The effect of ammonium chloride and sodium bicarbonate on the urinary excretion of magnesium, calcium, and phosphate

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Relatively few studies have been made in the control subject on the effect of ammonium chloride or sodium bicarbonate on the urinary excretion of magnesium, calcium, and phosphate. This paper reports such a study in 6 control subjects.

I. Material and methods

Six healthy ambulatory subjects, who were between the ages of 23 and 37 years, and who ranged in weight between 112 and 190 pounds, participated in the study (3 male medical students, 1 female medical student, 1 medical student's wife, and 1 female laboratory technician). They thoroughly understood the importance of the test, as to careful 24-hour collections of urine, and diet control. These subjects ate the same self-selected diet for the 3 periods of 5 days each of the experiment and collected 24-hour samples of urine during the same period. No preservative was added to the urine when the subjects were taking ammonium chloride. Thymol was used as a preservative during the control period and when sodium bicarbonate was taken. Samples of blood were drawn on the third day of each 5-day period. The 3 periods of study were as follows and in the sequence listed, except in one subject (R. J.) in whom periods 1 and 2 were reversed: (1) control diet—5 days; (2) control diet plus 8 Gm. of $NaHCO_3$ (95.2 mEq. of sodium) daily—5 days; (3) control diet plus 8 Gm. of NH_4Cl (plain) (151.2 mEq. of calcium) daily—5 days. During the 2 days, or more in a few instances, between periods the subject ate any diet desired.

Levels of serum magnesium were determined by the method of Simonsen and associates,[1] and magnesium in the urine, by a modification of this method; serum and urinary calcium, by the method of Clark and Collip[2]; and serum and urinary phosphate, by the method of Simonsen and associates.[3] Levels of serum bicarbonate were determined by the Van Slyke titration method.[4] Urine pH was determined by the Beckman pH meter.

II. Results

The urine of all subjects was made more acid (pH 4.8-4.9), and the levels of serum bicarbonate fell below control values during ingestion of ammonium chloride. During the ingestion of sodium bicarbonate the urine pH became more alkaline (7.2-8.3), and there was a slight rise in the levels of serum bicarbonate, in all but one subject,

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Table I. *Effect of NH_4Cl on urinary excretion of magnesium, calcium, and phosphate*

Subject, sex, age	Magnesium			Calcium			Phosphate		
	Control period (mEq./5 days)	NH_4Cl* period (mEq./5 days)	Difference (mEq.)	Control period (mEq./5 days)	NH_4Cl* period (mEq./5 days)	Difference (mEq.)	Control period (mM./5 days)	NH_4Cl* period (mM./5 days)	Difference (mM.)
J.A. M, 24	52.54	58.71	+6.17	45.77	70.11	+24.34	147.8	165.8	+18
E.W. M, 23	85.45	91.00	+5.55	67.41	85.26	+17.85	207.6	198.7	−8.9
D.H. M, 31	53.19	56.40	+3.21	76.25	101.56	+25.31	145.45	160.1	+14.65
S.H. F, 28	33.05	35.01	+1.96	32.35	58.85	+26.50	115.41	132.95	+17.54
L.M. F, 30	40.96	46.08	+5.12	43.52	61.3	+17.78	114.05	138.2	+24.15
R.J. F, 37	26.80	34.75	+7.95	24.30	49.7	+25.40	113.0	156.9	+43.9
Mean			+4.99 ± 0.87† p < .01 > .001			+22.86 ± 5.1† p < .01 > .001			+18.2 ± 6.9† p = .05

*Eight grams of NH_4Cl per day by mouth.
†Standard error of the mean.

Table II. *Effect of $NaHCO_3$ on urinary excretion of magnesium, calcium, and phosphate*

Subject*	Magnesium			Calcium			Phosphate		
	Control period (mEq./5 days)	$NaHCO_3$† period (mEq./5 days)	Difference (mEq.)	Control period (mEq./5 days)	$NaHCO_3$† period (mEq./5 days)	Difference (mEq.)	Control period (mM./5 days)	$NaHCO_3$† period (mM./5 days)	Difference (mM.)
J.A.	52.54	47.47	−5.07	45.77	42.95	−2.82	147.8	130.9	−16.9
E.W.	85.45	79.66	−5.79	67.41	62.75	−4.66	207.6	194.3	−13.3
D.H.	53.19	54.76	+1.57	76.25	70.10	−6.15	145.45	116.9	−28.55
S.H.	33.05	29.52	−3.53	32.35	28.46	−3.89	115.41	97.3	−18.11
L.M.	40.96	35.87	−5.09	43.52	41.40	−2.12	114.05	117.23	+3.18
R.J.	26.80	29.7	+2.90	24.3	20.3	−4.0	113.0	103.8	− 9.2
Mean			−2.5 ± 1.5‡ p < .2 > .1			−3.81 ± 0.64‡ p < .01 > .001			−13.8 ± 4.3‡ p < .05 > .02

*See Table I for ages and sex.
†Eight grams of $NaHCO_3$ per day by mouth.
‡Standard error of the mean.

above the control levels, but not above the normal for this determination.

Table I documents the effect of ingestion of 8 Gm. of ammonium chloride per day for 5 days on the urinary excretion of magnesium, calcium, and phosphate in each subject as compared to the control period. The range of urinary electrolyte excretion of the different subjects is seen to vary widely in the control period. Despite this there was a mean increase in urinary magnesium (+4.99 mEq.), calcium (+22.86 mEq.), and phosphate (+18.2 mEq.), which was statistically significant during ingestion of ammonium chloride.

