

VENOUS LEG ULCERATION: SKIN AND SERUM ZINC CONCENTRATIONS

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Abstract. Zinc was measured in serum and in thigh skin in patients with venous leg ulceration and also in controls. Skin zinc concentrations were expressed in terms of area and dry weight. The mean serum zinc concentration was significantly lowered in the ulcer group. The thigh skin zinc concentration was elevated in patients with chronic venous leg ulceration. The difference was more marked if the zinc concentration was calculated per surface area of skin, but did not reach statistical significance.

Key words: Zinc wound healing; Leg ulceration; Trace metals; Zinc deficiency

The association between chronic leg ulceration from different causes, and lowered plasma or serum zinc concentrations has been demonstrated in several studies (1, 3, 4). Increased rates of healing in response to oral zinc sulphate in patients with low serum zinc have also been shown (7, 2). However, little is known of the relationship between the zinc content of the skin and the serum zinc concentration in leg ulceration. We now report determinations of both skin and serum zinc in patients with chronic venous leg ulceration and control subjects.

SUBJECTS AND METHODS

Thirty-two leg ulcer patients aged 26-86 (mean 71) were studied. No patients had been given systemic zinc treatment and there was no recent history of application of topical medications containing zinc, nor any history of associated systemic illness such as diabetes. The average diameter of the ulcerated area was about 6 cm. Most patients had suffered from venous leg ulceration for more than 10 years.

The control group for serum zinc estimation comprised 33 patients attending hospital as outpatients with minor genito-urinary and skin diseases. Fully informed consent for the investigation was obtained from all the patients.

The control group for skin zinc estimation comprised necropsy material from 16 patients who had died following an acute illness—myocardial infarction, cerebral haemorrhage, etc. There was no known associated chronic disease in any of these patients. Skin was obtained from these subjects within 48 hours of death.

Serum and skin zinc determinations were done by the method of Oon et al. (4). Punch biopsy specimens of skin were obtained by means of an electric high-speed drill. Digests were prepared in nitric acid and perchloric acid and zinc analyses carried out using an SP 1950 Atomic Absorption Spectrometer. Results obtained from a single sample of thigh skin ranged from 1.60 to 2.37 $\mu\text{g}/5\text{ mm}$ biopsy ($n=4$). Zinc analyses were carried out on serum from venous blood samples using the Atomic Absorption Spectrometer. All zinc analyses of both serum and skin were done blind.

RESULTS

The serum and skin zinc concentrations in the leg ulcer group and in the control group are summarised in Table I. The mean serum zinc level was significantly lowered in the leg ulcer group. By contrast, the thigh skin zinc concentration was elevated in patients with chronic venous leg ulceration. The difference was most marked when the zinc was calculated per surface area of skin, but did not reach statistical significance.

DISCUSSION

The results of this investigation provide further confirmation of the association between chronic venous leg ulceration and lowered plasma or serum zinc concentrations and raise important questions concerning the relationship between the serum and skin zinc concentrations in this condition.

The finding of lowered serum zinc concentrations in patients with venous leg ulceration is in agreement with the earlier reports of Greaves & Boyde (1), Halstead & Smith (3), and Hallbrook & Lanner (2). However, the relationship of the serum zinc to the whole body zinc content was unknown and it seemed possible that the zinc content of leg skin might be of greater clinical significance than the serum concentration.

Table 1. Mean serum and thigh skin zinc concentrations in a group of patients with venous leg ulceration and in 2 control groups

Clinical group	No. of subjects	Serum zinc (ug/100 ml)	Skin zinc	
			µg/g	ng/mm ²
Venous leg ulceration	30	85.2 ± 12.4	55.3 ± 31.7 ^a	19.3 ± 5.1 ^a
Controls	33	102.4 ± 17.0	—	—
Controls ^b	16	—	46.6 ± 18.0	17.4 ± 4.7

All values given ± S.D.

^a n = 27. ^b Necropsy material.

Our values for normal thigh skin zinc content were lower than those of our previous study (4). However, all the subjects of our earlier study were Asians living in Singapore. Schroeder et al. (6) in a geographical study of tissue zinc concentrations found consistently higher values for zinc concentration in tissues of natives of the Orient compared with US and other geographical areas. Values for kidney, lung and spleen were almost twice the corresponding US figures, which agrees well with our results.

Although slightly below the level of statistical significance, the finding of raised thigh skin zinc concentrations in patients with chronic venous leg ulceration was unexpected. This was not due to the reduced thickness of skin in venous stasis, as the difference was evident whether the skin zinc concentration was calculated as wt/wt or wt/area. It is of interest that a similar elevation of thigh skin zinc concentration in the presence of a lowered serum zinc has been reported in pulmonary tuberculosis (4). Taken together, these studies raise the possibility that a redistribution of zinc between blood and

skin may be a general feature of chronic infection and bacterial toxemia (5). However, the deranged metabolism which occurs as a non-specific consequence of diverse skin diseases (8) may also play a part. Clearly detailed metabolic studies of zinc in healthy subjects and patients with venous leg ulceration are required.

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REFERENCES

1. Greaves, M. W. & Boyde, T. R. C.: Plasma zinc concentration in patients with psoriasis, other dermatoses and venous leg ulceration. *Lancet* *II*: 1010, 1967.
2. Hallbook, T. & Lanner, E.: Serum zinc and healing of venous leg ulcers. *Lancet* *II*: 780, 1972.
3. Halstead, J. A. & Smith, J. C.: Plasma zinc in health and disease. *Lancet* *I*: 322, 1970.
4. Oon, B. B., Khong, K. Y., Greaves, M. W. & Plummer, V. M.: Trophic skin ulceration of leprosy: skin and serum concentrations. *Br Med J* *2*: 531, 1974.
5. Pekarek, R. S. & Beisel, W. R.: Effect of endotoxin on serum zinc concentrations in the rat. *Appl Microbiol* *18*: 482, 1969.
6. Schroeder, H. A., Nason, A. P., Tipton, I. H. & Balassa, J. S.: Essential trace metals in man: Zinc. Relation to environmental cadmium. *J Chron Dis* *20*: 1967.
7. Serjeant, G., Galloway, R. E. & Guerri, M. C.: Oral zinc sulphate in sickle-cell ulcers. *Lancet* *II*: 891, 1970.
8. Shuster, S. & Marks, J.: Systemic Effects of Skin Disease. Heinemann, London, 1970.

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