with severe acne may provide a rationale for the beneficial effect of oral zinc treatment seen in clinical practice [17]. The mineral zinc is emerging as vital nutrient for skin health and appearance. Zinc nutritional status is necessary for oil gland function, local skin hormone activation, wound healing, skin inflammation control and regeneration of skin cells. Zinc supplementation has been used with success in the treatment of many acne cases [19]. Studies indicated that most individuals consume only 8-9 mg/day of zinc from dietary sources, whereas the recommended daily acquirement (RDA) for zinc is set at 15 mg/day for adults [20]. A review reported by Dr. Preston, indicated that lack of zinc is a recipe for acne [21]. Nasiri et al. in 2009 concluded from their study that zinc as anti-inflammatory

element may play a role in the pathogenesis of acne, and there is a need for further studies [10].

The present study also found that serum magnesium level was significantly decreased in severe type of acne compared with mild acne patients. This element (Mg) is vital for the production of proteins and enzymes in every tissue of the body. This includes the proteins and enzymes of skin cells where new cells are constantly being produced. It is also absolutely essential for the proper use of the vitamin Pyridoxine [21]. The author of the latter review suggested taking supplements of about 500 mg of this mineral each day is essential.

Copper is an important element for numerous metalloenzymes and metalloproteins such as superoxide dismutase that are involved in energy and antioxidant metabolism. Human keratinocytes are susceptible to peroxidative damage because they contain high concentrations of polyunsaturated fatty acids and also possess a significant ability to generate a reactive oxygen species (ROS), mainly superoxide anion and hydrogen peroxide. Superoxide dismutase (Cu-metalloenzyme) protects human skin cell from this peroxidative damage [22]. Although, this study showed that there was no significant difference in serum copper level between patient and control groups; Further studies are needed to show the beneficial effect of Cu compounds in prevention and treatment of acne vulgaris.

Elements are also important to mammalian target of rapamycin (mTOR) protein. This serine and threonine protein kinase regulates protein translation through a rapamycin-sensitive pathway. mTOR protein integrates signals from mitogens and the nutrients, glucose and amino acids, to regulate cellular growth and proliferation. The study of Lynch et al. [23] indicated that Zn^{2+} regulates, but is not absolutely required for, mTOR protein kinase activity. Zinc also stimulated a recombinant human form of mTOR. The stimulatory effects of Zn^{2+} were maximal at $\sim 100 \mu M$ but decreased and became inhibitory at higher physiologically irrelevant concentrations. Micromolar concentrations of other divalent cations, Ca^{2+} , Fe^{2+} , and Mn^{2+} , had no effect on the protein kinase activity of mTOR in the presence of excess Mg^{2+} . These authors also suggested that zinc acts at multiple steps in amino acid- and insulin cell-signaling pathways, including mTOR, and that the additive effects of Zn^{2+} on these steps may thereby promote insulin and nutritional signaling. A study conducted by Saleh concluded that male Iraqi acne patients, particularly those suffering from the severe type, have a significant elevation of serum levels of growth hormone (GH) and insulin like growth factor-(IGF)-1, which can stimulate androgen hormone synthesis and secretion, leading to the proliferation of sebocytes and keratinocytes resulting in aggravation of acne [24]. The results of the study conducted by Savastano et al. [25] underlined that spleen enlargement, a parameter expressing low-grade chronic inflammatory status, was a major determinant of low IGF-I/IGFBP-3 ratio than hepatic steatosis *per se*. The investigators also found a significant negative correlation between all the components of the IGF-I axis investigated and fat mass % (FM %), insulin resistance, or hepatic steatosis severity. However, FM% was a better determinant of IGF-I and IGFBP-1 than HS *per se* in the same population. In Conclusion; the present study revealed significant association between each of Zn and Mg levels with the severity of acne. Further studies that deal with serum concentrations of zinc, magnesium and mTOR in severe acne patients are required.

Acknowledgments

We would like to thank Assist. Prof. Maysaa Jalal (Ph D student Clinical Biochem, Biochemistry Department, College of Medicine, Baghdad) for help with statistical calculations.

