

ORAL ZINC SULPHATE THERAPY IN ACNE VULGARIS: A DOUBLE-BLIND TRIAL

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Abstract. The effect of zinc sulphate and placebo was compared in a double-blind trial in 56 patients suffering from acne vulgaris. Serum vitamin A levels were studied in all, before and at the end of therapy. 29 patients received zinc sulphate 600 mg daily and 27 patients received placebo. Patients on placebo showed no improvement. After 12 weeks of treatment with zinc sulphate, 17 patients (58%) showed significant improvement. There was a statistically significant decrease in the number of papules, infiltrates and cysts. In zinc-treated cases there was statistically significant increase in serum vitamin A levels, while no change was found in the placebo group.

Acne vulgaris remains a therapeutic problem. Most of the topical treatments are aimed at peeling and keeping the skin clean. Amongst systemic therapeutic agents, broad spectrum antibiotics are being used. Tetracyclines are effective and preferred to other antibiotics. The drawback with antibiotics is that they must be used for very long periods and they have their own side effects.

Recently oral zinc has been reported to be beneficial in acne vulgaris (3, 5, 6, 12), whereas others have not found it useful (1, 8, 13). The exact mode of action of zinc is not known. It plays a part in a large number of enzyme activities in the metabolism of many compounds and also in epithelialization (10). Zinc appears necessary in various stages of the metabolism of vitamin A and a rise in vitamin A level has also been reported following zinc therapy (4). In view of the paucity of trials and their variable results (1, 3, 5, 6, 8, 12, 13), the present study was undertaken.

MATERIAL AND METHODS

Fifty-six acne patients (35 males and 21 females) were the subjects of this study. Only patients who had not been treated with standard accepted treatment such as tetracycline, topical vitamin A acids or topical sulphur preparations and having a minimum of 15 acne lesions on the face were included in the trial.

A detailed history, and physical examination and laboratory investigations (Hb, WBC, urine, stool, transaminases B sugar, serum Vit. A) were carried out in each patient before instituting the treatment. Only otherwise healthy patients were selected, with no involvement of liver, kidney.

Estimation of lesions

The number of papules (elevated infiltrated lesion less than 5 mm in diameter), pustules (lesion less than 5 mm, containing visible pus), infiltrates (indurated lesion larger than 5 mm in diameter) and cysts were counted at each visit to clinic every week. Comedones were not taken into account. Only acne lesions in well defined regions of face were counted. Changes in oiliness of face, associated seborrhoea and side effects were periodically recorded. A clinical photograph of each patient was taken before and at the end of the trial. The response to treatment was assessed by two different dermatologists, neither of whom knew the code to the treatment.

Serum vitamin A

The vitamin A level in serum was estimated in each patient at the beginning of the trial, after 6 weeks and at the end of the trial by the ultra spectrophotometric method (9).

Mode of administration

A double-blind trial was undertaken with active drug zinc sulphate and placebo (Lactose). Both zinc sulphate and lactose were dispensed in identical gelatin capsules containing 0.3 g by weight. All previous medication (if any) was withdrawn at least a week prior to the new treatment.

Each patient was provided with capsules to be taken orally twice a day after meals. Patients were instructed to avoid excessive exposure to sunshine and heat.

Those showing no response to treatment after 6 weeks of treatment were presumed to show absence of effect and, to avoid frustration for the patient, tetracycline and vitamin A acid treatment was instituted.

RESULTS

The results appear in Table 1. Those patients on placebo showed no improvement after 6 weeks of

Table I. Grades of improvement at the end of trial

Excellent improvement: decrease in lesion count by 75–100%. Moderate improvement: decrease in lesion count by 50–75%. Slight improvement: decrease in lesion count by 25–50%. Very slight improvement (or no response): changes in lesion count by 0–25%. Aggravation: an increase in lesion count

Drug	Weeks of therapy	Improvement				
		Excellent	Moderate	Slight	Very slight or no response	Aggravation
Zinc	6	3	10	1	11	2
	12	12	3	2	10	2
Placebo	6	–	–	–	16	11
	12	–	–	–	–	–

treatment. Rather, 11 patients showed an aggravation of their condition and the treatment was therefore discontinued. Of the 29 patients on zinc, 15 showed some improvement (Table I). 17 received treatment for 12 weeks with further improvement.

Table II shows mean and standard deviations. In the zinc-treated group there was a statistically significant decrease in the number of papules, infiltrates and cysts ($p < 0.05$) while there was little effect on pustular lesions ($p > 0.05$). However, the effect on infiltrates and cysts was the most marked (< 0.001). In the placebo group, there was no significant change in the number of papules, pustules and cysts ($p > 0.05$) but the number of infiltrates was significantly increased ($p < 0.05$).

