PLASMA ZINC LEVELS AND THE EFFECT OF ORAL ZINC IN ACNE VULGARIS

ASHOK GHORPADE, * B. S. N. REDDY † AND S. N. A. RIZVI ‡

Summary

The plasma zinc levels were investigated in 46 acne vulgaris cases and 20 normal controls. Statistically significant low plasma zinc levels were observed in both male and female acne patients as compared to normal controls. Administration of oral zinc sulphate, 220 mg three times a day for three months, resulted in significant elevation of plasma zinc levels with simultaneous marked clinical improvement. No significant reduction was observed in the sebum secretion rate before and after oral zinc therapy in 17 (7.8%) patients. However, a decrease in the oiliness of face was recorded in 30% of the cases. No major untoward effects were noted with therapy. Oral zinc sulphate was found to be an effective, safe and economic remedy in the treatment of acne vulgaris.

KEY WORDS: Acne Vulgaris, Plasma Zinc Levels, Oral Zinc Sulphate, Effect on Sebum

Acne vulgaris is one of the most common adolescent dermatological problems encountered universally by the physician in clinical practice. Inspite of a long list of medicines available, acne still remains to be a chronic problem with neither a permanent cure nor a preventable therapy. For the last two decades systemic antibiotics have assumed the main role in the management of acne. Patients are commonly treated with tetracycline or erythromycin often for prolonged periods[1]. Currently there is an increasing interest among dermatologists to find alternative remedies of comparative effectiveness to oral antibiotics but without the problems and restrictions inherent to these agents[2].

From the time of ancient Egyptians zinc and its derivatives have been used to promote wound healing[3]. More lately zinc has been found useful in the treatment of acrodermatitis enteropathica[4,5]. Recently it has been used as a therapeutic agent in acne vulgaris. Michaelsson et al[6] have shown that marked improvement in the papules, pustules and infiltrates of acne vulgaris can be obtained with oral zinc. In another study zinc was found to be as effective as tetracyclines in acne[7]. The usefulness of oral zinc in acne vulgaris was reported by various workers[8-13].

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However, Weismann et al[14] and Orris et al[15] observed no significant difference between the beneficiary effect of oral zinc and placebo in acne vulgaris.

Low serum zinc levels were observed in acne vulgaris by Michaelsson et al[16] but the studies of Briggs[17], Weismann et al[14] and Vahlquist et al[10] could not confirm this finding. The effect of oral zinc on sebum secretion is not clear. Burton and Goolamali[18] failed to observe any significant reduction in sebum production of acne patients after oral zinc therapy. However, Demetree et al[19] studied the sebum secretion rate in healthy controls before and after 3 weeks of oral zinc administration and found statistically significant decrease in the sebum production after oral zinc was given.

Thus it becomes clear that there is no unanimity of opinion on the role of zinc in therapy of acne vulgaris. To our knowledge the plasma zinc levels in acne vulgaris have not been studied in India so far. Hence we thought it important to estimate the plasma zinc levels in acne vulgaris and to study the effect of oral zinc on the clinical picture and sebum secretion rate in acne patients.

Material and Methods

The study included 50 cases of clinically diagnosed acne vulgaris attending the out-patient clinic of Skin & V. D. department, LNJP Hospital and associated Maulana Azad Medical College, New Delhi. Both sexes were included (37 males+23 females). The subjects were in the age group of 18-21 years. The duration of the lesions varied from 3 months to 8 years. None of the patients had any systemic disease or skin problem other than acne. They were not receiving any systemic or topical anti-acne treatment for 4 weeks preceding the study period. The patients were strictly advised not to use any other medication during the period of study apart from oral zinc.

In all the cases, a thorough clinical examination was carried out and the acne lesions were carefully graded according to the severity index described by Michaelsson et al[6] by counting the number of comedones, papules, infiltrates and cysts. The total severity index was calculated after assigning an individual severity index to each type of lesion, which ranged from 0.5 for comedone, 1 for papule, 2 for pustule, 3 for infiltrate and 4 for cyst. By multiplying the number of each type of lesion with its severity index and adding each sum, a total score corresponding to the total severity of the disease was obtained.

