

Zinc sulphate in rheumatoid arthritis

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SUMMARY To assess the antirheumatic activity of zinc sulphate, 27 patients with active rheumatoid arthritis took part in a 6-month, randomised, double-blind, between-group trial of oral zinc sulphate versus placebo. Twelve patients on zinc and 9 on placebo completed the trial, but no significant antirheumatic activity of zinc sulphate was demonstrated.

Zinc is involved in many biological processes related to inflammation. Plasma zinc levels are reduced in rheumatoid arthritis,¹⁻³ and the reduction of plasma zinc is related to the degree of osteoporosis as determined by the metacarpal index.¹ Simkin² reported clinical improvement in patients with rheumatoid arthritis treated with zinc sulphate, but another study failed to confirm this.⁴ Zinc has also been reported as being beneficial in patients with psoriatic arthritis.⁵

Patients and methods

A 6-month, randomised, double-blind, between-group trial was performed. Patients with classical or definite rheumatoid arthritis of at least one year's duration were admitted to the trial if they had active disease uncontrolled by nonsteroidal anti-inflammatory drugs. Patients who had received the following drugs in the preceding 3 months were excluded: gold, D-penicillamine, chloroquine, levamisole, and immunosuppressants. Patients received either zinc sulphate 220 mg t.d.s. or identical 'dummy' placebo capsules. In addition to the trial drugs patients continued to receive the anti-inflammatory analgesic drugs which they had been taking prior to the study.

Patients were assessed initially and then at 6-week intervals for 6 months. The observations made were: (1) Pain, on the 20-point visual analogue scale (VAS). (2) Pain, on the 4-point scale (1=nil, 2=mild, 3=moderate, 4=severe). (3) Morning stiffness, on the 5-point scale (1=½ h or less, 2=½-1 h, 3=1-1½ h, 4=1½-2 h, 5=2 h or more). (4) Patient's assessment of overall condition: 5-point scale (1=very poor, 2=poor, 3=average, 4=good, 5=very good). (5) Articular index (Ritchie). (6) Grip strength: bag

inflated to 20 mmHg, the sum of 2 readings being taken for each hand. (7) Ring size of proximal interphalangeal joints.

Laboratory measurements performed included: haemoglobin, white cell count, erythrocyte sedimentation rate (ESR, Westergren), titre of rheumatoid factor, urea, creatinine, and alkaline phosphatase. The results were analysed by Student's *t* test.

Twenty-seven patients were admitted to the trial; 14 received zinc (11 female) and 13 placebo (10 female). The mean age was 51 years in the zinc group and 57 years in the placebo group, and the mean disease duration was 4.5 years and 8 years respectively. While both groups had active disease which would allow any drug effect to be clearly demonstrated, the placebo group were slightly more severely affected.

Results

Two patients on zinc were withdrawn, one because of severe indigestion and one for noncompliance. Eight other patients on zinc noticed mild nausea at times, but side effects were not a great problem. Four patients on placebo were withdrawn, 3 due to lack of effect and one due to side effects. Twenty-one patients completed 6 months (12 on zinc and 9 on placebo).

The clinical and laboratory results are shown in Table 1. Although there was a slight trend towards improvement in both groups of patients, there was no statistically significant change in any of the parameters measured in either group of patients, except for a reduction in ring size ($p < 0.001$ in zinc group; $p < 0.05$ in placebo group), but the difference between the zinc and placebo groups was not significant ($p > 0.1$). There was no significant change in the titre of rheumatoid factor. There was a significant increase in the alkaline phosphatase level in the zinc group ($p < 0.01$).

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Table 1 Mean of measurements made initially and after 6 months' treatment

Treatment	Zinc		Placebo	
	Initial	6 months	Initial	6 months
Pain (VAS)	7.83	5.00	11.56	8.56
Pain (4-pt)	2.92	2.50	3.33	3.00
Morning stiffness (5-pt)	1.92	1.58	2.56	3.22
Articular index	21.2	19.6	27.8	26.3
Grip strength (mm)	367	411	300	337
Ring size (mm)	566	553*	568	559*
Patient's assessment (5-pt)	2.92	3.42	2.67	3.11
Hb (g/dl)	11.4	11.1	10.9	11.0
ESR (mm/1st hour)	49.4	44.7	61.2	64.3
Alkaline phosphatase (IU/l) (normal less than 300)	262	366*	246	261

*Statistically significant results ($p < 0.05$).

Discussion

Our results do not show any significant therapeutic effect of oral zinc sulphate in rheumatoid arthritis. A recent study³ showed that zinc levels correlated positively with serum albumin in rheumatoid patients and were inversely related to both ESR and globulin concentration, supporting the hypothesis that a low

plasma zinc level in rheumatoid arthritis is one of the nonspecific features of inflammation.

We confirmed previous observations of a rise in serum alkaline phosphatase values in rheumatoid patients treated with zinc.^{2,4} It has also been reported that zinc enhances the alkaline phosphatase activity in rheumatoid synovial tissue in vitro,⁶ but the significance of this is uncertain.

References

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