

Serum Zinc Levels and the Effect of Oral Zinc in Acne Vulgaris

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ABSTRACT

BACKGROUND

Acne vulgaris is a chronic inflammatory condition of the pilosebaceous unit which occurs in adolescent age groups. Physical and psychological scars can create social issues in the family, school and workplace. The disorder is multifactorial. There are plenty of recovery choices but are not satisfactory. We wanted to investigate the serum zinc levels and the therapeutic utility of oral zinc supplementation in acne vulgaris patients.

METHODS

This is a prospective study conducted over a period of one and a half years among one hundred acne patients who reported to the outpatient clinic of the Department of Dermatology, Venereology and Leprology with untreated patients of acne vulgaris.

RESULTS

Males were 65 % and females were 35 % with male : female ratio of 6.5 : 3.5. Most of the patients were students occupying 71 % of the study. Family history was observed in 46 % of patients, either in the siblings or in the parents. Premenstrual flare-up of acne lesions was noted in 71.42 % of female patients indicating a pivotal role of hormones in the pathogenesis of acne. Aggravation of lesions in summer was noted in 45 % of patients. Aggravation of acne lesions with different types of diet like non-vegetarian food, oily food and chocolates was noticed in 69 % of the study. History of usage of different types of cosmetics available in the market was noted in 76 % of the patients. In the present study, 62 % had lower than normal serum zinc levels and 38 % had normal serum zinc levels. Thus, serum zinc levels were found to be lower in both male and female acne patients in the majority (62 %) of the study patients and also normal healthy controls. The fasting serum zinc levels in the 62 patients before and after oral zinc sulphate were estimated after completion of 3 months treatment. Normal serum zinc levels were observed in all 62 patients treated.

CONCLUSIONS

Oral zinc sulphate is an effective, safe and economic remedy in the treatment of acne vulgaris. The extra advantage with oral zinc sulphate is that it is devoid of many adverse reactions commonly seen after prolonged use of systemic antibiotics.

KEYWORDS

Oral Zinc Sulphate, Acne Vulgaris

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BACKGROUND

Acne vulgaris is a chronic inflammatory condition of the pilosebaceous glands which is characterized by seborrhoea, comedones, erythematous papules, pustules and in more severe cases tender nodules and cysts leaving behind mutilating scars.¹ It is the most common disorder among the adolescent age group affecting 90 – 95 % of the mid teen population. A large variety of topical and systemic medications are available for the management of acne vulgaris, yet the treatment of acne is not entirely satisfactory. Oral and topical antibiotics and / or retinoids are the commonly used therapies. Some authors added oral zinc to the treatment of inflammatory acne with varying success.² Zinc is a trace element necessary for several important functions such as protein synthesis, DNA and RNA replication and cell division and hence, required for human growth and development. It occurs in many metallo-enzymes that play an important role in delayed type of hypersensitivity reactions, regulation of inflammation, normal keratogenesis, cell membrane stabilization and many enzymatic reactions, besides being a structural component of many hormones. Recalcitrant clinical course and emergence of resistance to common antibiotics in some cases has led to the trial of numerous novel agents in acne management.²

Acne-like papulopustular lesions occurring in zinc deficiency cases and their rapid improvement with zinc supplementation has led some investigators to assess the relationship between serum zinc levels and acne lesions. Further studies demonstrated low serum zinc levels in acne patients, although their levels do not correlate with the severity of the disease. Subsequently oral zinc has been used extensively in the management of acne vulgaris.³ However, this topic has not received much attention in Indian context except for a couple of sporadic reports despite the patients of acne are very common.³ In view of the facts highlighted above, the present study aiming at the evaluation of serum zinc levels and the effect of oral zinc in acne vulgaris assumes greater significance.

METHODS

The study comprised of one hundred consecutive patients of either sex, diagnosed as acne vulgaris and fifty healthy subjects as controls who have reported to the Out-Patient Department of Dermatology, Venereology and Leprology, during the period of December 2012 to May 2014.

Inclusion Criteria

- Untreated patients of acne vulgaris of either sex diagnosed on clinical grounds were included in the study.
- Patients who gave informed consent to undergo required investigations in the study.

