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Effect of Fluoride on Copper, Manganese and Zinc in Bone and Kidney

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Recently, there has been resurgence of interest in the biological effects of inorganic fluoride because of widespread prevalence of endemic and industrial fluorosis on one hand and fluoridation of community water supplies on the other. The toxic effects of excessive fluoride have been extensively studied and reviewed (HODGE & SMITH 1965 & 1977; WALDBOTT 1978). However, in the studies on fluorosis, little attention has been given to the effects of fluoride on physiologically essential metallic nutrients. Fluoride is known to interact with and alter the metabolism of calcium (RICH & ENSINCK 1961; REDDY & NARASINGA RAO 1971), magnesium (OPHAUG & SINGER 1976) and iron (WEGNER et al. 1976). So far, there is no report discussing the effects of excessive fluoride ingestion on some essential metallic micronutrients. The object of the present paper is to investigate changes in the levels of copper, manganese, and zinc in the kidney and bone (femur) of rat following fluoride toxicity.

MATERIALS AND METHODS

Twentyfour female albino rats, each weighing 125-170 g were segregated into three groups of 8 each and were subjected for 10 months to varied fluoride concentrations viz. 0 ppm (control), 10 ppm (group 1) and 25 ppm (group 2) in drinking water. Each animal was fed a balanced diet obtained from M/s. Hindustan Lever, Bombay, India. Thereafter, the animals were sacrificed and their kidneys and bone (femur) removed using stainless steel dissecting instruments. Tissues so procured were dried at 80°C in an oven for analysis with atomic absorption spectrophotometer according to BARKER et al. (1976).

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The processing briefly involved digestion of a known amount of dried tissue by nitric acid and perchloric acid followed by appropriate dilution with deionized water. The clear yellow solution so obtained was used for analysis with Perkin-Elmer Atomic Absorption Spectrophotometer Model 304.

All glassware and sampling bottles were cleaned in hot nitric acid to remove all possible contamination. In addition, a blank was run treated in exactly the same way as the tissue sample and appropriate corrections made.

RESULTS AND DISCUSSION

The present study demonstrates that fluoride alters the levels of copper, manganese and zinc in bone (femur) and of manganese and zinc in the kidney. It is known that bone and the kidneys by accumulating and excreting fluoride respectively determine to a large extent, the course of fluoride toxicity.

There is observed an increase (38%) in the levels of manganese in bone and decrease in manganese level in the kidney in group 2 (25 ppm fluoride). The increased content of manganese in bone is suggestive of increased affinity of manganese for fluoride, the latter is established to be maximally concentrated in bone (HODGE & SMITH 1965). Similar pattern with regards to magnesium has been reported in fluorotic bone and attributed to increased affinity of magnesium for fluoride (ZIPKIN et al. 1960). We believe that the sequestration of manganese by fluorotic bone may result in manganese deprivation in other organs as evidenced by observed decreased Mn level in the kidney in group 2 (25 ppm).

On the other hand, there is observed an increased of 34% in the zinc level of kidney and decrease (13%) in zinc level of bone in group 2. With the data available, these changes are difficult to account for.

The severe copper depletion observed in bone following fluoridation seems to be of great physiological significance and can be related to varied pathological changes reported following fluorosis. Copper depletion in bone is known to impair erythropoiesis hence causing anemia (LEE et al. 1976). On the other hand, following fluorosis, induction of anemia has been reported which has repeatedly been attributed to impaired

Table 1. Effect of fluoride on tissue levels of copper, manganese and zinc[a]

Element	Organ	Concentration of fluoride administered		
		0 ppm	10 ppm	25 ppm
Cu	Bone	8.8 ± 1.3	9.2 ± 1.8	5.2[c] ± 1.1
Cu	Kidney	20 ± 2	22 ± 3	22 ± 3
Mn	Bone	11 ± 1	12 ± 2	15[c] ± 3
Mn	Kidney	19 ± 3	21 ± 3	14[c] ± 2
Zn	Bone	360 ± 30	370 ± 50	310[b] ± 31
Zn	Kidney	170 ± 18	180 ± 23	230[c] ± 21

[a] Values are Mean ± S.D. (µg/g dry weight tissue).
[b] Significantly different from control ($p < 0.01$).
[c] Significantly different from control ($p < 0.005$).

hemoglobin synthesis (HODGE & SMITH 1965, HILLMAN et al. 1979). Also, if sufficient copper is not available to bone, the cross-linking of bone collagen is impaired due to reduced activity of lysyl oxidase - a cuproenzyme which plays a key role in crosslinking of collagen (PRASAD 1978). Incidently alterations in collagen metabolism and cross-linking have been reported in fluoride toxicity (PECK et al. 1965; Editorial in Fluoride, 1979).

The observed alterations in manganese and copper are very pronounced in bone, obviously due to more toxic action of fluoride on bone which is established to be the most severely affected organ in fluoride toxicity.

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