Comparison of oral treatment with zinc sulphate and placebo in acne vulgaris

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SUMMARY

In a double-blind study 91 patients with acne vulgaris were treated either with oral zinc sulphate (0.4 g daily) or with a placebo. Forty-eight patients received zinc treatment and 43 patients placebo. Significantly better results were demonstrated in favour of zinc after 12 weeks.

Despite modern resources acne vulgaris remains a therapeutic problem. Tetracyclines are effective in many cases but have some unwanted effects, such as gastrointestinal irritation and development of R-factor resistance.

Recently there has been a renewed interest in the use of zinc therapy for dermatological conditions. Moynahan (1974) and Michaelsson (1974) have shown the effectiveness of oral zinc treatment in cases of acrodermatitis enteropathica. This has led to further studies on zinc treatment and recently Michaelsson, Juhlin & Vahlquist (1977 a) have shown that oral treatment with zinc is effective also in acne.

In view of these reports a clinical trial to compare the effect of oral zinc sulphate with that of placebo was made at five dermatological clinics in Sweden. The investigation was performed between the months of November and March in order to avoid the beneficial effects of UV-light from the sun during late spring and summer. Thus, only those patients who completed their treatment before the beginning of April were included.

MATERIAL AND METHODS

Initially, the study included 112 out-patients with acne of grades 2 and 3 according to the Pillsbury classification (Pillsbury, 1961); for ethical reasons patients of grade 4 were not included in this study.

The patients were placed at random in one of two treatment groups. Daily for 12 weeks each patient was given two effervescent tablets, one in the morning and one in the evening, which contained either zinc sulphate (0.2 g corresponding to 45 mg Zn²⁺)* or placebo. The tablets were identical in appear-

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* Solvezinc®, AB Tika, Lund; a subsidiary of AB Astra, Sweden.
ance, colour and taste. Neither the doctors nor the patients knew until end of the trial which tablets 
were active and which were not.

Fifty-eight patients received zinc sulphate treatment and 54 placebo. The age of the patients in the 
zinc group ranged from 13 to 37 (mean 18.5) years and in the placebo group from 13 to 31 (mean 18.3) 
years.

The two groups were not different as regards age, sex, duration and intensity of symptoms.

Only patients who had not been treated medically (in any way that might interfere with the results) 
for at least 6 weeks prior to the investigation were included in the trial.

No simultaneous medication that could interfere with the results was allowed during this period. 
However, local treatment with salicylic acid in ethanol and/or a liniment containing sulphur and re-
sorcinol was allowed for simultaneous use during the trial period.

Each patient was examined by the same investigator before treatment and after 4, 8 and 12 weeks of 
treatment. At the start of the treatment and at each visit the examining doctor made a rough estimate of 
the number of papules and pustules. This was performed in the following way: Six groups numbered 
0, 1–5, 6–10, 11–20, 21–30 and >30 were used for the classification of the papules. At each visit the 
patient was assigned to one of these groups. The same procedure was used for estimation of the num-
ber of pustules.

This estimate provided the basis for the doctor’s evaluation. Colour slides were taken of each patient 
at the beginning of the trial. At each subsequent visit both doctors and patients gave their subjective 
opinion of the results in terms of: much improved, improved, somewhat improved, unchanged, worse 
or much worse. The colour slides were shown to the patients before they made their final judgment on 
the effect of the treatment.

In this study no investigations of serum zinc levels were made.

The statistical evaluation of the results was made by using \( \chi^2 \)-test, comparing the number of patients 
stated as much improved or improved with the rest in each treatment group.

RESULTS

Twenty-one patients did not finish the trial; the reasons are summarized in Table 1.

Of the remaining 91 patients, 48 were given zinc sulphate treatment and 43 placebo. The zinc 
group included 24 women and 24 men, the placebo group 20 women and 23 men.

The overall results of both doctors’ and patients’ subjective evaluations of the treatment are sum-
marized in Table 2. The statistical analysis of the patients’ subjective evaluations showed a significant 
difference (\( P < 0.05 \)) between the two regimens after only 4 weeks of treatment. This difference in-
creased throughout the trial (\( P < 0.02 \) after 12 weeks).