Exclusion Criteria

- Treated cases of acne vulgaris in whom the acne is inactive.
- Pregnant, lactating and women on oral contraceptives.
- Patients taking the following systemic drugs.

Amiloride (a potassium-sparing diuretic that may increase the levels of zinc in blood;) anti hypertensives ACE (Angiotensin-Converting-Enzyme) inhibitors may decrease the levels of zinc in blood like captopril and enalapril and antibiotics (two kinds of antibiotics, quinolones and tetracyclines may decrease zinc absorption). People with malabsorption diathesis, such as Crohn's disease or celiac disease may have problem in zinc absorption were excluded.

Patients presented with acne vulgaris were considered for the study. After obtaining informed written consent a detailed clinical history, systemic and dermatological examination was carried out and the details were recorded in a prepared chart in all patients. Close up photographs of the face with acne lesions were obtained before starting oral zinc treatment.

Estimation of serum zinc is done by Nitro-PAPS, end point assay. Estimation of fasting serum zinc levels by nitro-PAPS method using biochemical semi auto analyser was carried out in all patients and controls (Figure 3). Later in all these patients, the lesions of acne vulgaris were graded as mild, moderate, severe, and grading was given to every patient clinically (grade I, grade II, grade III, grade IV). Subsequently the patients with lower serum zinc levels were advised to take oral zinc sulphate tablets 200 mg (equivalent to 50 mg of elemental zinc) daily for a period of 3 months. They were followed up at fortnightly intervals by obtaining a close-up clinical photograph of the face with acne lesions and assessment of clinical improvement in acne by the physician and as well the subjective impression of the patient for a period of 3 months. The results obtained were tabulated carefully and subjected to statistical analysis to arrive at meaningful conclusions.

Statistical Analysis

The experimental data were expressed as mean \pm Standard deviation. The significance of the differences between treatments and respective controls was analysed using the Student's t-test and GraphPad InStat, Software, USA.

RESULTS

The present study comprised of total 100 clinically diagnosed acne vulgaris patients, and 50 healthy normal subjects as controls. Serum zinc levels were estimated in all these 150 subjects. Oral zinc sulphate tablets were given for 3 months to acne patients with low serum zinc levels. The observations of the study are tabulated as follows.

Age in Years	Males (%)	Females (%)	Total (%)
11 - 15	10 %	5 %	15 %
16 - 20	46 %	16 %	62 %
21 - 25	7 %	5 %	12 %
26 - 30	1 %	4 %	5 %
31 - 35	0	3 %	3 %
36 - 40	0	1 %	1 %
41 - 45	1 %	1 %	2 %
Total	65 %	35 %	100 %

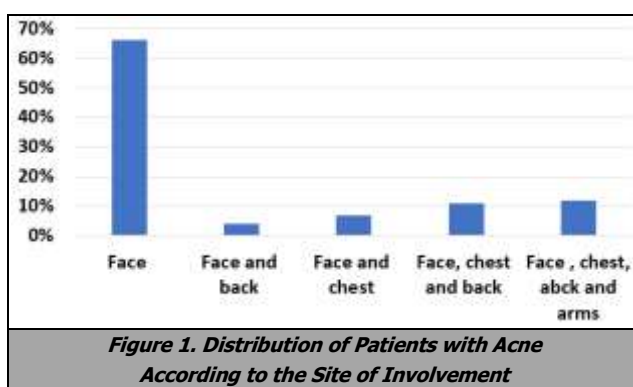
Table 1. Distribution of Patients with Acne According to Age and Gender

The age of the patients in the present study varied from 11 - 45 years. Highest number of patients were in 16 - 20 years age group. Maximum prevalence in males was seen at 18 years and in females at 18 and 19 years. (Table 7 and Figure 4).

