Original Article

Role of serum Zinc and Copper levels in patients with acne vulgaris

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ABSTRACT

Background: Acne vulgaris is a disorder in which hair follicles develop obstructing horny plugs (comedones) and the reason is unknown. The aim of the present study was to assess the relationship of zinc and copper to Acne vulgaris. **Material and Methods:** Young female patients in the age group of 13 to 19 years, with the problem of acne attending the out-patient department of Dermatology of a tertiary teaching general hospital over a period of six months, were included in this study. Female attenders (friends) of the patients of the same age, without acne comprised of the control group. Group 1 consisted of 50 patients with acne and group 2 was a control group having 25 normal individulas. The blood samples of patients and controls were collected on the scheduled date and analysed for serum zinc and copper levels at National Institute of Nutrition, Hyderabad by Atomic absorption spectrometry. **Results**: Mean Serum zinc levels in patients was 24.4 ± 2.4 whereas the levels in controls was 99.4 ± 4.5. The observation is that the mean value in acne patients is statistically significant and lower than controls ($p<0.001$). Mean serum copper levels in patients and control was 119±14 and 131.2±4.6 respectively. The observation is that mean value in acne patients is statistically significant ($p <0.001$). **Conclusion:** Zinc deficiency is one of the main causes of acne and zinc supplementation has got a marked role in its treatment. Whereas hypercupraemia needs further evaluation.

Key words: *Acne vulgaris, atomic absorption spectrometry, hypercupraemia, serum zinc, serum copper.*

Acne is one of the commonest skin disorders particularly in adolescents and young adults [1]. Acne vulgaris is a disorder of pilosebaceous unit in which hair follicles develop obstructing horny plugs (comedones) resulting in inflammation around the obstructed follicles, causing tissue destruction and scar formation [2]. Most cases of acne present with pleomorphic lesions consisting of papules, macules, comedones and nodules. Although the course of acne may be self-limiting the sequelae can be lifelong with pitted or hypertrophic scar formation [3]. It is a syndrome in which neither exogenous agents nor medications are primary causes but they are exacerbating factors [4]. One of the key features is excess sebum production from the sebaceous glands. While there is virtually no mortality associated with this disease, there is often significant morbidity seen [5]. Physical morbidity of acne results from scarring and from the adverse effects of treatment. Also important is the psychological morbidity of the disease on those afflicted, which affects self-esteem and quality of life. The burden of acne in terms of cost to society is not well defined, but the prevalence of the disease suggests that these costs are high.

Copper is the third most common mineral in the body. In addition to being important for many enzyme systems, copper is found throughout the musculoskeletal system, although the largest amounts are found in the brain and liver [6]. The formation and regulation of hormones such

as melatonin are under the control of copper, via its role in the blood protein ceruloplasmin and copper enzymes are also responsible for the production of a wide range of neurotransmitters and other neuroactive compounds, including the catecholamines and encephalins. Although copper deficiency per se is rare, due to the intricate interaction with zinc there can be deficiency as both compete during absorption.

Zinc deficiency is a lack of sufficient zinc to meet the needs of human beings. Hypozincemia is a condition where insufficient zinc is available for metabolic need. One-third of the world population is at risk of zinc deficiency, ranging from 4 to 73% depending on the country. Zinc deficiency is the fifth leading risk factor for disease in the developing world. Acne vulgaris is one of the manifestations of zinc deficiency. Other dermatological diseases being psoriasis and acrodermatitis enteropathica [7]. Normal plasma zinc concentration is about 112 ± 12 µgm %. [8]. Girls experience even more acne at times of the month because their period regulates zinc and copper levels. When copper is higher than zinc, acne develops in many cases and is a symptom of a need for zinc and other minerals as well

Zinc deficiency promotes the conversion of testosterone to dihydro testosterone that promotes the production of sebum [9]. The sebum which accumulates converts into papules, pustules and so on, but if zinc deficiency is there it results in hypercupraemia [10]. Zinc competes with copper in intestinal absorption, so if zinc is less copper toxicity results. The ideal ratio of copper to zinc is 1:8 in favour of zinc [11]. The acne-like lesions in copper deficiency have lead investigators from different countries to assess the relationship between serum copper levels and acne [2-6]. Copper was combined to acne treatment and it is still being used with varying rates of success [7,8,11,12]. However, there is only one report available on serum copper levels in acne patients from India [13]. Acne vulgaris is one of the common skin diseases in young individuals all over India and it has a lot of social and psychological impact on the individual's behaviour and performance in his/her daily life. Many dermatologists from times immemorial treat Acne vulgaris with zinc supplementation. Hence the present study was planned with an aim to study the exact relation of zinc to acne and whether zinc deficiency was one of the cause for acne and how far copper interferes with serum levels of zinc and its role in acne.

