

Effect of resupplying zinc in zinc-deficient rats

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Summary

The effects of oral intake of zinc (Zn) were investigated using rats in a Zn deficient state. A Zn-deficient diet was fed to six-week-old male Sprague-Dawley rats for 60 days. Then, a diet containing 20 mg of Zn per 100 g of food was fed for the next 28 days. Abnormalities such as dermatitis, abnormal serum copper/zinc (Cu/Zn) ratio, and deformed thyroid improved. However, no germ or sperm cells were observed in the testis. These findings suggest that the effects of resupplying Zn are minimal in tissues affected by rapid cell death due to Zn deficiency.

Introduction

Zn is an essential trace element for normal biological functions as it is involved in more than 200 enzymatic activities. In Zn deficiency, various symptoms such as growth retardation, dysgeusia, dermatitis and suppressed immunocompetency are seen^{1),2)}. However, the pathology of these symptoms associated with Zn deficiency has not been fully elucidated. Therefore, we have been investigating the effects of Zn deficiency in rats by developing a Zn deficiency model³⁾. This Zn-deficient model exhibits symptoms similar to those observed in human zinc deficiency, including stunted increase in body weight, dermatitis, epilation, skin ulcer, thymic atrophy and testicular atrophy. In the present study, we clarify the pathology of these symptoms by resupplying Zn to Zn-deficient rats and histopathologically investigating the observed changes.

Methods

A Zn-deficient diet was fed to male six-week-old rats for 60 days. The Zn-deficient diet was prepared by not adding any Zn. The results of atomic absorption analysis showed that Zn was present in this diet at 50 micro g per 100 g of food. The rats had free access to distilled water.

After the end of the Zn-deficient diet period, the rats were fed a regular diet (20 mg of Zn per 100 g of food). A blood sample was collected under etherization from these rats at 29 days after the start of the regular diet to measure the levels of serum Zn and Cu. In addition, the skin, thymus and testes were removed, fixed in 10% formalin, embedded in paraffin, and sectioned thinly according to the conventional methods for histopathological analyses. For comparison, the same tests were conducted on rats that were not fed the Zn-deficient diet.

Results

Compared to the rats that received only the regular diet, rats that received the Zn-deficient diet for 60 days were noticeably thinner, exhibited dermatitis in the eyelids, around the mouth and at the tip of the four extremities, and mild epilation (Fig. 1). In addition, two of the seven rats that were fed the Zn-deficient diet died on days 55 and 57. On the other hand, none of the seven rats that were fed the regular diet died or exhibited abnormal findings.

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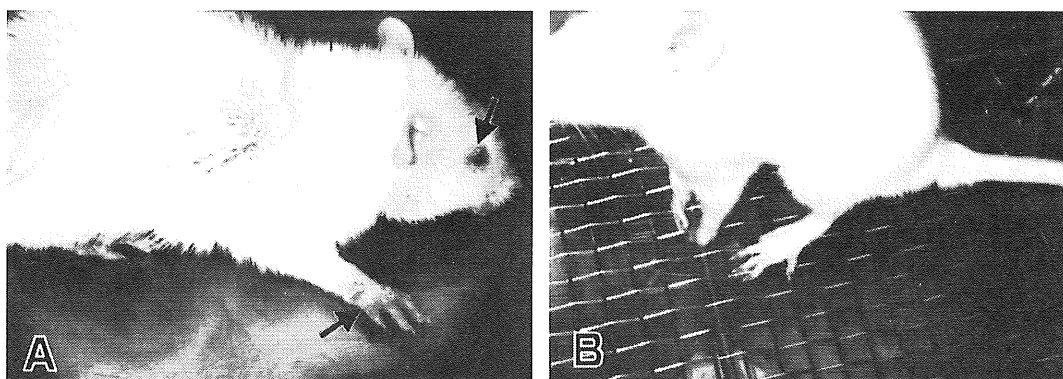


Fig. 1 Zinc deficiency models. A; Before a dietary therapy. B; After a dietary therapy.