Occupation	Percentage
Students	71 %
Employees	16 %
Housewives	4 %
Laborers	9 %
Seasonal Variation	
Summer	45 %
Winter	9 %
Nil	46 %
Family History	
Present	46 %
Absent	54 %
History Of Using Cosmetics	
Present	76 %
Nil	24 %
Relation To Diet	
Present	69 %
Absent	31 %
Aggravation of lesions with their premenstrual period N (%)	35 (71 %)

Table 2. Distribution of Patients with Acne with Other Details

Majority of patients were students 71 %. Remaining of them were employees, housewives and labourers. Aggravation of acne was noted in summer in 45 % patients followed by 9 % patients in winter and 46 % patients had no seasonal variation. In the present study, 46 % of the patients gave a positive family history of acne. At least one parent was affected in 30 of these cases and a positive history in the siblings was present in 4 of the cases.



76 % gave history of usage of cosmetics of different types and different brands. Whereas 24 % gave no history of usage of cosmetics. 69 patients gave history of aggravation of acne with their different types of diets like non-veg, oily food, chocolates whereas 31 patients did not give any history of relation with diet.

In the present study, out of 35 female patients 25 patients gave history of aggravation of lesions with their premenstrual period.

Sixty six patients (66 %) had acne lesions exclusively on face. Face was involved in all the 100 patients. 4 patients (4 %) had lesions on face and back. 7 (7 %) of them had lesions on face and chest. 11 patients (11 %) had lesions on face, chest and back sites. Remaining 12 (12 %) patients had lesions on all four sites.

Severity Index (Acne Grading)	Males		Females		Total No. of Patients
	No. of Pts.	%	No. of Pts.	%	
Grade - I	16	53.33	14	46.66	30
Grade - II	19	70.37	8	29.62	27
Grade - III	26	70.27	11	29.72	37
Grade - IV	4	66.66	2	33.3	6

Table 3. Distribution of Patients with Acne According to the Severity Index of Lesions (Acne Grading)

Majority of patients has shown acne grade III (37) (26 male patients + 11 female patients) followed by Grade I (30) (16 males + 14 females), the results have also shown that, 70 % of male patients showed Grade II and III, only 33.3 % of the total study population showed Grade IV respectively.

Patients	Mean Serum Zinc Levels $\mu\text{g} / 100 \text{ mL}$			t Value	P Value
	Acne Vulgaris Patients (100)	Normal Controls (N = 50)			
	Low Levels (N = 62)	Normal Levels (N = 38)			
Males	64.99 \pm 16.16	83.55 \pm 7.62	84.02 \pm 5.80	19.97	< 0.0001
Females	69.68 \pm 13.98	85.70 \pm 6.49	85.35 \pm 7.46	15.96	< 0.0001
Total	66.65 \pm 15.52	84.38 \pm 7.61	84.62 \pm 6.54		

Table 4. Mean Serum Zinc Levels in Patients with Acne and Normal Controls

The results obtained in the present study showed the mean serum zinc levels was lower in male patients when compared with female patients, whereas, the control group has shown the normal serum zinc levels (84.62 \pm 6.54), the zinc levels in test group were statistically significantly lower when compared with the control group.

Cases	Serum Zinc Level $\mu\text{g} / 100 \text{ mL}$		t Value	P Value
	Initial	After 3 Months		
Males	64.99 \pm 16.16	89.59 \pm 8.49	t=22.98	P < 0.0001
Females	69.68 \pm 13.98	90.23 \pm 8.64	t=19.74	P < 0.0001
Total	66.65 \pm 15.52	89.64 \pm 8.67		

Table 5. Improvement Noted in Mean Serum Zinc Levels in Acne Vulgaris Patients before and after Giving Oral Zinc Sulphate

In the present study the mean initial serum zinc levels was compared with the patient's serum zinc levels after 3 months of zinc treatment. It was observed that, there was statistically significant (p < 0.001) difference in the serum zinc levels in the patients treated with zinc with 3 months when compared with the initial group.



Figure 2. Images Showing the Improvement in the Lesions before and after Three Months of Oral Zinc Therapy

DISCUSSION

In the present study, it was noted that, acne is more common in adolescents of 16 - 20 years age group. The oldest patient was 45 years and youngest was 11 years old. These findings are in agreement with earlier studies. Bloch et al found that 18 year old individuals had the increased prevalence of clinical acne on the face comprising 35 % males and 23 % females. Acne occurs earlier in boys of 10 years age group than in girls of that group, however, in later ages the maximum prevalence is seen in girls (18 years) later than the boys (17 years). In a study done by Adityan and co-workers it was observed that, majority of the patients were in the age group of 16 - 20 years and 21 - 25 years.⁴ In the present study, the pattern of sex distribution shows that the incidence in males was higher than in females with male to female ratio is 7:3. Similar observation was also seen in a study done by Hinrichsen and co-workers.

