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ORAL ZINC SULPHATE THERAPY FOR ACNE VULGARIS

K. Weismann, S. Wadskov and J. Søndergaard

From the Departments of Dermatology, Rigshospital and Hvidovre Hospital, University of Copenhagen, Denmark

Abstract. A double-blind controlled clinical trial was performed to evaluate the effect of oral zinc sulphate, 0.6 g daily, on acne vulgaris. Twenty patients received zinc sulphate tablets and 19 were given placebo tablets. Thirteen of the zinc group and 12 of the placebo group received their medication throughout a 12-week period, while the remaining patients were treated for 4 or 8 weeks. In all patients the numbers of papular and pustular acne lesions on the face and the back were significantly reduced, while larger infiltrates remained practically unaltered during the trial, which was performed from March through May 1975. No statistically significant difference in the improvement of the groups was demonstrable. Pretreatment serum zinc values, which were normal in all patients, rose significantly in the zinc group as well as in the control group, but the increase in the former was significantly higher. The negative therapeutical results might be attributable to the limited number of patients or related to the zinc dosage. Furthermore, the results might have been influenced by the unexplained rise in serum zinc values in the control group. A possible weak beneficial effect of zinc might also have been camouflaged by the seasonal variation in the severity of acne which was noted in this study.

Key words: Acne vulgaris; Zinc sulphate; Zinc therapy

New principles for treatment of acne are currently being investigated throughout the world. Unfortunately, however, few prove to be effective. Oral zinc therapy might be an alternative effective principle (4). In acrodermatitis enteropathica (1, 3, 5, 7, 8) and in zinc deficiency, caused by long-term parenteral nutrition (2, 9), the inflammatory skin changes, including acneiform eruptions and seborrhoeic lesions on the face, disappear promptly when the patients receive systemic treatment with zinc. In a double-blind controlled clinical trial we have therefore attempted to evaluate the effect of oral zinc sulphate in acne vulgaris.

MATERIAL AND METHODS

Thirty-nine volunteer patients (30 males and 9 females) suffering from acne vulgaris were included in the study. The mean age in the male group was 22 years (range 17–33 years), and 24 years (range 17–37 years) in the female group. Only patients who had not been treated with tetracycline, topical vitamin A acid or benzoyl peroxide preparations were accepted for the trial, and a minimum of 15 papular or pustular acne lesions on the face was required. The study was performed during March, April and May 1975.

Treatment with zinc sulphate or placebo was performed as a randomized double-blind trial. Zinc sulphate (Solvezink®, AB Tika, Lund, Sweden) was given as effervescent tablets of 0.2 g $ZnSO_4 \cdot 7H_2O$ (=45 mg Zn^{2+}), and for placebo, lactose tablets of identical appearance and taste were used. The patients were instructed to ingest one tablet dissolved in a glass of water three times daily immediately after the meals. No other treatment was permitted and sunbathing was prohibited during the trial. At each control visit to the clinic 2, 4, 8 and 12 weeks later, the remaining tablets were counted to ensure that the medication had been taken as prescribed.

Serum zinc was determined in each patient before and after 4 and 12 weeks of treatment. The blood samples were taken between noon and 3 p.m., the patients having been fasting for at least 5 hours. Special zinc-free glasses were used and care was taken to minimize the risk of contamination. The zinc analyses were performed by Medicinsk laboratorium A/S, Copenhagen, using atomic absorption spectrophotometry.

The number of papules (elevated infiltrated lesions less than 5 mm in diameter), pustules (lesions less than 5 mm, containing visible pus) and infiltrates (indurated or cystic lesions larger than 5 mm in diameter) were counted at each visit, always by the same clinician. Comedones were not counted. Only acne lesions in well-defined regions were recorded, which included the face and the back. The face region was defined as the area limited by the border of the scalp and two lines drawn from the distal part of the right and left mastoid processes to the anterior edge of the sternocleidomastoid muscles, joining a horizontal line at the level of the laryngeal prominence. The test area on the

Table I. *Results of oral zinc sulphate and placebo treatment in acne vulgaris*

Left: for each of the acne lesions in the zinc group and the placebo group: n = number of patients; $\bar{X}$ = mean number of lesions; S.D. = standard deviation. *Right:* the changes from the initial values to those after 4, 8, and 12 weeks are evaluated by means of Wilcoxon's signed rank sum test: n = number of patients showing a change; RS = sum of signed ranks; p = probability value; n.s. = not significant ($p>0.05$)

	Week 0			Week 4			Week 8			Week 12		
	n	$\bar{X}$	S.D.	n	$\bar{X}$	S.D.	n	$\bar{X}$	S.D.	n	$\bar{X}$	S.D.
Papules												
Zinc	20	28.4	16.2	20	20.6	17.4	14	19.1	12.3	13	13.0	8.0
Placebo	19	41.3	21.2	19	27.4	20.9	14	24.1	22.5	12	21.8	15.8
Pustules												
Zinc	20	9.8	14.3	20	5.7	7.6	14	4.1	4.1	13	9.3	12.4
Placebo	19	7.1	9.0	19	3.5	4.1	14	3.6	3.6	12	3.4	2.8
Infiltrates												
Zinc	20	6.2	9.4	20	6.6	10.6	14	2.9	5.3	13	5.1	7.5
Placebo	19	3.3	4.6	19	3.4	5.2	14	1.3	1.5	12	2.4	3.2

back was limited by two vertical lines at the right and left posterior axillary folds and two horizontal lines through the vertebra prominens and the inferior scapular angles.

