Urinary Oxalate Excretion during Intravenous Infusion of Diuretics in Man

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Dear Sir,

Intrarenal oxalate handling has been studied in rats by infusion of ¹⁴C-oxalate, ³H-inulin, organic acids, and various inhibitors of organic acid secretion [1–3]. In these studies a net secretion of oxalate in the early proximal tubule was demonstrated [2], being the result of tubular secretion and reabsorption [1]. Secretion is an active carrier-mediated process [4]; reabsorption and passive diffusion are quantitatively less important than secretion [5]. Infusion of the diuretic agents furosemide and chlorothiazide lowered the fractional oxalate excretion [6]. This was probably not related to the site of diuretic action but to inhibition of tubular oxalate secretion; possibly, the diuretics – being organic acids – compete with oxalate for the secretory transport sites [6]. In another study, volume expansion was found to have no effect on oxalate excretion [3]. We are unaware of studies in man examining intrarenal oxalate handling. In earlier studies in man, we found a constant ratio of about 2 between the clearances of ¹⁴C-oxalate and creatinine [7, 8]. In this letter, we present the oxalate excretion in two studies before and after intravenous infusion of diuretics in healthy subjects. The studies were performed during maximal water diuresis and infusion of inulin for assessment of the GFR. All studies were performed on an intake of 200 mmol/day Na. One study was performed in 7 male subjects (24–29 years). After 1 h of recumbency, two 20-min baseline urine portions were collected, and an intravenous injection of 1 mg bumetanide was given, followed by intravenous infusion at a rate of 0.5 mg/h. After 45 min equilibration, three 15-min urine portions were collected.

A similar study was performed in 5 male subjects (23–28 years), who received an intravenous injection of 500 mg acetazolamide, followed by intravenous infusion at a rate of 250 mg/h. This study was repeated during volume expansion induced by ingestion of 0.5 mg 9- α -fluorocortisone acetate b.i.d. during 1 week. Urinary oxalate was measured by an enzymatic method [9]. The results (evaluated by analysis of variance and the least significant difference test) are presented in table 1. The loop diuretic bumetanide gave a 1.3- to 1.5-fold increase in oxalate excretion ($p < 0.05$). Since the inulin clearance – and thus the filtered load of oxalate – did not increase, the rise in oxalate excretion must be caused either by an increased tubular secretion or a

decreased tubular reabsorption. The results with the proximal acting carbonic anhydrase inhibitor acetazolamide were comparable to those of bumetanide. The inulin clearance (and thus the filtered load of oxalate) was lowered ($p < 0.05$), but the net oxalate excretion remained unaltered, which also points to increased tubular secretion or decreased tubular reabsorption. In contrast to the observations in animals with furosemide and chlorothiazide [6], bumetanide and acetazolamide apparently do not compete with oxalate for binding to secretory transport sites in the dose used by us. However, the doses per kilogram body weight in the animal studies were considerably higher than the doses currently used in humans. Since it is not likely that diuretics enhance tubular secretion, a decrease in tubular reabsorption is more obvious. This suggests that in the human kidney reabsorption plays a more important role than in the rat. Chronic volume expansion had no effect on oxalate excretion, although the inulin clearance in-

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Table 1. Mean oxalate excretion ($\pm$ SEM) during intravenous infusion of bumetanide and acetazolamide

Oxalate excretion, $\mu\text{mol}/\text{min}$

C-inulin, ml/min

baseline 0–20 min

baseline 20–40 min

infusion 85–100 min

infusion 100–115 min

infusion 115–130 min

baseline 0–40 min

infusion 85–130 min

Bu(n = 7) AC(n = 5) AF(n = 5)

0.23 ± 0.03 0.21 ± 0.04 $0.33 \pm 0.05^*$ 0.28 ± 0.02 $0.31 \pm 0.05^*$

0.27 ± 0.04 0.29 ± 0.03 0.29 ± 0.04 0.23 ± 0.03 0.27 ± 0.04

0.31 ± 0.05 0.30 ± 0.04 0.29 ± 0.03 0.29 ± 0.03 0.28 ± 0.03

116 ± 6 118 ± 6

128 ± 12 131 ± 13 $141 \pm 10^*$ $114 \pm 8^*$

C-inulin = Inulin clearance; Bu = bumetanide study; AC = acetazolamide control study; AF = acetazolamide study after 1 week of 9- α -fluorocortisone acetate treatment; * $p < 0.05$.

creased. In sum, the effects of diuretics on oxalate excretion were unexpected. To investigate the possibility of using diuretics (or other drugs affecting the transport of organic acids) as oxaluretic drugs, more studies – both acute and chronic – should be performed.

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