The fasting blood samples were collected initially from all acne patients and 20 carefully matched healthy controls and the plasma zinc levels were estimated according to the method of Song et al[20]. In 17 acne cases, the sebum secretion rate was determined by the method of Strauss and Pochi[21]. Following this, 220 mg zinc sulphate capsules ($ZnSO_4 7H_2O$) corresponding to 45 mg of elemental zinc were given orally, three times a day, for a period of 3 months to all patients. Clinical evaluation of lesions was carried out at the time of initial visit and at 2,4,6, 8,10 and 12 weeks by using the same severity index as mentioned earlier. At the end of 3 months, the plasma zinc levels were again estimated in all patients. Similarly, the sebum secretion rate was determined in the 17 patients in whom it was estimated earlier.

Results

46 patients completed the study. There were four drop-outs. Two patients discontinued from the study because of nausea and vomiting due to the oral

TABLE 1

Mean plasma zinc levels in 20 controls and in 46 cases of acne vulgaris

Cases	Mean Plasma Zinc Levels /μg100 ml		't' value	'p' value
	Acne Cases (46)	Controls (20)		
Males	55.85 ± 8.37 (46 — 100)	85.27 ± 10.06 (70 — 100)	8.931	<0.001
Females	61.10 ± 10.36 (46 — 80)	77.11 ± 6.26 (68 — 84)	4.144	<0.001
Total	58.13 ± 9.65 (46 — 80)	81.6 ± 9.48 (68 — 100)	9.132	<0.001

Figures in parenthesis indicate the ranges

zinc and two defaulted because of personal reasons. The mean plasma zinc levels in 20 healthy controls and 46 acne patients (26 males + 20 females) are shown in Table 1. In normal controls, the plasma zinc levels varied from 68–100μg/100 ml (mean = 81.6 μg%) and in acne patients, the levels were in the range of 46–80μg/100 ml (mean = 58.13 μg%). Thus, the plasma zinc levels were found to be lower in both male and female acne cases than in normal controls (Fig. 1A) and this difference was statistically significant ($P < 0.001$). Although the plasma zinc levels were slightly lower in male acne cases than in females, this difference was found to be statistically not significant ($P > 0.05$). No specific relationship was noted between the plasma zinc levels to age of patient or duration of lesions.

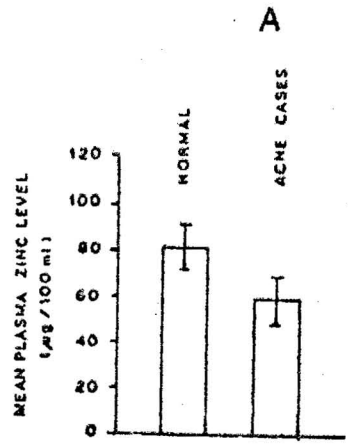

Fig. 1-A Mean plasma zinc levels in normal controls and acne vulgaris cases.

The mean plasma zinc levels in the 46 patients before and after oral zinc sulphate are summerized in Table 2. There was a significant rise in the mean plasma zinc levels of both male and female patients from initial 58.13μg to 78.13μg after 3 months of oral zinc (Fig. 1B). The percentage of increase in male patients was slightly more than in females.

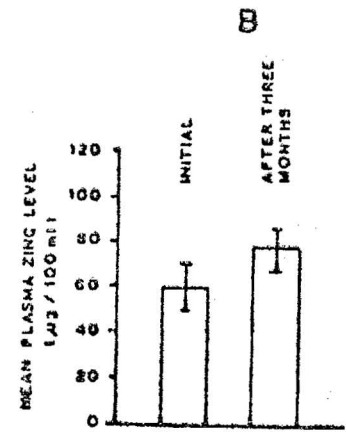

Fig. 1-B Mean plasma zinc levels in acne cases before and after 3 months of oral zinc sulphate.