MATERIAL AND METHODS

This project was approved by the ethics committee (No. GMC/EC/App/0358/17-18; dtd. 25, April, 2018 of the medical college/hospital.

Young female patients in the age group of 13 to 19 years, with the problem of acne attending the out-patient department of Dermatology of a tertiary teaching general hospital over a period of six months, were included in this study. Female frimeds of the patients of the same age, without acne comprised of the control group. The subjects were divided into two groups, 50 acne patients were labelled as group-1 and 25 Normal controls without acne were labelled as group-2. The purpose of research was explained to every subject included in the study and an informed consent was obtained. Haemoglobin levels were assessed in every subject using finger prick test and those patients whose haemoglobin level was less than 10 gms/dl were excluded as copper deficiency can manifest as anemia which may further lower serum copper values [14].

After an overnight fast, blood samples of patients and controls were collected on the scheduled date and analysed for serum zinc and copper levels at National Institute of Nutrition, Hyderabad by Atomic absorption spectrometry (SVL spectronics, India). All glassware used in the process were made zinc-free by immersing overnight in 6% hydrochloric acid (HCL), subsequently they were washed and rinsed thoroughly with distilled water and double-distilled water and dried in a hot air oven. Plastic disposable syringes with needles for collecting blood samples, plastic storage vials with caps and plastic pipettes were used without any pretreatment. A clean closed room was chosen to avoid contamination while collecting the blood sample. The patient was made to sit comfortably on a stool and a rubber tourniquet was tied around the arm about 4 inches above the cubital fossa. With a plastic disposable syringe fitted with a sterile needle about 4ml of venous blood was drawn and transferred immediately into a centrifuge tube which were then plugged with a sterile cotton plug. Individual centrifuge tubes were numbered with their respective patient numbers.

Each blood sample was centrifuged for about 20 minutes at 3500 RPM and supernatant serum was transferred gently into a plastic storage vial using an automatic pipette. For each sample transfer, a separate pipette tip was used. Storage vial was numbered with their respective numbers and kept in deep freeze chamber.

Throughout the procedure, gentle and minimum handling was done to avoid haemolysis.

Serum zinc and copper were estimated by means of Atomic absorption spectrophotometer (As205) using flame spectroscopy. After obtaining Appropriate standards from NIST (National institute of standard and technology, Hyderabad, India), Standard reference materials (SRMS) were prepared. 1 ml of serum diluted to 10 ml with deionized water in clean 10 ml volumetric flasks. Instrument was switched on and hollow cathode lamp for particular element was put in place. Instrumental and gas flow settings and aspiration rate were established to optimize the signal and minimize background noise. Parameters for particular estimation were given. Deionized water was aspirated to set baseline to read zero absorbance. Working standards for particular element was aspirated from most dilute to most concentrated and a graph was then plotted. Normal as well as patients samples were run and values were recorded with the help of printer. Finally values were calculated considering the dilution factor.

The mean values of serum copper in patients group and control group were tested for statistical significance by using independent sample "t" test. The P-value <0.01 was considered significant.

RESULTS

The study subjects were divided into 2 groups. Group 1 consisted of 50 patients with acne. Normal controls were 25 in number without acne and they were labeled as group-2. Mean Serum zinc levels in patients was 24.4 ± 2.4. Mean Serum zinc levels in controls was 99.4 ± 4.5. The observation is that the mean value in acne patients is statistically significant and lower than controls ($p<0.001$). Mean serum copper levels in patients was 119±14. Mean serum copper levels in controls was 131.2±4.6 The observation is that the mean value of copper is lowered in acne patients when compared to controls and is statistically significant (.p <0.001) (Table 1, figure 1).

Levene's test was carried out to assess the equality of variances and it showed that both the groups of zinc and copper do not follow normal distribution. Comparison between zinc and copper values were assessed using Pearsons correlation in both groups which showed negative correlation and were significant (Table 2).

