Sodium Chloride-Dependent Oxalate Absorption in the Human Gut

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We investigated the effect of sodium chloride intake on oxalate and calcium metabolism in the human body. In healthy subjects with a simultaneous intake of sodium oxalate (4 μmoles/kg body weight) and sodium chloride (1.2 mmoles/kg body weight), the change in oxalate-creatinine ratio was 2.04 ± 0.74, and 3.25 ± 1.29 (means ± SD), respectively, after 2 and 4 hours of oxalate intake (n = 8). The magnitude of the change in the ratio was significantly greater in the case with simultaneous intake of sodium chloride and sodium oxalate in comparison to the case with an intake of sodium oxalate alone ($P < 0.05$ and $P < 0.01$ after 2 and 4 hours of intake of oxalate, respectively). In subjects with an intake of sodium chloride alone, the change in calcium-creatinine ratio was 49.07 ± 29.96 and 0.363 ± 0.309 (means ± SD), respectively, after 2 and 4 hours of sodium chloride intake (n = 3). The results suggest that high sodium intake can be one of the risk factors for urolithiasis.

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INTRODUCTION

Calcium oxalate is the most common component of urinary stones. Oxalate metabolism has not been fully elucidated. Recently, oxalate transport systems in the brush border membrane of the proximal tubule cells have been studied. Oxalate is interchangeable with the hydroxyl or chloride iron.[1] Furthermore, oxalate-bicarbonate exchange activities are found in the membrane preparations of brush border and basolateral membrane vesicles. Sodium oxalate cotransport activity was recognized on the brush border membrane from the rat proximal tubule cell.[2] In the ileal brush border membrane of the rabbit, oxalate can be exchanged for OH^-, Cl^-, $SO4^{2-}$, and oxaloacetate.[3] No Na-oxalate cotransport system in rabbit ileal brush border membrane has been demonstrated.[4] Several reports contributed to elucidating the effect of sodium on urolithiasis. Urinary sodium excretion has a significant correlation with urinary calcium excretion both in normal subjects and stone formers.[5] It was suggested that salt intake should be restricted, to decrease the risk of hypercalciuria.[6] However, it has not been investigated whether high sodium intake in the diet itself increases oxalate absorption in the small intestine.

The purpose of this study was to confirm the effect of sodium chloride on oxalate and calcium absorption in the human small intestine. We found that sodium chloride-dependent absorptions of oxalate and calcium occur in the human small intestine and that the intake of sodium chloride increases urinary excretion of oxalate and calcium.

MATERIALS AND METHODS

The protocol for this study was approved by the Human Subject Committee of the Mie University School of Medicine. All subjects were fully informed of the nature of this study and volunteered to participate. Nine subjects were obtained from the medical staff of Mie University School of Medicine. None had any history of renal urolithiasis and renal dysfunction. In this study, all subjects were fasted for 12 hours after their last meal of the previous day, which was free from dietary restrictions. Urine samples were collected from all subjects prior to study, and 2 and 4 hours after intake of sodium oxalate. During the 4-hour period, all subjects rested and drank 150 mL of water after collection of each urine sample. Eight subjects received sodium oxalate (4 μmoles/kg body weight) together sodium chloride (1.2 mmoles/kg body weight) After an at least 1-week interval, the same subjects received the same dose of sodium oxalate. To elucidate the effect of sodium chloride on urinary oxalate excretion, sodium chloride (1.2 mmoles/kg body weight) was administered to 3 control subjects. Also, these subjects took water alone. Concentrations of urine sodium, potassium, and chloride were determined by electrode studies,[7] creatinine by the method of Jaffe,[8] and oxalate by the method of Ichiyama.[9]

Excretions of oxalate, and calcium were also represented as ratios of individual excretion to creatinine excretion (Ux/Ucreat where x represents ox, or Ca). Changes in these individual ratios were determined by ratios obtained at 2 and 4 hours after intake of sodium oxalate. The following formula was used: Ux/Ucreat (at time +2 hours or +4 hours) ÷ Ux/Ucreat (at time 0 hours). All data was expressed as means (± SD). Student's t test was used in the statistical analyses and a P value < 0.05 was considered to be statistically significant.

RESULTS

The effects of simultaneous intakes of sodium oxalate and sodium chloride, and of sodium oxalate alone on oxalate excretion are summarized in Fig. 1. No significant differences could be found in Uox/Ucreat between subjects with intake of sodium chloride and sodium oxalate, and those with intake of sodium oxalate alone. Then, we calculated the change in Uox/Ucreat as described under Materials and Methods (Fig. 1). Changes in Uox/Ucreat were 2.04 ± 0.74 and 3.25 ± 1.29 (means ± SD) at 2 and 4 hours, respec-

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tively, after intake of sodium oxalate and sodium chloride. When sodium oxalate alone was administered to the same patients, changes in Uox/Ucreat were 1.12 ± 0.22 and 0.96 ± 0.19 (means ± SD), respectively, at 2 and 4 hours after intake of sodium oxalate. Thus, changes in Uox/Ucreat were significantly greater in subjects with simultaneous intake of sodium chloride and sodium oxalate, when compared to those with intake of sodium oxalate alone ($P < 0.05$ and $P < 0.01$ at 2 and 4 hours after intake).

