Lead Increases Urinary Zinc Excretion in Rats

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Abstract

The major purpose of this study was to determine whether acute or chronic Pb exposure would increase urinary excretion of zinc in the rat. Four groups of unanesthetized rats were given 0, 0.03, 0.3, or 3 mg Pb (as acetate) kg intravenously, and urinary excretion of zinc, sodium, and potassium was monitored for 6 h. Only at the highest dose was urinary Zn excretion significantly elevated; there were no significant changes in sodium and potassium excretion at any dose. Two other groups of rats were studied for 9 weeks in metabolism cages before and during administration of either 500 ppm Pb (as acetate) or equimolar Na acetate in the drinking water. Two days after Pb treatment and continuing through day 35, Zn excretion was elevated in the Pb-exposed animals; beyond this day, zinc excretion became similar in the two groups. The difference in Zn excretion was not the result of lower water intake by the Pb-treated animals. At sacrifice (70 days after starting Pb exposure), Pb-exposed animals had lower Zn content of the plasma and testis, but there was no difference in kidney Zn. Plasma renin activity was significantly higher in Pb-exposed animals. We conclude that chronic Pb exposure in rats can result in some degree of decreased tissue zinc, which is, at least in part, secondary to increased urinary losses of zinc.

Index Entries: Zinc excretion, and lead; lead, and urinary Zn excretion; zinc deficiency; lead, effect on zinc balance; zinc, in testis; renin, effect of lead on; lead, effect on renin.

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Introduction

We previously demonstrated that the acute administration of lead to anesthetized dogs produced a rapid marked increase in the urinary excretion of zinc (1). The present studies test the hypothesis that chronic administration of lead, in doses that do not produce renal damage, would elevate urinary zinc excretion, thereby possibly contributing to the development of zinc deficiency. To our knowledge there have been only three published studies that deal with the chronic effects of lead on zinc metabolism: In a study of mice, Seth et al. (2) found no effect of lead administration on the concentrations of zinc in kidney and liver; El-Gazzar et al. (3), in a study with rats, found that the addition of 100 ppm Pb to drinking water caused a decrease in plasma, liver, and bone zinc concentrations; Mahaffey et al. (4), also studying rats, found that 200 ppm Pb decreased kidney, brain, and femur zinc. In none of these studies was urinary excretion of zinc measured.

To test the effect of Pb exposure on zinc excretion, rats were given either lead acetate (500 ppm Pb) or sodium acetate chronically in their drinking water and their urines were collected daily or three times weekly, using metabolism cages. However, before undertaking this long-term experiment, we studied the acute effects of lead in this same species to satisfy ourselves that lead can enhance zinc excretion in species other than dog.

Methods

Acute Lead Exposure

Male rats weighing 275–300 g (Charles River, Wilmington, Mass.) were housed five per cage and placed on Teklad Rat and Mouse Chow (zinc content = 28 ppm). On the day of the experiment, the animals were randomly assigned to one of four experimental groups (N = 6 per group) receiving 0, 0.03, 0.3, or 3 mg. Pb (as Pb acetate) /kg. The lead solutions or sodium acetate for the control animals was freshly prepared in 5% dextrose; they contained 1.71 mg acetate/mL (equal to the acetate in the 3 mg/kg dose) and were administered intravenously in a volume of 0.1 mL/100 g body weight. Immediately prior to the injection, each animal received 2 mL demineralized water/100 g body weight via stomach tube (to insure adequate urine flows) and was then lightly anesthetized with ether. The femoral vein was exposed for injection of the treatment dose, after which the incision was closed with wound-clips. Each animal was placed in a stainless steel solder-free metabolism cage for collection of urine during the next 6 h. At the end of this period, the animals were removed from the cages and their bladders were emptied manually by firm pressure on the abdomen; this urine was added to the total collection. Each animal was then anesthetized with sodium pentobarbital (50 mg/kg, ip), and a terminal blood sample was collected by aortic puncture, using EDTA as anticoagulant.