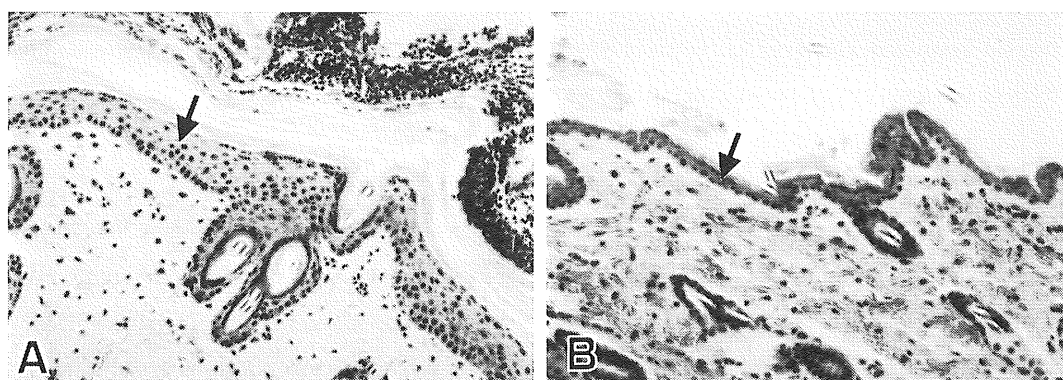


Fig. 2 Photomicrographs of skin. A; Before a dietary therapy. Hyperkeratosis with parakeratosis are observed in the stratum corneum epidermidis. B; After a dietary therapy.

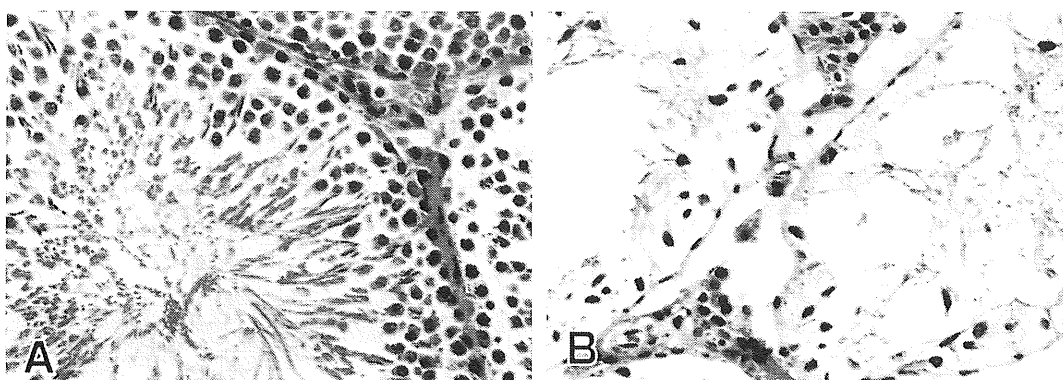


Fig. 3 Photomicrographs of testis. A; Control (normal). B; After a dietary therapy. A decrease in spermatozoa and a loss of sperm cells are observed in all cases.

Resupplying zinc brought about the following five changes in rats 1) While on the Zn-deficient diet, the body weight of the rats hardly increased, but after resupplying Zn, the body weight of the rats increased rapidly. At four weeks after making the switch from the Zn-deficient diet to the regular diet, there was an average increase in body weight of 36.8 g (range: 20 - 52g). During the same period, the average increase in body weight for the rats that received the regular diet the entire time was 13.7 g (range: 2 - 22g). 2) The levels of serum Zn and Cu normalized (Table 1). The average serum Zn and Cu levels for the rats that were fed the Zn-deficient diet were 101.8 ± 20.0 and 108.0 ± 16.1 micro g/dl, respectively; and those for the rats that were fed the regular diet were 109.1 ± 17.4 and 111.2 ± 32.4 micro g/dl, respectively. 3) In stratified squamous epithelial cells, increased keratinization and hypertro-

phied sebaceous glands disappeared (Fig. 2). 4) Thymic atrophy dissipated. 5) In the testis, no spermatocyte or sperm cells were seen, and severe atrophy was confirmed (Fig. 3), exhibiting the same findings as in the Zn-deficient rats.

Discussion

In the present study, stunted increase in body weight, dermatitis, epilation, testicular atrophy and dermatitis were observed before resupplying Zn, and these findings are often associated with Zn deficiency. Of these symptoms, stunted increase in body weight, serum Zn and Cu imbalance, dermal lesion and thymic atrophy were shown to easily recover without administering an excessive amount of Zn even when Zn deficiency was advanced.

While on the Zn-deficient diet, two of the seven rats died of pneumonia. Also, the remaining five rats were not in a good physical shape and had nasal discharge. Zn deficiency induces rapid thymic atrophy³⁾, and this thymic atrophy is thought to be related to suppressed immunocompetency. In the present study, the physical condition of the rats was favorable after resupplying Zn, and thymic atrophy was no longer seen, suggesting that immunological function was improved by resupplying Zn.

On the other hand, even after resupplying Zn, the testis did not return to normal. Zn deficiency induces rapid apoptosis of germ cells, eliminating these cells. As a result, Zn deficiency is associated with marked testicular atrophy^{3),4)}. The results of the present study suggest that the effects of resupplying Zn are mostly nonexistent in tissues, such as the testis, that exhibit less resistance to Zn deficiency and susceptibility to cell death.

Acknowledgements

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