Next we examined the effect of sodium chloride on urinary excretion of calcium. The simultaneous intake of sodium chloride and sodium oxalate did not increase Uca/Ucreat at 2 and 4 hours after intake. Also, intake of sodium oxalate alone did not increase UCa/Ucreat at 2 and 4 hours after intake. In subjects with an intake of sodium chloride alone, UCa/Ucreat increased profoundly. Therefore, we calculated the change in UCa/Ucreat in these cases (Fig. 2). In subjects with an intake of sodium chloride alone, the change in Uox/Ucreat was 49.07 ± 29.96 and 0.363 ± 0.309 (means ± SD), respectively, at 2 and 4 hours after intake (n = 3). In those with intake of sodium oxalate alone, the changes in UCa/Ucreat were 2.11 ± 3.02 and 4.11 ± 9.56 (means ± SD) at 2 and 4 hours, respectively. When 3 subjects took sodium chloride, the changes in UCa/Ucreat were 0.97 ± 1.17 and 2.11 ± 2.55 (means ± SD) at 2 and 4 hours, respectively, after intake.

DISCUSSION

This study showed that oxalate absorption in the small intestine of the human may be dependent upon the presence of sodium chloride. There are no previous reports of the presence of a putative Na-oxalate co-transport system in the intestine. In this study, therefore, the possibility of sodium being exchanged for protons,[10] and subsequently oxalate being transported through an oxalate-H symport system remained to be determined. Also, oxalate may be absorbed

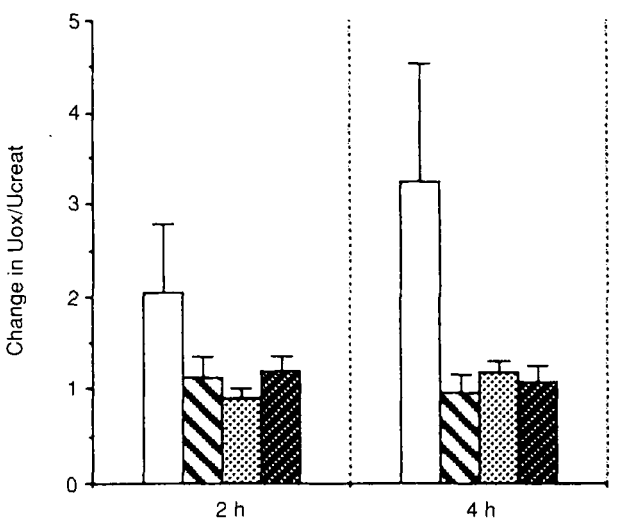

Fig. 1. The changes in Uox/Ucreat in subjects with simultaneous intake of sodium chloride and sodium oxalate (□) (n = 8), with sodium oxalate alone (▨) (n = 8), with sodium chloride (□) (n = 3), and with intake of none (■) (n = 2).

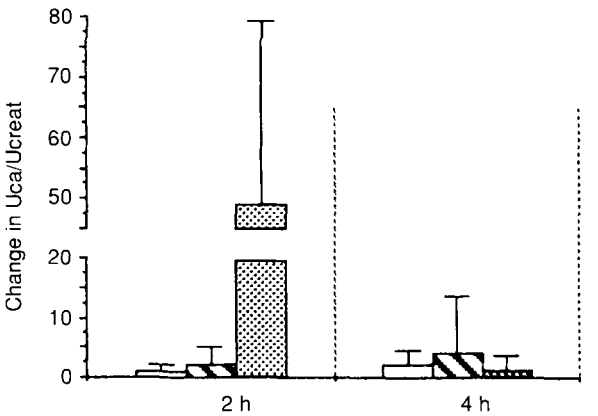

Fig. 2. The changes in UCa/Ucreat in subjects with simultaneous intake of sodium chloride and sodium oxalate (□) (n = 8), with sodium oxalate alone (▨) (n = 8), and with intake of sodium chloride (□) (n = 3).

via oxalate-Cl exchange. Recently, there has been significant progress in the studies which were related to oxalate absorption from intestine.[11,12] The stomach is a powerful and critical organ in oxalate absorption from intestine.[20] Oxalate flux across the proximal colon of the rabbit showed dependency on the pathway involving Na^+, Cl^-, $HCO3^-$. Koul and his associates previously investigated an oxalate transporter in LLC-PK1 cells and reported similar transport systems to those reported here.[13] Possibly, such oxalate transporters exist for a variety of cells, transporting oxalate across the cell membrane to maintain intracellular pH as a potential anion-buffering system.

Dietary calcium has been reported to inhibit and delay oxalate absorption in the stomach and intestine of rats.[14] Calcium intake has also been suggested to decrease urinary oxalate excretion.[15] These observations agree with our own. Sodium oxalate intake did not increase UCa/Ucreat more than sodium chloride intake alone (Fig. 2). These results indicate that oxalate intake decreases calcium absorption from the alimentary tract. Also, our data show the effect of sodium chloride on calcium absorption (Fig. 2). Intake of sodium chloride alone increased urinary calcium excretion from 60 to 3000 (mg calcium/g creatinine). These results do not indicate ordinary functions, but a specialized situation. Although the calcium pump and vitamin D3 are involved in calcium absorption,[16] there is a possibility that Na^+/Ca^+ exchange activity might be an alternative pathway for calcium absorption in the gut.

Dietary therapy rather than a lifelong medication to prevent stone recurrences might be recommended, since an effective pharmacological agent is not available for the treatment of oxalate stone formers.[17] The benefits of dietary therapy result from oxalate restriction at appropriate calcium intake levels[18] as well as from proper dietary sodium restriction, since sodium stimulates both oxalate and calcium absorption from the gut.

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