Clinical photos were obtained before and at the end of the trial under standardized photographic conditions to facilitate comparison. The overall clinical effect of the treatment was evaluated at each visit both by the patient and the clinician.

The results were statistically analysed by Wilcoxon's rank sum test and Student's t-test.

RESULTS

By the end of the trial when the code was broken, 20 patients (15 males and 5 females) were found to have received treatment with zinc sulphate and 19 patients (15 males and 4 females) had received the placebo. Thirteen patients of the zinc group and 12 of the control group received the medication throughout the 12-week period, while the remaining patients were treated for 4 or 8 weeks (Table I). The only patients who were excluded after 4 or 8 weeks were those who did not turn up for control or failed to take the tablets as prescribed.

In the placebo group and the zinc-treated group a clinical improvement of acne was noted by the clinicians and the patients during the trial. With a single exception the numbers of papules and pustules were significantly reduced after 4, 8 and 12 weeks, whereas the number of infiltrates was unaltered in the two groups, apart from a significant decrease after 8 weeks in the control group (Table I). There was, however, no statistically significant difference between the groups in the reduction of papules, pustules or infiltrates when compared with the control group ($p>0.05$, Wilcoxon's rank sum test). No significant difference was found in the number of acne lesions in the two groups before the trial ($p>0.05$, Wilcoxon's rank sum test).

After 4 weeks, serum zinc levels in the zinc-treated group rose from 13.05 ± 1.87 μmol/l (mean ±S.D.) to 17.75 ± 3.04 μmol/l. At the end of the trial the value was 18.15 ± 4.49 μmol/l. The levels after 4 and 12 weeks were significantly higher than the initial serum zinc concentrations ($p<0.001$, Student's t-test). At the beginning of the trial, serum zinc was 13.58 ± 1.46 μmol/l in the control group. After 4 weeks the mean value was 14.33 ± 1.53 μmol/l, and after 12 weeks 15.39 ± 2.12 μmol/l. These values are significantly higher than the pre-treatment values ($p<0.05$ after 4 and 12 weeks, Student's t-test). However, the increase in serum zinc after 4 and 12 weeks was significantly higher in the zinc-treated group than in the control group ($p<0.001$ and $p<0.05$, respectively, Student's t-test). In Medicinsk laboratorium A/S the normal range of serum zinc is 10.6–17.7 μmol/l (females) and 11.4–18.9 μmol/l (males) (10).

Side effects were recorded in 5 patients receiving zinc. All had nausea, in one case followed by vomiting, within a quarter of an hour after ingestion of the tablets. Because of this, the treatment was stopped in 2 patients; in 3 the medication was continued as the discomfort soon disappeared.

0–4 weeks			0–8 weeks			0–12 weeks		
n	RS	*p*	*n*	RS	*p*	*n*	RS	*p*
10	120	0.05	13	66	0.05	12	75	0.01
17	104	0.05	14	85	0.01	12	59	0.05
17	100	0.05	12	57	0.05	12	1	n.s.
15	106	0.05	12	24	n.s.	9	34	0.05
13	−9	n.s.	9	22	n.s.	8	14	n.s.
15	−9	n.s.	10	41	0.05	9	10	n.s.

DISCUSSION

The results show that oral zinc sulphate in doses of 0.6 g daily did not alleviate the acne in the limited number of patents included in this study. Thus, no reduction in the number of papules, pustules and infiltrates was observed after treatment for up to 3 months with zinc when compared with a similar group of acne patients given a placebo. The lack of effect of zinc could not be explained by the fact that the patients did not take the tablets, as this was controlled at each visit by counting the remaining tablets and, at the end of the trial, confirmed by a significant rise in serum zinc. Neither could the failure be attributed to the type of acne, since the two gruops were properly matched for type and severity; nor could it be due to an improper evaluation technique. Two clinicians may obtain quite different results even by using a strict system of classification. In this study, however, this was excluded, as each patient was always seen by the same clinician.

The therapeutical failure might be attributable to the dosage of zinc which resulted in a slow increase of serum zinc to about the upper normal limit. The rise in serum zinc levels in the control group remains unexplained, but might reflect seasonal variations in zinc metabolism. Strain & Pories (6) have found a marked elevation of the zinc content of human hair during the summer months, and they suggest a connection between alteration in zinc metabolism and remission of seborrhoea and acne during summer. Thus, it cannot be excluded that the changes in the serum zinc level might have influenced the severity of acne in the control and zinc-treated groups.

In no case did we find low or subnormal serum zinc concentrations suggestive of latent zinc deficiency, which might have indicated the involvement of zinc in the pathogenesis of acne vulgaris.

Recently, Michaëlsson (4) studied the combined effect of oral zinc sulphate and vitamin A, and oral zinc alone (0.6 g zinc sulphate daily) on acne vulgaris. She found a significant decrease in the number of papules, pustules and infiltrates in the zinc-treated groups when compared with groups receiving placebo or vitamin A alone. At present, until further details are published, we are unable to explain the discrepancy between our results and those obtained by Michaëlsson.

The significant improvement in the severity of acne in both the zinc group and the control group was probably due to the well-known seasonal variation of acne in temperate climates. The trial was performed in the spring to ensure that all patients would achieve some alleviation of their acne, and therefore carry on with their medication. The weather during the trial was unusually fine with many sunny hours. This might not only explain the overall improvement of acne in the patients, but might even to some extent have camouflaged a possible weak beneficial effect of the zinc. Further controlled clinical studies performed during other seasons of the year might explain this.

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K. Weismann, M.D.
Department of Dermatology
Rigshospital
Blegdamsvej 9
DK-2100 Copenhagen
Denmark