The sebum secretion rate in 17 acne patients are shown in Table 3. A slight reduction in the sebum secretion

TABLE 2

Mean plasma zinc levels in 46 acne vulgaris cases before and after giving oral zinc sulphate

Cases	Plasma zinc level μg/100 ml		't' value	'p' value
	Initial	After 3 months		
Males	55.85 ± 8.37 (46 — 80)	76.23 ± 8.69 (64 — 102)	25.16	<0.001
Females	61.10 ± 10.36 (46 — 80)	80.60 ± 10.24 (60 — 100)	20.65	<0.001
Total	58.13 ± 9.65 (46 — 80)	78.13 ± 9.75 (60 — 102)	31.90	<0.001

rate was observed from the initial 2.66 mg/10cm²/3hours to 2.63 mg/10cm² hours after 3 months of oral zinc therapy but this difference was statistically not significant ($P > 0.05$). However, a decrease in the oiliness of face was noted in 14 patients (33%) after therapy.

Increase in the plasma zinc levels in both males and females after oral zinc, resulted in considerable clinical improvement. The severity index showed statistically significant decrease from the initial value of 138.84 to 71.90 after three months of theray, $P < 0.001$ (Table 4). Males had more severe acne initially and showed greater degree of improvement than females. The percentage of reduction in the total severity was 49.71 in males and 44.67 in females. The reduction in mean severity index of both males and females are shown in Fig. 2. In both the sexes, reduction in the severity of lesions started from second week onwards. Maximum decrease in the severity index curve was seen at 6 weeks in females, while in males the reduction in the severity index continued upto 12 weeks.

The percentage reduction in total severity index is further outlined in Table 5. The predominant lesions observed in this study were papules, comedones, pustules and infiltrates in that order. Only one patient had cystic acne.

After 3 months of therapy, statistically significant improvement was observed in individual lesions as shown in Table 6. The reduction in comedonal lesions in male patients was not significant. Marked improvement was noted in pustules, infiltrates and papules in that order. These showed a mean reduction of 55.46%, while non inflammatory lesions (comedones) showed

TABLE 3

Mean sebum secretion rates in 17 acne patients before and after zinc sulphate orally

Cases	Sebum Secretion Rate (mg/10 □cm 3 hours)		't' value	'p' value
	Initial	After 3 months		
Males (10)	3.16 ± 0.29 (2.50 — 3.45)	3.15 ± 0.32 (2.36 — 3.40)	0.790	>0.05
Females (7)	1.94 ± 0.18 (1.72 — 2.15)	1.90 ± 0.17 (1.63 — 2.12)	0.809	>0.05
Total (17)	2.66 ± 0.67 (1.72 — 3.45)	2.63 ± 0.69 (1.63 — 3.40)	1.110	>0.05

TABLE 4

Mean Severity Index in 46 acne patients before and after giving oral zinc sulphate for 3 months

Cases	Mean Severity Index		% decrease	't' value	'p' value
	Initial	After 3 months			
Males (26)	172.65 ± 111.70 (51.5 — 574.5)	86.82 ± 58.53 (21.5 — 219)	49.71	6.051	<0.001
Females (20)	94.88 ± 54.62 (35.5 — 231.5)	52.50 ± 27.19 (20 — 108)	44.67	5.173	<0.001
Total (46)	138.84 ± 100.27 (35.5 — 574.5)	71.89 ± 51.02 (20 — 219)	48.21	7.173	<0.001

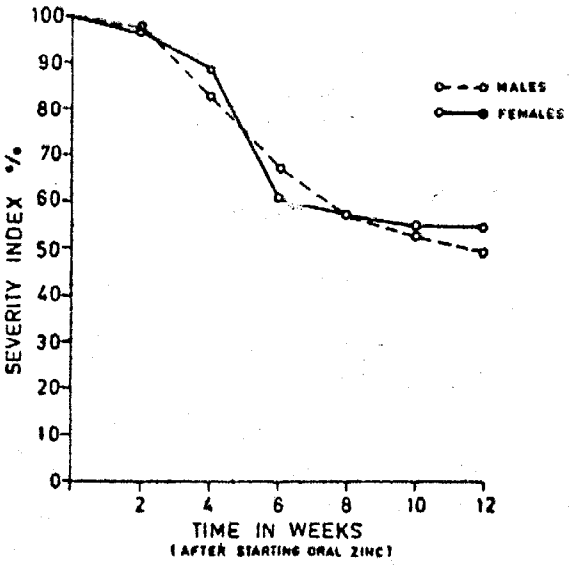

Fig. 2 Mean severity index at biweekly intervals after starting oral zinc in male and female acne cases.

