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## **EVALUATION OF ZINC SULPHATE THERAPY IN LONG STANDING BURN CASES AND ITS EFFECT ON BURN WOUND HEALING. A CONTROLLED CLINICAL TRIAL**

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### **Summary**

A clinical trial was set to demonstrate the effect of zinc salt on the local & general condition of burned patients. One Hundred cases were selected with long standing burn with generalized weakness and features of zinc deficiency and delayed burn healing. They were divided into two groups. Group one received zinc salt. Group two received placebo. Those treated with zinc showed good improvement both in local and general condition, although 10 patients showed no improvement but these patients need a lot more than zinc to improve. From this trial, zinc is recommended as an efficient adjuvant in the treatment of all long-standing burn cases

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### **Introduction**

**Z**inc is a trace element that present in a relatively high concentration throughout the body<sup>1</sup> especially skin, bones, teeth and soft tissue, also in plasma bound to macroglobulin and albumin<sup>2</sup>.

The whole body of an adult contains 1.4-2.3 grams of zinc, with an average zinc level of 2.5 µgm/ml in the whole blood or 2.7 µgm/ml in plasma<sup>3</sup>.

Changes in the level of zinc occur in plasma and cells in various illnesses including stress conditions, severe infections and acute tissue injuries as; burn and severe trauma<sup>4</sup>. Large dose of

steroids or surgical stress produces rapid depression in serum zinc level<sup>5</sup>.

A number of enzymes are zinc dependent<sup>6</sup>. DNA & RNA polymerase have been shown to be zinc dependent enzymes<sup>7</sup>.

As there is an increase metabolic demand for zinc during collagen synthesis in the process of tissue repair, which explain the gain in wound tensile strength. The inhibitory effect of the deficiency on wound healing is the same as if these enzymes were depressed<sup>8</sup>, the utilization of amino acids in the synthesis of protein is impaired<sup>9</sup>, this account for the delay in wound healing and epithelialization of wound and burned area.

Hallbook and Lanner observed a more rapid healing of chronic leg ulcers and burn in patients with high serum zinc

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level than those with lower level<sup>8</sup>. There is a significant decrease in zinc in serum and tissue samples taken from burned patients during treatment<sup>10</sup>. Henkin and Associates showed that hypogeusia (loss of taste acuity) and dysgeusia (disorder of taste), had a good response to zinc therapy<sup>11</sup>. Follis demonstrated that zinc deficiency could produce alopecia and gross skin lesions (thickening or hyperkeratosis) with failure of complete nuclear degeneration of skin epithelial cells<sup>12</sup>. Moreover, zinc deficiency may lead to anorexia and reduction in food consumption<sup>13</sup>, and cause weakness and fatigability by decreasing bone osteoplastic activity and muscle wasting as well as inhibiting protein synthesis<sup>14</sup>, proved by the observation of low plasma protein level in cases with zinc deficiency leading to low levels of immunoglobulin<sup>15</sup>.

The aim of the study is to demonstrate the effect of zinc supplement on enhancement of skin healing in burned patients admitted to the hospital, who show features of the deficiency.

## Patients and Methods

This is a five years clinical trial conducted on 100 patients admitted to plastic and burn unit in Saddam Teaching Hospital in Basrah between 1994 - 1998. The nature of the study was explained to the patients before starting the treatment.

On admission full clinical history and examination were done as well as investigation, to find out the patients who might be deficient in zinc e.g. alopecia, anorexia, high infection rate, etc. (Table III).

Oral zinc test was on the schedule in the beginning but was dropped later because the patients were confused in their interpretation of the taste.

Due to the unavailability of atomic absorption spectrophotometry at the time this clinical trial was conducted, serum

zinc level estimation was not included.

The hundred patients were randomly assigned into two groups:

Group 1, received orally 200 mg of zinc sulphate t.d.s dissolved in 5% dextrose water in addition to other local treatment, vitamins and antibiotics. Children under the age of 12 years received orally 50 mg of zinc sulphate three times daily (British National Formulary, BNF 1992). This treatment was continued for 2-4 weeks depending on the response of the patient which appeared in the form of subjective & objective improvement.

Group 2; the control group, received 5% dextrose water mixed with bitter taste to mimic the taste of zinc sulphate, and the patients were taking local treatment, vitamins and antibiotics for a period of three weeks. After 3 weeks, patients in this group received oral zinc sulphate but they were not included in the first group.

All patients were assessed weekly by weighing and for signs of improvement, they were inspected frequently for regrowth of the hair, mobility and signs of wound healing. Data were analyzed statistically using student t-test and P value, to compare the significant differences between the two groups.