References

1. Vora S, Ovhal A, Jerajani H, Nair N, Chakraborty A (2008) Correlation of facial sebum to serum insulin-like growth factor-1 in patients with acne. *Br J Dermatol* 159: 990-991.
2. Aesoph, Lauri M (1998) A Holistic approach to skin protection. *Nutrition Science News* 3: 204-208.
3. Boelsma E, Hendriks HF, Roza L (2001) Nutritional skin care: health effects of micronutrients and fatty acids. *Am J Clin Nutr* 73: 853-864.
4. Katzman M, Logan AC (2007) Acne vulgaris: nutritional factors may be influencing psychological sequelae. *Med Hypotheses* 69: 1080-1084.
5. Dreno B, Foulc P, Reynaud A, Moysé D, Habert H, et al. (2005) Effect of zinc gluconate on propionibacterium acnes resistance to erythromycin in patients with inflammatory acne: in vitro and in vivo study. *Eur J Dermatol* 15: 152-155.
6. Niren NM, Torok HM (2006) The Nicamide Improvement in Clinical Outcomes Study (NICOS): results of an 8-week trial. *Cutis* 77: 17-28.
7. Pohit J, Saha KC, Pal B (1985) Zinc status of acne vulgaris patients. *J Appl Nutr* 37: 18-25.
8. Verma KC, Saini AS, Dhamija SK (1980) Oral zinc sulphate therapy in acne vulgaris: a double-blind trial. *Acta Derm Venereol* 60: 337-340.
9. El-Saaie L, Abdel-Aal H, El-Mahdy H, Abdel-Aal AM (1983) Serum copper, iron and zinc in cases of acne vulgaris. *J Med* 14: 125-136.
10. Nasiri S, Ghalamkarpour F, Yousefi M, Sadighha A (2009) Serum zinc levels in Iranian patients with acne. *Clin Exp Dermatol* 34: e446.
11. Daniel F, Dreno B, Poli F, Auffret N, Beylot C, et al. (2000) [Descriptive epidemiological study of acne on scholar pupils in France during autumn 1996]. *Ann Dermatol Venereol* 127: 273-278.
12. Smithard A, Glazebrook C, Williams HC (2001) Acne prevalence, knowledge about acne and psychological morbidity in mid-adolescence: a community-based study. *Br J Dermatol* 145: 274-279.
13. Al-Battat RA (2006) Scarring and non scarring facial acne vulgaris and the frequency of skin diseases. A thesis submitted to the Scientific Council of Dermatology and Venereology- Iraqi Board for Medical Specializations.
14. Cappel M, Mauger D, Thiboutot D (2005) Correlation between serum levels of insulin-like growth factor 1, dehydroepiandrosterone sulfate, and dihydrotestosterone and acne lesion counts in adult women. *Arch Dermatol* 141: 333-338.
15. Toyoda M, Morohashi M (2001) Pathogenesis of acne. *Med Electron Microsc* 34: 29-40.
16. Meret S, Henkin KI. *Clin. Chem.* 1971; 17: 369. Cited by: Gowenlock H A, McMurray R J, McLauchlan MD. *Varly Practical Clinical Chemistry*. 1988, 6th ed. Heinemann Medical Books.
17. Michaëlsson G, Vahlquist A, Juhlin L (1977) Serum zinc and retinol-binding protein in acne. *Br J Dermatol* 96: 283-286.
18. Amer M, Bahgat MR, Tosson Z, Abdel Mowla MY, Amer K (1982) Serum zinc in acne vulgaris. *Int J Dermatol* 21: 481-484.
19. *The Doctors? Vitamin and Mineral Encyclopedia* (S. Hendler). Simonand Schuster, 1990: 195-207 (zinc).
20. *Nutrition for Living* (1988) (2ndedn), The Benjamin/Cummins Publishing Companies; 338.
21. Preston R (2002) *Acne-how to prevent and overcome acne forever*. International Institute of Nutritional Research.
22. Wong WY, Flik G, Groenen PM, Swinkels DW, Thomas CM, et al. (2001) The impact of calcium, magnesium, zinc, and copper in blood and seminal plasma on semen parameters in men. *Reprod Toxicol* 15: 131-136.
23. Lynch CJ, Patson BJ, Goodman SA, Trapolsi D, Kimball SR (2001) Zinc stimulates the activity of the insulin- and nutrient-regulated protein kinase mTOR. *Am J Physiol Endocrinol Metab* 281: E25-34.
24. Saleh BO (2012) Role of growth hormone and insulin-like growth factor-I in hyperandrogenism and the severity of acne vulgaris in young males. *Saudi Med J* 33: 1196-1200.
25. Savastano S, Di Somma C, Pizzi G, De Rosa A, Nedi V, et al. (2011) Liver-spleen axis, insulin-like growth factor-(IGF)-I axis and fat mass in overweight/obese females. *J Transl Med* 9: 136.