15.44% reduction. The average inflammatory lesion count (%) at biweekly intervals after starting oral zinc sulphate in females and males is shown in Figs. 3A & B respectively. Marked improvement was observed in the clinical picture after three months (Fig. 4).

No major untoward effects were observed in this study with oral zinc except mild gastrointestinal symptoms in the form of nausea and vomiting in 6 out of 50 patients. On continuation of therapy, these symptoms subsided in all except in two, who ultimately discontinued from the study.

Discussion

The normal plasma zinc levels as estimated by different workers vary

TABLE 5

Percentage reduction to total severity index after 3 months of oral zinc sulphate

% Severity reduction	Number of Cases			
	Males	Females	Total	%
Less than 30	2	—	2	4.35
31—60	18	13	31	67.39
61—80	5	3	8	17.39
No significant change	1	1	2	4.35
Worsening	—	3	3	6.52
Total	26	20	46	100.0

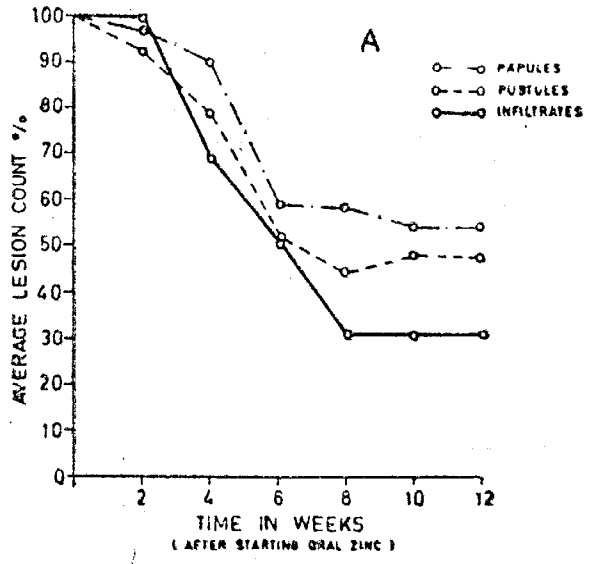

Fig. 3-A Mean count of lesions at biweekly intervals after starting oral zinc in female acne cases.

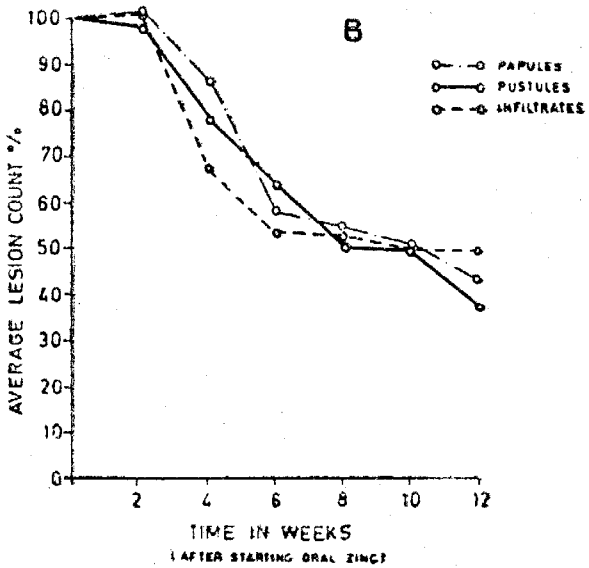

Fig. 3-B Mean count of lesions at biweekly intervals after starting oral zinc in male acne cases.

