PROCEEDINGS OF THE SOCIETY FOR EXPERIMENTAL BIOLOGY AND MEDICINE 151. 380-381 (1976)

Plasma Zinc Levels in Nephrectomized and Ureteral Ligated Rats (39215)

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Plasma zinc concentration has been reported to be decreased in a great variety of conditions (1). A consistent decrease in liver disease has been found (2, 3), but the influence of the kidney on plasma zinc concentration has not been as well defined (4).

Decreased plasma zinc levels have been reported in patients with renal artery stenosis and renal parenchymal disease in the absence of significant renal failure (5), and also in uremic patients (4, 6). Condon and Freeman observed low plasma zinc levels in 21 of 31 patients in renal failure. They found a consistent lowering of plasma zinc in rats made uremic by ureteral ligation (7). Our study was undertaken to examine the effects of nephrectomy (unilateral and bilateral) and ureteral ligation (unilateral and bilateral) on the plasma zinc levels of normal and zinc-supplemented rats.

Materials and methods. Two-month-old virgin female (230 ± 10 g) rats of the Long-Evans strain were purchased from a commercial source and housed in stainless steel cages. Deionized water and rat chow were fed *ad libitum*. After a 12-week acclimation period, 36 rats were randomly chosen to receive supplemental zinc. A solution of zinc acetate (488 μM) was substituted for drinking water and continued until the end of the experiment (23 days). This concentration of zinc in drinking fluid has been shown to be above the level necessary for optimum growth but below any apparent toxic level (8).

Food was removed from the cages approximately 24 hr prior to surgery. Under ether anesthesia one of the following procedures was performed: (a) sham operation; (b) unilateral nephrectomy; (c) bilateral nephrectomy; (d) unilateral ureteral ligation; (e) bilateral ureteral ligation; and (f) no operation. The sham operation consisted of laparotomy and a minimal manipulation of the kidneys.

Blood samples (5–8 ml) were obtained 24 hr after surgery by aortic puncture following sodium pentothal anesthesia. Clotting was prevented by using approximately 40 IU of heparin (zinc free)/ml of blood. Zinc levels were determined on diluted (1:3) plasma samples by atomic absorption spectroscopy.

Results. The range of plasma zinc levels in the unsupplemented rats was 69–117 μg/100 ml. In the zinc-supplemented normal rats the range was 78–173 μg/100 ml. Sham operation resulted in a significant lowering of plasma zinc in both groups.

Comparisons of plasma zinc levels *within* the unsupplemented and zinc-supplemented groups are shown in Table I. There was no statistically significant difference between the plasma zinc levels of the sham-operated and either the unilateral nephrectomized or unilateral ureteral-ligated rats.

In the rats not given additional zinc, the mean plasma zinc levels were highest in the unoperated rats and lowest in the bilateral ureteral ligated rats. The bilateral nephrectomized rats and bilateral ureteral-ligated rats showed significantly lower mean zinc levels than the sham-operated rats, which had lower mean zinc levels than the unoperated animals.

In the zinc-supplemented rats, the mean plasma zinc concentrations were also lowest in the bilateral ureteral-ligated rats. However, supplementation of the bilateral nephrectomized rats raised their mean plasma zinc level to that of the sham-operated controls.

Comparisons of plasma zinc levels *between* the unsupplemented and zinc-supplemented groups are shown in the same table. Supplementation had no significant effect on either the sham-operated, unilateral nephrectomized, or bilateral ligated rats. There was a significant increase in the mean plasma zinc concentration of the unilateral ligated and bilateral nephrectomized animals that received supplemental zinc. In normal unoperated rats, supplementation

TABLE I. PLASMA ZINC LEVELS IN NEPHRECTOMIZED AND URETERAL-LIGATED RATS.

Treatment	Not zinc-supplemented	Zinc supplemented
	Plasma zinc* (μg/100 ml)	Plasma zinc* (μg/100 ml)
Unoperated	89 ± 2.2 (26)	117 ± 7.7 (10)
Sham operated	69 ± 1.6 (10)[a,b,h]	75 ± 4.0 (5) [e,f,g,h]
Unilateral Nephrectomy	78 ± 4.2 (4) [a,i]	80 ± 11.6 (6)[c,d,e,i]
Unilateral ligated	64 ± 4.0 (5) [b]	85 ± 4.8 (5)[d,f]
Bilateral nephrectomy	60 ± 2.1 (18)	72 ± 2.3 (4)[c,g]
Bilateral ligated	45 ± 1.3 (12)[j]	46 ± 2.4 (6)[j]

* Means ± SE. In parentheses are the number of rats. Means designated by the same superscripts are not significantly different ($P > 0.05$).

[a,b] Unsupplemented group.

[c–g] Supplemented group.

[h–j] Comparison between groups.

caused a significant increase of plasma zinc from a mean of 89 to 117 μg/100 ml.

Discussion. The kidney does influence plasma zinc concentration. Our results show that bilateral nephrectomy or bilateral ureteral ligation results in a lowering of plasma zinc which is significantly greater than that following a sham operation.

The mechanism by which removal of both kidneys lowers plasma zinc is unknown. It does not involve urinary loss of zinc since urine output is reduced to zero. The facts that bilateral ureteral ligation causes an even greater lowering of zinc and that this change resists correction by zinc supplementation indicate that the mechanism involved in the lowering of plasma zinc by ureteral ligation may be different than that responsible for the decrease resulting from bilateral nephrectomy. There may be a third mechanism leading to a fall in plasma zinc since sham operations regularly lower zinc concentration. Unfortunately, no concrete details of any of these mechanisms are known, at present. It has been suggested that since plasma zinc is largely protein bound, decreases in plasma zinc may reflect changes in some carrier protein (7).

Summary. The effect of nephrectomy and ureteral ligation on the plasma zinc levels of zinc-supplemented and unsupplemented rats was studied. Bilateral nephrectomy, and to a greater extent bilateral ureteral ligation, resulted in a significant lowering of plasma zinc in the unsupplemented rats. Sham operation caused a lesser but significant lowering of plasma zinc which was not different from the effect of unilateral nephrectomy or unilateral ureteral ligation. Adding zinc to the drinking fluid of the bilateral nephrectomized rats raised their plasma zinc levels to that of sham-operated controls, but had no effect on the plasma zinc levels of the bilateral ureteral-ligated rats.

We thank Mr. Antonio B. Ogo for his technical assistance.

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Received July 7, 1975. P.S.E.B.M. 1976, Vol. 151.