Majority of the patients had a family history of acne at least one parent was affected in the present study. A survey in Germany showed that acne had been present in one or both parents in 45 % of school boys with acne but in only 8 % of parents in whom the children had no acne.¹ These reports suggest that hereditary may have a role in the aetiology of acne but it may not be the only factor.

The reason for the students may be due to cosmetic and psychological importance. According to Koo, psychiatric morbidity associated with the acne includes impaired self-image / self-esteem, social impairment, depression, anger, which are very common in young students.⁵ It is important to note that majority (71 %) of the acne patients are students in the present study. Majority of the females (71.42 %) had history of premenstrual flares of their acne. The reason for this exacerbation has been attributed to premenstrual hydration of the ductal pores causing increased resistance to sebum out flow leading to ductal obstruction and aggravation of acne. Khanna and co-workers noticed an improvement of acne in the post menstrual phase in their study.⁶ There is a widespread consensus that acne generally improves in summer but there is no proof regarding this. The explanation for summer exacerbation is the comedogenic effect of ultraviolet radiation. Excessive sweating, especially in a tropical climate, can lead to blockage of duct and thus increase in acne. In the present study also, 45 % of the patients gave history of aggravation of the acne lesions in summer. Only few patients (9 %) gave history of aggravation of their lesions in winter. 46 % of the patients gave no history of seasonal variation in relation to their lesions. Gfesser and co-workers found during summer regression of acne seen in one third of the patients, aggravation in another third of the patients, and no seasonal variation in the rest of one third patients.

In a study by Rasmussen and co-workers, 60 % of the patients felt that chocolates and fatty foods were responsible for the flare up of their acne lesions. In the present study also 69 % of the patients felt that fatty food including fried and oily food stuffs, non-vegetarian food and chocolates were responsible for the flare up of their acne lesions. This finding is in agreement with the Rasmussen study, but not with Fulton and co-workers and the reason for this may be due to the fact that the findings in the study by Fulton are based on the clinical trials and not on history given by the patient.⁸

In the present study, 76 % of the patients gave a history of using cosmetics, which includes greasy and non-greasy. 24 % of the patients did not give any history of cosmetic usage in the present study which well correlates with other studies.⁹

In the present study 25 patients had given history of duration of illness of 1 year, and 34 patients duration of more than 1 month. In the present study 66 % patients had acne lesions exclusively on face. Face was involved in all the 100 patients. 4 % patients had lesions on face and back. 7 % of them had lesions on face and chest. 11 % patients had lesions on face, chest and back sites. Remaining 12 % patients had lesions on all four sites. Acne occurs more common on the face was noted in other studies also.

In the present study, I - IV scale was used as narrated by Tutakne and Chari.¹⁰ This method helps in evaluating the lesions of the patients and to choose the modality of treatment. In the present study, thirty patients (30 %) had grade I acne, 27 % had grade II acne, 37 % had grade III acne, 6 % had grade IV acne. Most of the patients are with grade III acne. Grading method used in the present study, is similar to those used by many others.¹¹

The normal serum zinc levels in acne vulgaris patients as estimated by different workers varied between 70 to 125 µg / 100 mL of serum. Reports from the Western hemisphere have shown higher serum zinc values than those from the Eastern hemisphere. Each laboratory has different ranges, but many had obtained reference value of 70 – 125 µg / 100 mL serum.

Serum zinc levels in acne patients have been studied by many workers with varying results. They demonstrated low zinc levels in male patients with severe acne. Female patients did not show any definite change. They also found a definitive decrease in serum levels of retinol binding difference in serum zinc levels between acne patients and healthy controls.