## Results

Age range of the patients (Table I), it was 1 – 40 years with a mean of 6.25 in both groups. The age of 15 – 20 years have the higher number being 22 in first group and 25 in the second group. There is no significant difference between the two groups in regard to age of the patients.

Occupation of the patients (Table II), most of the patients were housewives (46 patients in both groups) next were students (20 patients).

Sex distribution (Fig. 1) show high female/male ratio = 3:1, females number =73 and males number = 27. Most of the

burn cases were housewives that is why the females number is higher.

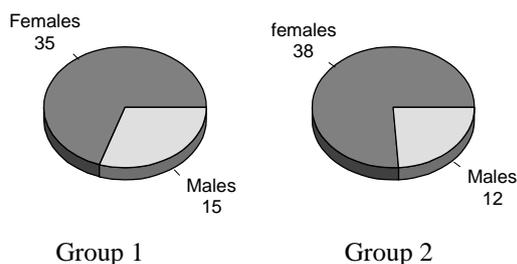


Figure 1. Sex distribution of the cases.

Age	Zinc group	Control group
1 - 5	2	3
5 - 10	0	1
10 - 15	4	5
15 - 20	22	25
20 - 25	8	6
26 - 30	5	3
30 - 35	5	5
36 - 40	4	2
Total	50	50
Mean+/- SD	6.25+/-6.77	6.25+/-7.75

Table I. Age distribution of the patients.

Occupation	Zinc group	Control group
Housewives	24	22
Children	2	4
Students	9	11
Soldiers	6	5
Laborers	5	4
Civil Servants	2	4
Total	50	50

Table II. Occupation of the patients.

Duration between getting burn and starting of zinc therapy (Fig. 2), most of the cases were admitted after a period of 4 – 8 months following their illness, and that is the period when they gave up treatment and start to get the deformity.

The clinical feature (Table III) were the same in both groups with no statistical difference. It was found that the most common symptoms were anorexia (91

cases) followed by alopecia (89 cases) and generalized weakness (86 cases).

Clinical features	Zinc group	Control group
Alopecia	46	43
Anorexia	44	47
Weakness	41	45
Infection & delayed healing	39	34
Taste impairment	31	27
Hyperkeratrosis	17	10

Table III. The clinical features on presentation.

Duration of treatment with zinc (Table IV), those with short illness were treated for 2 weeks, patients with long history were treated for 4 weeks, while five patients needed multiple doses after an improvement following a 4 weeks treatment. It seems that best results were obtained after 3-4 weeks treatment with zinc.

Duration of Treatment	No. of Patients
2 weeks	6
3 weeks	20
4 weeks	19
Multiple doses	5
Total	50

Table IV. Duration of treatment with zinc sulphate.

The outcome of treatment (Table V), following the course of zinc sulphate treatment, patients showed a subjective improvement including; improvement in appetite in 74% of the first group as compared with 14% of the control group which is highly significant ( $P < 0.01$ ), also there were an improvement in the taste in 24% of them. The objective improvement show significant increase in wound healing and decreased infection in 72% of the cases as compared with 30% of the control group cases. Increased movement was noticed in 64% of the patients in comparison with 20% of the control group. The regrowth of hair was highly significant

in the zinc treatment group (in 58% of the cases) while non of the patients in the control group had regrowth of the hair.

Out come of Treatment	Zinc group	Control group
1. Subjective		
Improve appetite	37	7
Improve taste	12	5
2. Objective		
Decrease infection & Increase healing	36	15
Increase movement	32	10
Re growth of hair	29	0
Gaining weight	13	6
3. No improvement	10	30

**Table V. The final outcome of treatment**

Haemoglobin, serum protein and body weight had a remarkable increase in the zinc group. Some patients show no improvement at all; those constitute only 20% of the patients treated with zinc. While in the control group no improvement form 60% of patients.

## Discussion

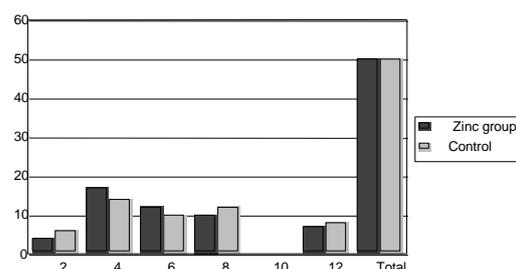
The trace element zinc is normally found in high concentration in seafood and meat<sup>16</sup>. These are the expensive source of protein, which cannot be easily offered by low socioeconomic class. Grains are relatively rich in total zinc but a considerable proportion of it is lost in the milling process.