<table>
<thead>
<tr>
<th>Table 1. Reasons for discontinuing the treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reason</td>
</tr>
<tr>
<td>Deterioration</td>
</tr>
<tr>
<td>of condition</td>
</tr>
<tr>
<td>Side effects</td>
</tr>
<tr>
<td>Inability to attend</td>
</tr>
<tr>
<td>Failed to co-operate</td>
</tr>
<tr>
<td>Total</td>
</tr>
</tbody>
</table>

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Acne vulgaris treated with zinc sulphate

TABLE 2. The doctors’ and the patients’ ( ) subjective evaluations

<table>
<thead>
<tr>
<th>Treatment period (weeks)</th>
<th>Much improved</th>
<th>Improved</th>
<th>Somewhat improved</th>
<th>Unchanged</th>
<th>Worse</th>
<th>Much worse</th>
</tr>
</thead>
<tbody>
<tr>
<td>4*</td>
<td>Zinc</td>
<td>9 (11)</td>
<td>17 (14)</td>
<td>11 (13)</td>
<td>5 (7)</td>
<td>3 (1)</td>
</tr>
<tr>
<td>4*</td>
<td>Placebo</td>
<td>7 (8)</td>
<td>8 (5)</td>
<td>13 (15)</td>
<td>7 (9)</td>
<td>5 (3)</td>
</tr>
<tr>
<td>8*</td>
<td>Zinc</td>
<td>10 (11)</td>
<td>18 (18)</td>
<td>8 (10)</td>
<td>8 (7)</td>
<td>2 (-)</td>
</tr>
<tr>
<td>8*</td>
<td>Placebo</td>
<td>8 (9)</td>
<td>11 (7)</td>
<td>10 (16)</td>
<td>10 (7)</td>
<td>2 (2)</td>
</tr>
<tr>
<td>12</td>
<td>Zinc</td>
<td>20 (23)</td>
<td>18 (13)</td>
<td>2 (7)</td>
<td>6 (4)</td>
<td>2 (1)</td>
</tr>
<tr>
<td>12</td>
<td>Placebo</td>
<td>13 (14)</td>
<td>10 (8)</td>
<td>8 (12)</td>
<td>8 (7)</td>
<td>4 (2)</td>
</tr>
</tbody>
</table>

* Five patients were unable to call back after 4 weeks and 4 patients after 8 weeks.

The statistical analysis of the doctors’ subjective evaluations showed no significant differences at the visits after 4 and 8 weeks, but showed a significant difference after 12 weeks of treatment (P < 0.01). The results of the statistical analysis are shown in Fig. 1.

Some side effects—predominantly gastrointestinal—were recorded, but there were no differences regarding types and severity between the two regimens (Table 3).

DISCUSSION

Michaëlsson et al. (1977a) showed a beneficial clinical effect of oral zinc sulphate treatment in acne vulgaris by using a lesion-counting technique. This method is suitable for controlled studies of clinical effects in acne, but can hardly be applied to clinical practice. More often results of treatment have to be evaluated by the doctor and patient by subjective means. We were interested to see if it was possible to

![Figure 1](image-url)
detect the beneficial effect of zinc treatment in acne by using a subjective technique though the investigation was performed in a strictly double-blind manner, comparing the effects of zinc and placebo treatment.

Our investigation showed a significantly better effect from zinc treatment compared to placebo. The topical treatment is certainly responsible for part of the improvement in both the placebo group and the zinc group. However, the difference between the groups was clear in spite of this treatment. After 12 weeks treatment with zinc sulphate 75% of the patients were content with the therapeutic results.

The mechanism by which orally administered zinc helps acne vulgaris is still poorly understood. Michaëlsson et al. (1977a) have suggested that there might be a zinc deficiency in puberty. The zinc absorption may be influenced by dietary factors and excessive losses of zinc may also be responsible. Recent investigations on the relationship between serum zinc and retinol-binding protein in acne (Michaëlsson et al., 1977b) have given support to the theory that zinc is essential for maintaining normal blood levels of vitamin A. Both these compounds are important for normal epithelial differentiation.

The present study has shown that orally administrated zinc sulphate has a clear effect in cases with papular and pustular acne. The treatment seems to be safe, easily administered and with very few side-effects. It can also be used in combination with different kinds of topical treatment, for instance retinoic acid.

**ACKNOWLEDGMENTS**

Professor Bengt Källén helped with the statistical calculations. Zinc and placebo tablets were provided by TIKA, AB, Sweden.

**REFERENCES**


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