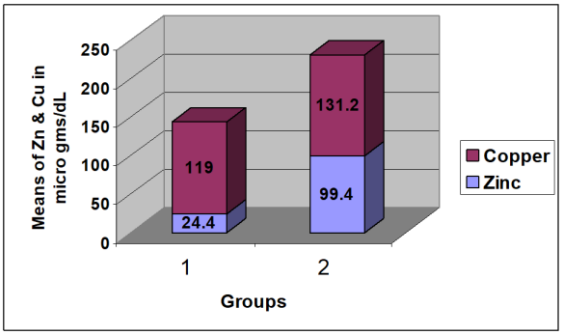

Figure 1: Comparison of zinc and copper levels in group 1 and 2

Table-2: Showing pearson correlation among the 2 groups for zinc and copper

		Group 1		Group 2	
		Zn	Cu	Zn	Cu
Zn	Pearson Correlation	1	-.378**	1	-.612**
	Sig. (2-tailed)		.007		.001
	N	50	50	25	25
Cu	Pearson Correlation	-.378**	1	-.612**	1
	Sig. (2-tailed)	.007		.001	
	N	50	50	25	25

***Correlation is significant at the 0.01 level (2-tailed)*

DISCUSSION

Acne vulgaris is a common dermatological disease with psychological impact in adolescents. Adverse effects were mild cosmetic problems to the advanced stage. In the present study serum zinc and copper levels were estimated by atomic absorption spectrophotometry to show the relationship to acne. Two groups were taken; Group-1 were patients of acne and Group-2 were controls without acne. In both groups only females aged 13 -19 were taken.

Mean Serum zinc levels in patients with acne was 24.4±2.4 in comparison to controls which was 99.4±4.58. The mean zinc level in patients was significantly lowered compared to controls. The mean values were found to be statistically significant at $p<0.001$. These findings correlate with other studies by Mohammed A et al and Michaelson G et al. The study included female students aged 16-20 years with acne, results showed significantly lower mean zinc levels compared to the control group. Their study reported mean zinc levels at 30.6±2.5, which is in agreement with our present study which showed mean zinc concentration to be 24.4±2.4 [15,16].

Table-1: Showing mean ±S.D zinc and copper levels in patients and controls

Group		N	Range(µg/dl)	Mean (µg/dl)	Standard Deviation	Standard Error mean
Zn	Patients	50	16.5– 30.1	24.4120	2.445	.34582
	Control	25	55.6 -92.8	99.4960	4.58189	.91638
Cu	Patients	50	100.0 – 132.0	119.0400	14.09383	1.99317
	Control	25	120-139	73.2280	4.64799	.92960

Zinc deficiency promotes the conversion of testosterone to dihydrotestosterone which promotes the production of sebum and dilatation of sebaceous glands, thus sebum accumulates resulting in acne [17]. Hence, zinc deficiency is one of the causes of acne. Present study and data support this fact. After the statistical analysis both the groups i.e. patients and controls were found to be non-homogenous and non-parametric as shown by parametric "t" test, so non-parametric statistical test that is "U" test is performed which also gives the same result. All the samples were fasting samples which rule out the possibility of any interference with zinc absorption as the cause of hypozincaemia. All possible measures were taken to avoid extraneous zinc concentration and haemolysis. One of the criteria for zinc deficiency as reported by Ai-guoma et al [18] was anaemia due to menstrual irregularities, but in our present study anaemia was an exclusion criteria so this was not an interfering factor.

Mean Serum copper levels in patients was 119± 14. Mean serum copper of control group was 131.2±4.64 in present study copper levels were lower in patients in comparison to controls. The actual relation between copper and zinc is inverse because there is a zinc metal transporter znt-4 called as divalent cation dct-1associated with the transport of copper cations, hence there is competition between transport of copper and zinc for absorption [19]. As per the studies of Michaelson G et al [16] zinc levels were lowered with the concomitant rise of copper but the present study is not in accordance with that study in case of copper levels. Copper levels were on the upper limit of the international reference range, which is 70-140µg/dl, which is the limitation of this study. This could be due to low sample size, variation in the method of analysis and the model of the instrument used in the technique. From the present study, we can positively conclude that zinc supplementation can cure acne as zinc deficiency is the main cause for the acne.

CONCLUSION

The main aim of this study was to establish the relation of acne with two trace elements zinc and copper. Relation of zinc with acne showed a clear picture i.e. the mean levels were decreased in all 50 patients enrolled in this study, but simultaneous significant decrease in copper levels was not seen in all patients instead copper was on the upper limit mean being 119.4±14, which is very near to international reference range that is 70-140µg/dl. Thus we can positively conclude that zinc deficiency is one of the main causes of acne and zinc supplementation has got a marked role in its treatment, whereas hypercupraemia needs further evaluation.

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