between 70 to 125 ug / 100 ml of plasma[22-27]. Reports from the western hemisphere have shown higher plasma zinc valuses than those from the eastern hemisphere. In our study, the mean plasma zinc level in normal controls was 81.6 ug/100 ml. It is known that animal foods contain a high concentration of zinc. Certain agents (phytates and phosphates) present in the cereals may decrease the absorption of zinc by chelation. Since our population is largely vegetarian, it is possible that the relative lack of animal foods and excess of cereals in the diet have contributed to the comparatively lower zinc levels in our normal controls. Prasad et al[28] have shown that in tropical countries where sweating is excessive, upto 2-3 mg of zinc can be lost through sweat. This might be another factor contributing to low plasma zinc levels as observed in our study.

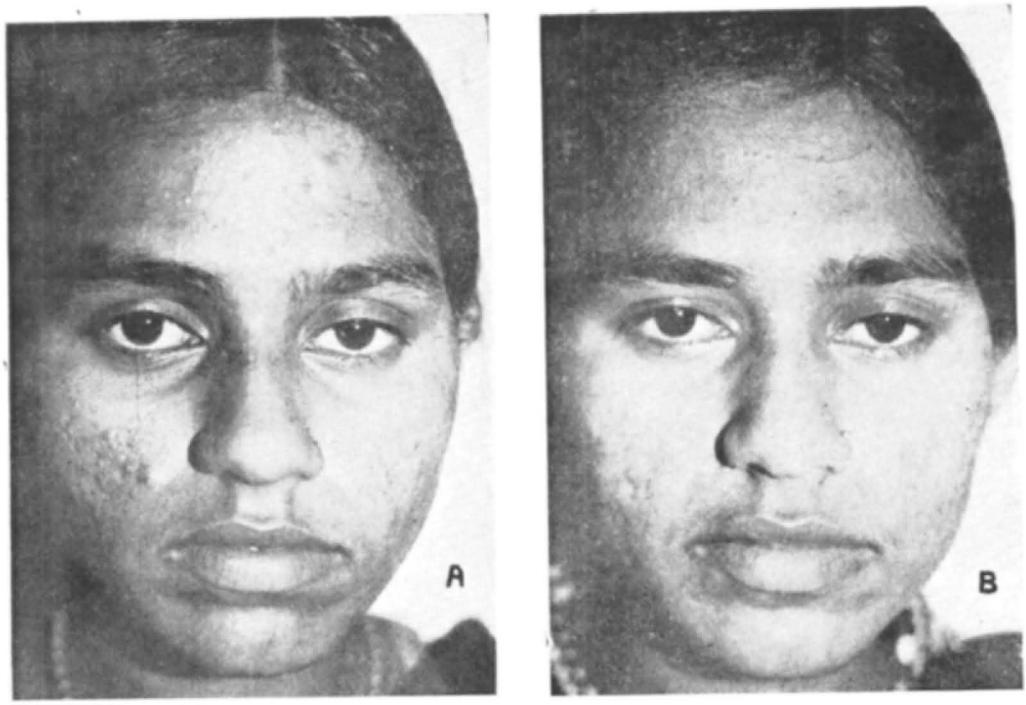

Fig. 4 The clinical picture of acne lesions in a female patient before (A) and 3 months after zinc therapy (B).

TABLE 6

Mean count of different types of lesions in 46 acne cases befo·e and after oral zinc for 3 months

Type of lesion	Ini-tial	3 mon-ths	% reduc-tion	't' value	'p' value
Papules	102.74	49.00	52.30	6.376	<0.001
Pustules	7.57	3.09	59.18	8.327	<0.001
Infiltrates	5.32	2.40	54.89	6.952	<0.001
Come-dones	23.70	20.04	15.44	3.511	<0.001

Earlier reports show decrease in zinc levels to be significantly low in male cases with severe acne than in normal controls and cases with mild acne[7]. The serum zinc levels in female acne patients although lower than in normal controls was not significant statistically. The reasons for the observed low levels of zinc in acne vulgaris patients have not been understood completely. According to Fitzherbery[29], the requirement of zinc during puberty shows a significant rise, which persists until the age of 18-19 years and longer in males than in females.