A decrease in oiliness of the face and associated seborrhoea were observed in 17 patients on zinc treatment, while no such change was observed in any of the patients on placebo.

Four patients on zinc complained of nausea. In one, treatment was discontinued because of vomiting and in 3 others who continued with drug therapy, there was no discomfort. At 6 and 12 weeks of therapy, no abnormal changes were observed at routine blood and urine examinations.

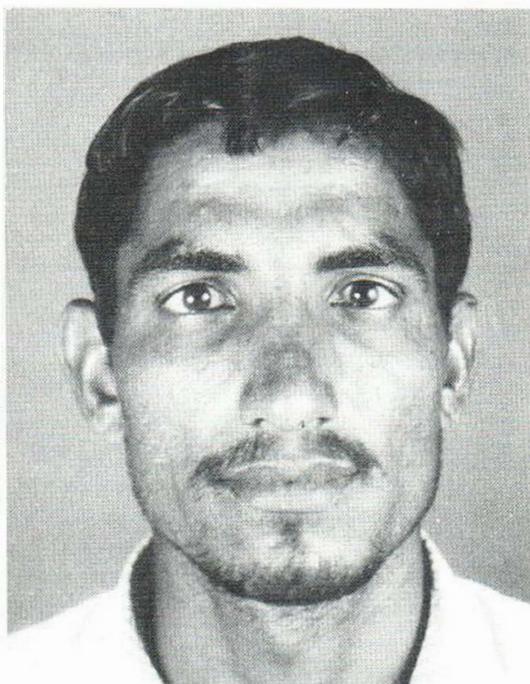
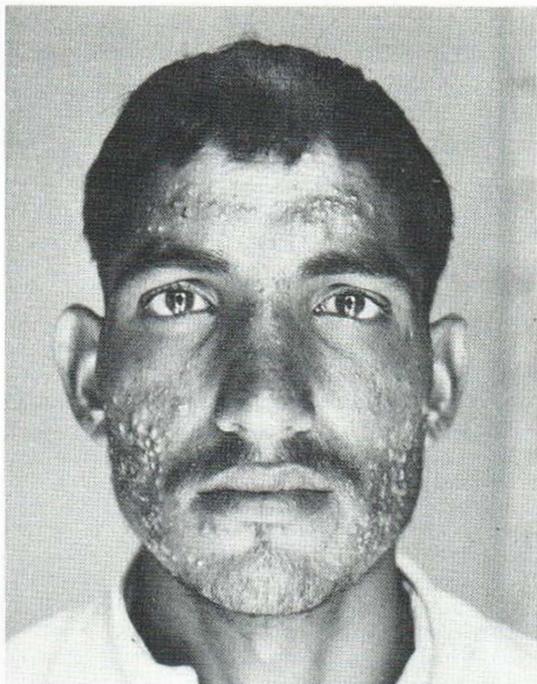
Serum vitamin A levels were estimated before starting the treatment, after 6 weeks and at the end of the trial. After 6 weeks, serum vitamin A levels in the zinc-treated group (29 patients) rose from $20.93 \pm 4.65 \mu\text{g}/100 \text{ ml}$ (mean \pm S.D.) to $24.36 \pm 5.02 \mu\text{g}/100 \text{ ml}$ and at the end of the trial (i.e. 12 weeks) the value was $31.12 \pm 5.8 \mu\text{g}/100 \text{ ml}$. The rise in serum vitamin A level was significant ($p < 0.01$).

In the placebo group, the vitamin A level before treatment was $23.93 \pm 4.98 \mu\text{g}/\text{ml}$ (mean \pm S.D.) and at 6 weeks it was $21.87 \pm 4.77 \mu\text{g}/100 \text{ ml}$, thus showing an absence of any significant change ($p > 0.05$), as shown in Table III.