El-Saaiee and co-workers¹² could not demonstrate any change in zinc levels between acne patients and control group, all of them demonstrated a beneficial effect of oral zinc in acne. Their results were lower than those of Michaelsson and co-workers. Women, whether diseased or healthy, showed a significantly lower mean serum zinc levels as compared to men. Michaelsson and co-workers, in contrast, did not show any decrease in the levels in females.

Ghorpade and co-workers¹³ studied 46 cases of acne vulgaris and 20 controls. They found a significant decrease in the zinc levels in both males and females as compared to normal controls of same age. Madadi and co-workers¹⁴ studied serum zinc levels and other trace elements in acne patients and found significant decrease in the serum zinc levels as compared to controls.

In the present study, fifty healthy controls (28 males, 22 females) were estimated for their serum zinc levels. All fifty patients had serum zinc levels ranging from 71 – 98 µg / 100 mL, the mean serum zinc level being 84.62 µg %.

It is known that animal foods contain high concentration of zinc. Certain agents (phytates and phosphates) present in the cereals may decrease the absorption by 50% of zinc by chelation. Since Indian population is largely vegetarian, it is possible that the relative lack of animal foods and excess of cereals in the diet have contributed to comparatively lower zinc levels in the normal controls of this study. Serum zinc levels of normal controls of this study is in accordance with the study of Ghorpade and co-workers.¹³

In the present series, the serum zinc levels were estimated in one hundred acne patients. Sixty-two patients (62 %) had lower than normal serum zinc levels ranging from 42 – 68 µg / 100 mL. It is found that very low serum zinc levels were noted in grade IV (severe) acne when compared with other grades. Thus, low serum zinc levels were found lower in both male and female acne patients in majority of the total one hundred acne patients studied in the present series.

The clinical improvement in the lesions was found to be very much variable in individual patients of the total 62 % treated. Out of 62 patients treated, very minimal response was noted in 21 patients (33 %) though their lower serum zinc levels improved to normal levels. Remaining 41 patients (67 %) showed average to maximum response. These observations about the improvement of lesions and zinc levels after treatment with oral zinc sulphate for 3 months are in accordance with the study of Ghorpade and co-workers,¹³ where 58 % of the subjects of the study showed significant improvement of the acne.

As the patients in the present study were strictly advised not to use any other medications during the period of study apart from oral zinc, the benefit with oral zinc seems to be self-evident. The clinical improvement of lesions was also reflected with the increase in serum zinc levels of the patient before and after treatment.

In both the sexes reduction in the severity of the lesions started from second follow up visit onwards (1-month completion of treatment). Maximum clinical improvement was seen at fourth visit (3 months after completion of treatment).

After 3 months of therapy statistically significant clinical improvement was observed in individual lesions. The reduction in comedonal lesions in male patients was not significant. Marked clinical improvement was noted in pustules and papules.

Only few side effects were observed among the patients treated with zinc in the present. Mild gastrointestinal symptoms in the form of nausea and vomiting noted in 12 (19.35 %) patients out of 62 patients who had taken treatment. On continuation of therapy these symptoms subsided. Similar observations were noted by Ghorpade and co-workers.

Zinc is an important component of several enzyme systems and its deficiency can influence local steroid metabolism of sebaceous gland which plays a major role in the pathogenesis of acne.¹³ The levels of retinol binding protein (which reflects the amount of vitamin A available to the tissues) were found to be low in acne patients, and the administration of zinc and vitamin A result at increase of retinol binding protein level. Zinc may act by inducing the release of vitamin A, thus improving the condition of low vitamin A levels in acne vulgaris. Probably a combination of these factors may be responsible

CONCLUSIONS

Acne lesions occur in adolescent age group more commonly in males. Factors that aggravate acne lesions include summer season, diet with non-vegetarian food, oily food, chocolates and milk products causing exacerbation.

Low serum zinc levels occur in acne vulgaris patients, more so in patients with inflammatory lesions. A significant improvement of acne lesions has been noted with oral zinc therapy. The number of patients studied in the present series is limited (hundred only) but the conclusions arrived are important and point out the need of further studies with

large number of patients to ascertain the exact role of oral zinc therapy in acne either as an adjunctive or alternative.

Data sharing statement provided by the authors is available with the full text of this article at jebmh.com.

Financial or other competing interests: None.

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