Michaelsson et al[16] reported low serum zinc levels and retinol binding protein (RBP) in acne cases. According to these authors, one possibility is that these patients have a real zinc deficiency leading to a defective synthesis of RBP and a resultant deficiency of vitamin A. The laboratory criteria for the diagnosis of zinc deficiency are not completely clear at present and it is not certain whether a low plasma zinc level is indicative of real zinc deficiency in the body. Low plasma zinc level may be a reflection of an impaired zinc nutrition in many, while in others it may indicate a shift of zinc from plasma to another body pool or alternatively represents a late sign of zinc deficiency[36]. However, the critical test for zinc deficiency is a definite clinical response to zinc supplementation. Since the plasma

zinc levels were observed to be significantly lower in acne and a definite clinical improvement was noted in the lesions after oral zinc therapy in the present series as well as in other studies [7,16], it may be reasonable to assume that a relative zinc deficiency exists in acne vulgaris. However, it may not be possible to establish whether this is due to increased zinc requirement in adolescent age group as observed by Fitzherbery[29] or the result of stress and inflammatory reaction to the disease process in acne vulgaris as explained by Michaelsson et al[16] or combination of both these factors.

Increase in the plasma zinc levels after giving oral zinc resulted in a sight reduction in the sebum secretion rate of acne cases studied in the present series but this decrease was found to be statistically not significant. Similar observations were reported by Burton and Goolamali[18]. Hence it may be conceived that oral zinc has no major effect on the sebum secretion rate in acne patients, although one cannot exclude the possibility of qualitative changes in the different components of sebum. This aspect has not been studied so far.

The beneficial role of oral zinc in the treatment of acne has been reported by many workers[8,9,10,11,13]. In the present study also, significant clinical improvement in acne after three months of oral zinc therapy was observed. The response was better in inflammatory lesions than in comedones. In a double blind study, Michaelsson et al[7] found that oral zinc sulphate was as effective as tetracycline in the treatment of acne vulgaris and hence recommended it as an alternative remedy to tetracycline. The results observed in our study prove that oral zinc sulphate is an effective, safe and economic remedy in the treatment of acne vulgaris. The added advantage with this medicine is that it is devoid of many adverse reactions commonly seen after prolonged use of systemic antibiotics. None of the patients studied in this series had any major untoward effects except mild gastrointestinal symptoms in the form of nausea and vomiting, which subsided on continuation of therapy in most of the cases.

The exact mechanism of action of zinc in acne vulgaris is not clear. Several views were expressed to explain its beneficiary role. Zinc may interfere with the inflammatory process in acne by virtue of its ability to (1) stabilize the biological membranes and influence the phagocytic activity of the macrophages[31], (2) adversely affect the neutrophil chaemotaxis and complement activation[32] and (3) inhibit the histamine release from mast cells[33]. Zinc is an important constituent 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. The levels of retinol binding protein RBP (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 resulted in the increase of RBP levels[10,13,16]. Zinc may act by inducing the release of vitamin 'A' thus improving the condition of low vitamin 'A' levels in acne vulgaris[34]. Probably, a combination of these factors may be responsible for the therapeutic response of oral zinc in acne.

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Announcement...

Dear Colleague,

On behalf of the Organising Committee of the Conference, I have the pleasure in inviting you and your friends for your co-operation and active participation in the VIIth National-Conference of IASSTD in Bombay on 26th & 27th February, 1983. This is an advance intimation to you to adjust your programme to attend the Conference and also to give you ample time to work on your paper.

Scientific Programme :

The Scientific Programme will include Guest lectures by eminent authorities, Orations and Scientific Sessions. Those who are interested in sending Scientific Papers on any aspect of Sexually Transmitted Diseases are requested to forward the abstracts of their papers not exceeding 150 words to the Chairman, Scientific Committee, Dr. S. G. Deshpande, before 15th December, 1982 and full text of the Paper by 10th January. 1983. The detailed programme will follow shortly.

Dr. J. K. Maniar,
Org. Secretary.