Table II. Mean and standard deviations of lesion counts during treatment period

For each of the acne lesions in the zinc group and the placebo group: n = number of lesions, \bar{x} = mean number of lesions, S.D.: standard deviation. The changes from initial values of those after 6 and 12 weeks: p : probability value, S: significant, NS: not significant, HS: highly significant

Lesions	Drug	Week 0			Week 6			Week 12		
		n	\bar{x}	S.D.	n	\bar{x}	S.D.	n	\bar{x}	S.D.
Papules	Zin	29	29.38	12.50	29	17.79	12.04	17	7.41	4.61
	Placebo	27	19.33	4.05	27	20.22	4.92			
Pustules	Zinc	29	5.34	7.31	29	2.96	15.81	17	0.29	0.30
	Placebo	27	3.70	4.78	27	2.92	3.24			
Infiltrates	Zinc	29	1.65	2.89	29	1.38	2.02	17	0.29	1.17
	Placebo	27	0.70	2.23	27	1.92	2.81			
Cysts	Zinc	29	0.52	1.58	29	0.48	0.87	17		
	Placebo	27	0.63	1.78	27	0.59	1.61			



DISCUSSION

The results show that oral zinc sulphate in doses of 0.6 g daily give significantly better results than does placebo. After 12 weeks of treatment 58% of patients on zinc therapy were satisfied with the therapeutic results, while none of those on placebo showed any therapeutic response.

Michaëlsson et al. (6) compared the combined

effect of oral zinc and vitamin A with oral zinc alone, on acne vulgaris. They found a significant decrease in the number of papules, pustules and infiltrates in the zinc-treated group when compared with the group receiving placebo or vitamin A alone. Later they (5) compared the effect of oxytetracycline with oral zinc in acne patients and found that improvement in both groups was 70%. Hillström et al. (3) showed significantly better effect with zinc sulphate than with placebo.

Burton & Goolamali (1) found no clinical improvement in acne patients given 660 mg of zinc sulphate per day. Likewise Weismann and associates (13) and Orris et al. (8) could not demonstrate better results with zinc sulphate in their studies. However, Weismann et al. (13) noted clinical improvement in both placebo and zinc-treated groups. They attributed the alleviation in the severity of the acne in both groups to seasonal variations of acne in a temperate climate. Strain & Pories (11) have reported a marked rise in zinc content in human hair during the summer months, thus suggesting a relation between changes in zinc metabolism and remission of seborrhoea and acne in summer. The improvement found in both the zinc and the placebo group in Weismann's cases can be

Statistical significance

0-6 weeks	0-12 weeks
$p < 0.05$ S	$p < 0.05$ S
$p > 0.05$ NS	
$p > 0.05$ NS	$p > 0.05$ NS
$p > 0.05$ NS	
$p > 0.05$ NS	$p > 0.001$ HS
$p > 0.05$ S	
$p > 0.05$ NS	$p > 0.001$ HS
$p > 0.05$ NS	

Table III. Results of serum vitamin A-assessment of zinc and placebo treatment

n =number of patients, \bar{x} =mean value, S.D.=standard deviation, p =probability value, S=significant, NS=not significant, HS=highly significant

	Week 0			Week 6			Week 12			Statistical significance	
	n	\bar{x}	S.D.	n	\bar{x}	S.D.	n	\bar{x}	S.D.	0-6 weeks	0-12 weeks
Zinc	29	20.95	4.65	29	24.36	5.02	16	31.12	5.8	$p < 0.05$ S	$p < 0.001$ HS
Placebo	27	23.93	4.98	27	21.87	4.76				$p > 0.05$ NS	

explained on the basis of an increase in zinc during summer, thus indicating the role of zinc in acne.

The mechanism by which zinc is helpful in acne is poorly understood. Michaëlsson et al. (6) suggest that there might be deficiency of zinc at puberty, which may well be of importance. Dietary factors probably influence absorption too—and hence the level of blood zinc.

The role of vitamin A in acne is established and is indirectly measured in the blood in the form of retinol-binding protein (RBP). Michaëlsson et al. (7) have shown the relationship between serum zinc and RBP in acne, i.e. with an increase in serum zinc there was also an increase in RBP, thus suggesting the role of serum zinc through RBP. Subsequently, Vahlquist et al. (12) have also observed a rise in RBP and clinical improvement in acne in zinc-treated patients. Zinc itself is also involved—just as is vitamin A—in epithelial differentiation.

In our series, vitamin A levels were estimated before instituting zinc therapy and then at intervals of 6 weeks and 12 weeks of treatment. In cases where zinc therapy was given there was an increase in vitamin A level, more so in the 17 cases which showed significant clinical improvement.

Our findings support the observations of Michaëlsson et al. (6).

One would conclude that zinc is involved to some extent in acne. Chapil et al (2) have pointed out in their study that zinc has an anti-inflammatory effect too. Although some workers (1, 8, 13) have not found a beneficial effect of zinc in acne, it is suggested that more trials need to be conducted, as no serious side effects with oral zinc have yet been observed. Zinc may find a place in the treatment of acne and, if not as good as tetracycline, maybe as an alternative.

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