Variations in Cutaneous Zinc Concentrations after Oral Administration of Zinc Gluconate

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The assessment of zinc levels after oral administration of 100 mg of zinc gluconate was performed over a 72-hour period in 3 sectors: plasma, blister fluid and epidermis. The results show that zinc taken orally reaches the epidermis after 72 h and indicate the existence of an intermediary compartment between plasma and epidermis, represented by blister fluid, in which zinc concentration is 243.9±32.2 µg/l, that is, the ratio blister fluid/plasma = 0.33. *Key words: Zinc; Epidermis; Blister fluid; Kinetic study.* (Received January 17, 1984.)

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Zinc is a coactivator of a large number of enzyme systems in the organism (alkaline phosphatases, carbonic anhydrase, etc.). Today, links between zinc metabolism disorders and skin lesions are mentioned with increasing frequency, raising the problem of zinc's role in therapy, not only for local application but also for general administration. The present study was undertaken in an attempt to determine the variations in zinc skin concentrations after oral administration of zinc gluconate (Laboratoire LABCATAL) in control subjects.

MATERIALS AND METHODS

Control subjects

The study was carried out on 32 subjects in apparent good health who presented no extensive dermatosis. There were 27 men and 23 women, with a mean age of 35 years (range 20 to 60 years). No subject had received local or general zinc-based treatment within the recent past, and no woman was on oral contraceptive agents.

Methods

The skin was disinfected with zinc-free alcohol, and no local anesthetic was used. To avoid zinc contamination, instruments were sterilized in glass tubes, and surgical gloves were not used.

A suction cup was placed on the skin of a control subject, using a modified Kiistala apparatus. A drop in pressure of 300 mmHg during 2 h resulted in formation of 4 blisters. These blisters were punctured, and their content centrifuged. The blister dome was cut through with a scalpel to allow assaying of the zinc in 2 sectors: epidermis (the blister dome) and blister fluid. Samples were always taken from the inner side of the arm. Plasma zinc was also determined for each subject fasting.

The control population was divided into 3 groups, each identical as to mean age and proportion of men and women: Group I, 8 subjects; Group II, 12 subjects; and Group III, 12 subjects. At time T_0 (the same for all subjects in the 3 groups), zinc was assayed in 3 sectors: plasma, blister fluid and epidermis. Then all subjects were given 100 mg of zinc gluconate orally before a second zinc assay was performed for the 3 sectors at intervals of 24 h (Group I), 48 h (Group II) and 72 h (Group III). 100 mg Zinc gluconate = 15 mg zinc element.

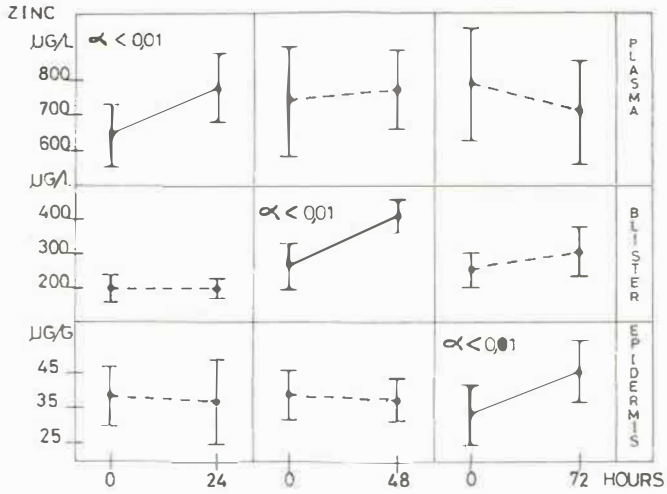

Fig. 1. Variations in zinc concentration in plasma, blister fluid and epidermis after oral administration of 100 mg of zinc gluconate at 24, 48 and 72 hours.

Zinc assay

Zinc was assayed by flame atomic absorption spectrometry, with correction of nonspecific absorption by Zeeman effect (Hitachi spectrometer, Model 180-80), in dissolution fluids prepared in the following conditions:

Blood and plasma. 0.25 ml of blood or 1 ml of plasma was introduced into a Pyrex tube in 1 ml of pure acid (Carlo Erba). The mixture was heated at 150°C until the fluid was clear. After cooling, deionized water was added to bring the fluid level to 5 ml.

Blister fluid. 0.2 ml of fluid was diluted in 1.8 ml of deionized water.

Dermis and epidermis. After drying at 105°C for 12 h, the sample was weighed, then introduced into a Pyrex tube in 0.5 ml of pure nitric acid (Carlo Erba). The tube was heated at 150°C until complete dissolution of the tissue fragment. Deionized water was then added to bring the fluid level to 3 ml.

Results are expressed in μg/l for plasma and blister fluid and in μg/g dry wt for epidermis. Statistical analysis was performed by determining variations and applying the paired Student's *t*-test.

