SPECIAL ARTICLE

Role of zinc in post-injury wound healing

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The importance of trace elements such as zinc is well recognized in the context of metabolic response to injury and wound healing. There is post-injury lowering of zinc as part of the so-called 'triggered' biochemical response to trauma even if the trauma is of relatively modest severity (Stoner, 1984). In the catabolic phase of metabolic response to trauma, which starts 24–48 h post-injury, the predominant feature is protein or muscle catabolism resulting in the release of amino acids for synthesis of glucose (gluconeogenesis) and production and excretion of urea nitrogen in the urine. Albumin concentration may fall for up to a week and then takes weeks to recover. The extent of zinc loss, which is linked to proteins, mainly albumin, correlates very closely with the amount of nitrogen loss in the urine (Cuthbertson *et al.*, 1972). As wound healing is known to be impaired in zinc deficient patients and animals (Hallmans, 1979), a combination of possible existing zinc deficiency and post injury reduction of zinc would be expected to delay wound healing.

Hypo-zinaemia is known to occur in cirrhosis of liver, malabsorption syndrome, poor diet, renal disease, diabetes, chronic debilitated conditions and in burns. Acute zinc deficiency causes anorexia, disfunction of smell and taste and mental and cerebellar disturbances, chronic deficiency results in growth retardation, anaemia, testicular atrophy, skin changes of hyperkeratosis and acanthosis and acrodermatitis enteropathica, alopecia and lowering of serum alkaline phosphatase. Borderline zinc deficiency may be common even in the U.S.A. (Prosad, 1976).

The serum and tissue zinc can be increased by oral administration of zinc sulphate, acetate or bicarbonate which are non-toxic in pharmacological doses and/or by the application of zinc oxide as paste, powder or tape over the wound (Hallmans, 1979) and by zinc tape on intact skin which absorbs zinc (Hallmans & Linden, 1979) thereby facilitating wound healing, zinc exerting a beneficial effect on collagen synthesis and epithelization (Hallmans *et al.*, 1980).

In order to understand the role of zinc in the management of post-injury patients with wounds, it is necessary to establish existing zinc status of the patients, deter-

mine the extent of trauma-related loss, take into account factors that are likely to influence serum zinc i.e. diabetes, use of diuretics etc, administer the necessary zinc supplements and measure the beneficial outcome, if any. A prospective study (Maitra, 1982) suggested that zinc oxide paste bandage reduced healing time of pre-tibial flap laceration in the elderly, a group of patients who may be expected to have an underlying hypozincaemia (poor diet, chronic debility and diseases), but the role of zinc was not investigated.

In a prospective study of 94 elderly female patients with pre-tibial flap lacerations, we investigated: (1) the serum zinc status of the injured patients; (2) whether there was any correlation between serum zinc and the healing of pre-tibial flap lacerations treated by zinc oxide paste bandage and; (3) any absorption of zinc from intact skin with this treatment. The conclusions from this study were: (1) the mean serum zinc levels of the injured were normal; (2) there was no correlation between serum zinc and healing time of the lacerations; and (3) there was no significant absorption of zinc from paste bandage. However, it suggested that older women with large wounds may be suffering from hypozincaemia and might therefore benefit from zinc therapy. This hypothesis needs to be tested in a strictly controlled trial which may prove difficult to undertake.

Some of the difficulties of conducting a trial of this type in the clinical environment of a busy A&E department were illustrated in our study — firstly, the problem of identifying a matching control group with regard to age and sex which are likely to influence serum zinc level. Secondly, elderly patients are likely to be on medication i.e. steroids, diuretics or suffer from diseases such as diabetes: conditions which are known to influence serum zinc levels. Thirdly, injured patients might be less active and this factor of relative immobilization could favour zinc loss. Fourthly, the validity of the use of antibiotics in the presence of positive microbial culture, which may occur from surface contaminants, and how this would affect zinc status. Fifthly, the diagnosis of zinc deficiency may be problematic. The laboratory criteria for diagnosis of zinc deficiency are not completely established (Prosad, 1976). Small variations in zinc levels during treatment, might be due to normal fluctuations in the patients and laboratory analysis rather than actual zinc loss or gain. Response to zinc therapy is probably one of the best indicators of zinc insufficiency which favours zinc retention in the body. In order to confirm zinc retention it is necessary to perform metabolic balance studies using [^{65}Zn], however, these are difficult to perform. Sixthly, it would also be necessary to measure 24h of urinary zinc excretion which is decreased in chronic deficiency but increased in post-injury catabolic phase. Finally, measurement of zinc-dependent enzymes such as serum alkaline phosphatase would be necessary to provide additional evidence of zinc status, but may be impossible to achieve in the out-patient clinical context of the trial involving elderly patients.

In conclusion, research into post-injury zinc metabolism affecting wound healing is fraught with difficulty in the A&E clinical setting because of the diversity of patient population and the nature of wounds commonly encountered, as well as the factors previously discussed. However, recovery of patients following trauma depends on the understanding of the protein-energy requirements which are closely related to post-injury negative nitrogen balance and associated hypozincaemia and hyperzincuria. In this context, the strategy of trauma research would be

to concentrate on defining the extent of the zinc loss and measure the effect of supplemental therapy in selected patient groups of differing injury severity taking into consideration the likely influence of co-existing factors and recognizing the underlying scientific limitations.

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