The soil of Iraq and neighboring countries, Syria, Turkey, Iran and Egypt is poor in zinc. The total contents of zinc in wheat are lower than that from most other countries<sup>17</sup>. When patients who are on a low zinc intake encountered a situation that required more zinc supplement, these patients will definitely pass into state of zinc deficiency.

The majority of patients admitted with burn are between 15 – 35 years of age (Table I), this is the active age group of life who are involved in active work e.g. housewives, industrial workers as chem-

ical and electrical industries, and service men.

Patients included in this series were either neglected at home or transferred from other hospitals; they were immobile and had lost weight. Seventy-five out of the 100 cases were admitted after 4 – 8 months of illness (Fig. 2). Patients showed all features of emaciation and weakness with stiff joints and inability to move some of them have multiple deficiencies. Those patients admitted within six months of the accident showed improvement with a short course of treatment.



**Fig. 2: The duration between time of burn and starting of treatment**

The most common features of zinc deficiency in this series (Table III) were fall of hair, anorexia and fatigability. Fall of hair was noticed by the patients themselves, they were worried of being bald. Anorexia may not be absolute; patients may show dislike for certain food that can be attributed also to taste impairment and anaemia. Weakness and fatigability are big problems, movement can stimulate anabolism but as long as the patient remain immobile in bed catabolism continues. Immobility leads to disuse atrophy of the muscles, which becomes worse by hypoproteinemia. Zinc supplement will improve protein synthesis but building the body demand active movement starts in bed first. Taste impairment resulted from atrophy of taste buds<sup>12</sup> is reversed by zinc administration as founded by Henkin et al<sup>19</sup>, sixty out of 100 patients showed taste impairment in both groups. Gross

skin thickening were observed in different forms in both groups which may appear in the form of thickening or hyperkeratinization<sup>13</sup>, it may also present as scaling or cracking of the skin, 27 patients showed some kind of skin lesions, it was not a prominent feature and usually the patient considered it as minor and attributed it to dirtiness. Any value of 10gm/dl haemoglobin and 6gm/dl serum protein were considered as normal. Sixty seven patients showed normal haemoglobin and 58 have normal serum protein in spite of generalized features of multiple deficiencies which was a paradox explained by repeated blood transfusions, still 33 patients showed low haemoglobin and 42 patients showed low serum protein.

Forty five out of fifty patients (Table IV) received zinc for 3 – 4 weeks, which is the average period for treatment, during this period patients expected to show sign of improvement. Only 6 patients showed improvement within 2 weeks of treatment. Duration of treatment depends on duration of illness and degree of emaciation. Five patients required more than 4 weeks of treatment to show some improvement, neglected cases with multiple deficiencies required food, vitamins and zinc to improve.

To detect the changes or improvement expected from the patients, the results were divided into subjective, objective and no improvement. Improvement of appetite was the main change detected by the patients as both zinc supplement and decreased stress would improve the appetite, which was also affected by the changes in sense of taste, and smell<sup>18</sup>. Thirty-seven patients on zinc treatment showed better appetite, which was significant if compared with seven patients on placebo. Thirty six patients on zinc treatment showed signs of decreased wound infection and sepsis with sign of healthy granulation tissue and increased epithelialization of the wound, this could be explained by

improvement in the action of RNA and better synthesis of proteins and collagen tissue reflected as sound wound healing<sup>19</sup>. As a result of increased protein synthesis, muscle bulk would increase, if combined with reassurance and gentle physiotherapy, patients would start moving. Thirty-two patients on zinc treatment have good movement although their wounds were still not completely closed. Ten of the patients on placebo started movement explained by good food, drugs and reassurance.

Hair fall in the form of alopecia or thinning of the hair is the result of decreased protein synthesis and general malnutrition leads to weak hair follicles and fragile hair shaft. In a study done by Ead RD<sup>20</sup>, alopecia areata were treated by zinc, he didn't find any benefit of this element. In this study 29 patients on zinc and non of the patients on placebo showed improvement on short course of zinc treatment, yet improvement was not immediate as old hair have to fall and new hair grow, this new hair show no tendency to fall or break.

As a sequel of increased protein synthesis, improved diet intake, active movement and anabolism with improvement of patient morals, weight will be gained in 13 of the zinc treated patients. Ten of the patients showed no improvement due to multiple deficiencies, some of them refused food intake and active movement due to psychological factors as they were already suicide cases and required psychotherapy, they may get benefit from another dose of zinc after few weeks.

## Conclusion

From this clinical trial, it was found that zinc salts are highly beneficial for all patients who are bed confined for long duration due to burn and cutaneous ulcers. They may have a little improvement at the beginning, but the situation changes after few days.

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