RESULTS

In statistical terms, the mean values for the 32 patients at time T_0 in the 3 sectors were plasma zinc, 728.1±77.8 μg/l; epidermal zinc, 37.3±3.1 μg/g; and blister fluid zinc, 243.9±35.2 μg/l dry wt. Blister fluid zinc/plasma zinc = 0.33.

Results of the kinetic study (Fig. 1)

In Group I, 24 h after oral administration of zinc gluconate, an isolated rise in plasma zinc was noted (T_0=643.1±82.01 μg/l; T_{24}=793.3±106.4 μg/l; t=5.44, p<0.01). On the other hand, no significant rise was noted for blister fluid zinc (T_0=203.3±49.5 μg/l; T_{24}=206.6±25.1 μg/l; t=0.34, not significant) nor for epidermal zinc (*T*ufi0=39.3±9.2 μg/g dry wt; T_{24}=38.4 ±12.9 μg/g dry wt; t=0.01, not significant).

In Group II, 48 h after oral administration of zinc gluconate, there was no longer a significant difference in plasma zinc level (T_0=745.2±150 μg/l; T_{48}=769.3±10 μg/l; t=0.12, not significant). On the other hand, there was a significant increase in blister fluid zinc (T_0=262.8±65.9 μg/l; T_{48}=418.6±52 μg/l; t=3.94, p<0.01) and no rise in epidermal zinc (T_0=39.1±7.3 μg/g dry wt; T_{48}=38.3±6.2 μg/g dry wt; t=1.98, not significant.

Finally, in Group III an isolated rise was noted in epidermal zinc concentration at 72 h (T_0=33.7±8.04 μg/g dry wt; T_{72}=45.5±12.1 μg/g dry wt; t=4.02, p<0.01), whereas there

Table I. *Cutaneous zinc values according to region*

Authors	Region	Epidermis (μg/g)	Dermis (μg/g)	Epidermis + dermis (μg/g)	Method
Michaelson (1)	Shoulder	56±4	24±2		AAS
Molokhia (2)	Interscapular region	56±8.8	Upper dermis 12.5±3.1		NA
Molokhia (3)	Foreskin	132.3±53.6	43.2±13.6		NA
Michaelson (1)	Mammary region	45±6			AAS
Molokhia (4)	Abdomen	70.5±26.3	12.6±4.7		NA
Molokhia (3)	Abdomen	67.3±18.9	10±3.4		NA
Michaelson (1)	Buttocks	62±15	25±1		AAS
Dachowski (5)	Thigh			46.6±18	AAS
Beng Bee Oon (6)	Thigh			80	AAS
Molokhia (3)	Sole of foot	49±14.3	24.9±9.5		NA
Parkinson (7)	Average (all sites)			1.7	AAS

AAS = atomic absorption spectrometry, NA = neutron activation.

was no increase in plasma zinc (T_0=796±179 μg/l; T_{72}=714±151 μg/l; t=1.43, not significant) nor in blister fluid zinc (T_0=266±47 μg/l; T_{72}=313±77 μg/l; t=1.8, not significant).

DISCUSSION

The zinc levels for epidermal samples taken on the inner side of the arm at time T_0, thus prior to oral administration of zinc gluconate, were relatively low (37.3±3.1 μg/g) in comparison with those of other regions explored. Table I indicates the different values reported in the literature according to region studied. On the whole, these results provide clear confirmation of the regional variations in cutaneous zinc levels already emphasized by Molokhia and Portnoy (3).

The study of suction blister fluid has already led to numerous applications (8–10). In qualitative terms, this fluid is identical in content to plasma as has been demonstrated, especially by an electrophoretic test. However, the concentration of each of the elements is lower than in plasma (11). Notably, with regard to proteins, the ratio blister protein/plasma protein is directly related to the molecular weight of each protein (12). On the whole, suction blister content is close to that of interstitial fluid (13).

Most of the zinc was bound to proteins: 28% to α_2 macroglobulin and 60% to albumin (14). Thus, it may be considered that the zinc level value for blister fluid (243.9±25.2) and the ratio blister zinc/plasma zinc = 0.33 are in correlation with the coefficient of filtration of these vector proteins (albumin = 0.29; α_2 macroglobulin = 0.14) (12).

Moreover, in kinetic terms there was a 24-hour delay between the rise in plasma zinc and that of blister fluid, which indicates that blister fluid is not a simple plasma filtrate.

This observation raises the hypothesis of an intermediary compartment apparently corresponding to the interstitial sector. Thus, our kinetic study is in agreement with the work of Herfst on the interstitial origin of blister fluid (13).

Finally, with respect to Group III, the kinetic study demonstrates that orally administered zinc gluconate does reach the epidermis, but with a 72-hour delay, resulting in a rise in epidermal zinc. This factor points clearly to the problem of the exact role of zinc at the level of the epidermis and its mechanism in therapeutic action. Prospective studies in this area are already under way.

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