Table II gives the results of ingestion of sodium bicarbonate on the urinary excretion of these same ions. Four of the 6

Table III. *Review of changes in urinary electrolyte excretion with ingestion of NH_4Cl (from the literature)**

Investigator and year	*Number of subjects*	*NH_4Cl (Gm.)*	*Increase over control electrolyte excretion*			*Type of Comparison*
			Ca (mEq.)	*Mg (mEq.)*	*PO_4 (mM.)*	
Wiley et al.,[5] 1933	1	5.2	22	8	14	Total increase during 6 days on NH_4Cl over 6 days of control period
Tibbetts and Aub,[6] 1937	1	12–18	7	8.3		Total increase during 6 days on NH_4Cl over 6
	1	12–18	28	48	27	days of control period
Martin et al., (This study, 1959)	6	8	22.86	4.99	18.2	Total increase (mean for group) during 5 days on NH_4Cl over 5 days of control period
Keith et al.,[7] 1926	1	10.5	5.5	1.7	3	1 day on control—3 days on NH_4Cl. Figures given are maximum 24-hour increase while on NH_4Cl
Sartorius and Pitts,[8] 1949	1	15	23.8	3.7		Maximum 24-hour increase on NH_4Cl over
	1	10.5			19	mean 24-hour excretion of 5-day control period
Martin et al. (This study, 1959)	6	8	7.11†	3.45†	8.37†	Maximum 24-hour increase in electrolyte excretion on NH_4Cl over mean 24-hour excretion of 5-day control period (mean for group)†

*Rearranged and calculated to compare with our results.
†All highly significant mean changes.

subjects showed a decrease in urinary excretion of magnesium, whereas 2 showed a rise as compared to the control period. The mean change was not statistically significant. All subjects showed a decrease in the urinary excretion of calcium, with a mean decrease of 3.8 mEq., which was a significant mean change. All but one subject showed a decrease in urinary excretion of phosphate, but the mean decrease was not highly significant.

No significant changes in the values for serum magnesium or calcium, as determined on the third day of each test period, were found. Some minor to moderate variations in the levels of serum phosphate occurred in a few subjects, but without any definite pattern.

Discussion

Presumably, healthy subjects are in magnesium, calcium, and phosphate balance, and excrete any excess of these ions ingested. If each subject ate the same diet in each of the test periods, although different for each subject, change in the excretion of electrolyte should represent the effect of the drug taken, and not the amount of dietary electrolyte.

Thus, this project was designed to see not only whether there were changes in the urinary excretion of magnesium, calcium, and phosphate after ingestion of ammonium chloride or sodium bicarbonate, but whether there was an average or mean response to these drugs, despite variation of age, sex, weight, and intake of electrolytes. This was done purposely, since acidifying or alkalinizing agents are given to patients of different age, sex, and weight and on diets which differ as to the content of magnesium, calcium, and phosphate.

The results clearly show an increased urinary excretion of magnesium, calcium, and phosphate in all subjects after acidifica-

tion of the urine with ammonium chloride. Furthermore, there was a mean response for the group, which was statistically significant, despite variations in sex, weight, age, and urinary output of electrolytes during the control period.

Only four studies (6 control subjects) have previously been reported[5-8] on the effect of ammonium chloride on the urinary excretion of magnesium, calcium, and phosphate. Table III summarizes this data. The material from the literature, where possible, has been rearranged and recalculated, to compare with our data, although amounts of ammonium chloride and periods of study were not always similar. Increases in the urinary output of magnesium, calcium, and phosphate during therapy with ammonium chloride was shown in all studies. The amount of these increases varied from our results in some instances. In part this may be due to differences in the amount of drug used and the period and design of the study.

Jabir and associates[9] reported acute increases in the excretion of magnesium after ingestion of ammonium chloride, but the design of his experiment does not allow comparison with our results.

Although the effects of acidifying salts on the excretion of calcium is well known, little attention has been paid to their effect on excretion of magnesium in urine.

Previous studies from our laboratory[10] have shown a fall in the level of serum magnesium and marked increases in the output of magnesium in the urine in patients with congestive heart failure who were receiving prolonged diuretic treatment with ammonium chloride and Mercuhydrin. The present study documents increased urinary output of magnesium in control subjects after the administration of ammonium chloride. The possibility of depletion of body magnesium with repeated and prolonged use of ammonium chloride, particularly if the dietary intake of magnesium is low, is thus a possibility, particularly if more potent diuretics, such as the mercurials or chlorothiazide, follow the use of ammonium chloride. The effects of depletion of magnesium in the experimental animal are well known. The studies of Flink[11] have delineated the clinical picture of magnesium deficiency.

Only one other study in one subject[5] has dealt with the effect of sodium bicarbonate on the urinary excretion of magnesium, calcium, and phosphate. In this study, changes in urinary electrolytes during 6 days of ingestion of 100 mEq. of $NaHCO_3$ over a 6-day control period were as follows: decrease in calcium of 7.5 mEq.; increase in magnesium of 7 mEq.; increase in phosphate of 1 mM. Ingestion of sodium bicarbonate in our study caused a decreased urinary excretion of magnesium in 4 subjects, of calcium in 6 subjects, and of phosphate in 5 subjects. The mean change was highly significant only for calcium (−3.81 mEq.).

Summary

Six normal subjects showed mean or average increases, which were statistically significant, in urinary output of magnesium (+4.99 mEq.), calcium (+22.86 mEq.), and phosphate (+18.2 mM.) during 5 days of ingestion of ammonium chloride, as compared to a 5-day control period. This occurred despite differences in the intake of electrolytes, age, sex, or weight. The possible significance of the loss of magnesium during diuretic therapy was discussed.

During ingestion of sodium bicarbonate there was a mean decrease over the control period which was statistically significant only for urinary output of calcium (−3.81 mEq.).

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