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Research Article

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EFFECTS OF ETHANOL ADMINISTRATION ON URINARY EXCRETION OF MAGNESIUM AND OTHER ELECTROLYTES IN ALCOHOLIC AND NORMAL SUBJECTS *

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Although clinical magnesium deficiency is now recognized frequently in chronic alcoholics, its cause or causes are not clear. A poor dietary intake is undoubtedly important, but it is unlikely that magnesium deficiency results from dietary depletion alone, since it has been quite difficult to produce experimental dietary magnesium deficiency in man (2). Earlier workers have shown that the kidneys are reasonably efficient in conserving magnesium (2, 3). Thus, it is likely that some additional mechanism may be responsible for magnesium deficiency associated with chronic alcoholism. Recent studies have indicated that ethanol may induce increased urinary excretion of magnesium (4, 5). The purpose of the present study was to determine the effect of an acute ethanol load on urinary excretion of magnesium and other electrolytes, and to make preliminary observations on the mechanism responsible for an observed increase in urinary excretion of magnesium.

METHODS

Fifteen studies were performed on nine normal and four alcoholic subjects. Two of the alcoholic subjects had significant hypomagnesemia at the time of study, while the other two had been repleted before study. One alcoholic subject was restudied several weeks later when he was readmitted to the hospital with acute alcoholic intoxication. All subjects were on a normal hospital diet and were fasted overnight before the experiments, which began at 8:00 a.m. Water-loading was achieved with 20 ml of water per kg of body weight and was maintained for the duration of the study by replacing the fluid volume excreted. Inulin and para-aminohippurate (PAH) were added to 5% glucose in water and administered, after a priming infusion, at a rate of 5 ml per minute by a constant-infusion pump. After a 45- to 60-minute equilibration period, serum and urinary sodium, potassium, calcium, magnesium, chloride, phosphate, pH, inulin, and PAH were measured during three successive 20-minute control periods. Blood and urinary lactate and citrate values and total urinary organic acids were obtained in the control subjects and in four ethanol-loaded subjects.

After the control periods, 30 ml of 100% ethanol with a small amount of water was given orally, and 5% ethanol in 5% glucose solution with inulin and PAH added was infused at a rate of 5 ml per minute. After a 20-minute equilibration period, measurements were made during successive 20-minute test periods and compared with the control results. Most studies terminated after three test periods, but three ethanol-loading experiments were extended for longer periods to ascertain the duration of effects after ethanol administration.

Three control experiments were conducted identically with the others except that no ethanol was given. Urine collections were obtained by voluntary voiding except in two studies where bladder catheterization was necessary.

Magnesium was measured by the molybdivanadate method (6), and other electrolytes were determined by standard laboratory techniques. pH measurements were made with a Beckman zeromatic pH meter with expanded scale. Inulin was determined by the method of Schreiner (7), and PAH by that of Smith and associates (8). Lactate was measured by the Marcus modification of Barker's and Summerson's procedure (9), and the method of Beutler and Yeh (10) was used for citrate. Total organic acids were determined by a modification of the method of Palmer (11). The methods for calculating correlation coefficient and probability are described by Snedecor (12).

RESULTS

The results of all studies are summarized in Table I. The most significant and consistent finding was a marked increase in magnesium excretion after the administration of ethanol in all ethanol-loaded subjects. Figure 1 graphically

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shows the mean values of magnesium excretion during the three control periods as compared to the mean values of the three test periods for each ethanol-loaded subject. The mean increase for all test subjects amounted to 167% over control values, with a range of 90 to 357%, and is statistically significant ($p < 0.001$). There was no significant difference between normal and alcoholic subjects.

A consistent but less striking increase in urine calcium excretion occurred in all subjects (Figure 1). The mean increase amounted to 89% over control values, ranging from 36 to 180% ($p < 0.005$).

On the other hand, urine potassium excretion showed a definite decrease after ethanol administration in all patients except one (Figure 1). A mean decrease of 44% was observed ($p < 0.01$). These results confirm the reports of others (13, 14).

No statistically significant changes were observed in the excretion of other electrolytes, in contrast to previous studies showing decreases in urinary sodium and chloride excretion (13, 14). Urinary pH (Table I) and blood electrolytes (Table II) were also unaltered. (We have no satisfactory explanation for the lower plasma potassium concentrations found both before and after ethanol infusion in the ethanol-loaded subjects.) Inulin and PAH clearances (Table II) likewise remained relatively constant so that the changes in magnesium, calcium, and potassium after eth-

TABLE I

Urinary excretions before and after ethanol

Subject	Age	Period	Flow	Na^+	K^+	Ca^{++}	Mg^{++}	Cl^-	Phos≡	Lactate	Citrate	Total organic acids	pH
	yrs		*ml/min*	*μEq/min*	*μEq/min*	*μEq/min*	*μEq/min*	*μEq/min*	*μq/min*	*μq/min*	*μq/min*	*μEq/min*	
Controls													
1. NM*	38	Before	12.1	117	24	8	21	43	24	150	318	140	5.8
		After	13.5	118	19	11	25	48	20	242	431	131	6.1
2. WM	31	Before	15.0	231	81	10	15	115	46	47	433	165	6.9
		After	17.4	258	77	8	14	126	56	55	411	147	7.1
3. WM	22	Before	22.7	364	44	10	9	285	75	223	415	106	6.8
		After	20.8	380	59	13	11	366	67	183	354	75	7.0
Mean of controls		Before	16.6	237	49	10	15	148	48	140	389	137	6.5
		After	17.2	252	52	11	16	180	47	160	399	118	6.7
		% Change	+4	+6	+5	+12	+11	+22	−2	+14	+3	−14	+3
Ethanol-loaded													
1. Ind. M	38	Before	12.9	148	72	17	10	130	51				
		After	15.7	180	36	27	27	152	47				
2. NM*	38	Before	17.7	166	47	12	11	136	16				
		After	17.8	152	17	19	25	117	9				
3. WM	41	Before	16.2	149	61	12	5	90	79				
		After	19.1	170	36	27	9	92	94				
4. NM*†	29	Before	12.9	229	42	7	3	198	24				
		After	15.3	270	20	14	13	217	18				
5. Ind. M*	36	Before	21.9	249	40	21	3	195	61				
		After	24.7	361	22	30	15	273	55				
6. WM	31	Before	14.0	118	61	24	8	90	62				
		After	20.7	298	39	65	26	214	110				
7. WM	34	Before	13.1	212	82	11	5	156	64			109	6.6
		After	14.4	235	36	20	16	174	40			169	6.4
8. WM	39	Before	14.0	139	99	13	4	118	95	155	160	76	6.2
		After	17.3	237	68	26	13	192	84	181	213	89	6.3
9. NM*†	29	Before	9.9	145	30	8	1	91		1,076	125		6.6
		After	11.7	173	25	13	2	118		1,184	119		6.5
10. WM	50	Before	6.6	112	35	17	5	83	70		145	74	6.2
		After	6.6	139	38	23	11	125	60		143	96	6.0
11. WM‡	28	Before	12.4	130	42		10	418	54	83	192		6.3
		After	14.3	134	14		19	502	32	95	245		6.3
Mean changes		Before	14.2	165	58	15	7	161	58	438	156	86	6.4
		After	16.6	218	33	28	17	206	55	487	180	118	6.3
		% Change	+17	+32	−44	+89	+167	+28	−5	+11	+16	+37	−1

* Indicates alcoholic subject.
† No. 4 and No. 9 are the same subject. Not included in mean changes except for lactate, citrate, and pH.
‡ Received double dose, 60 ml, of ethanol.

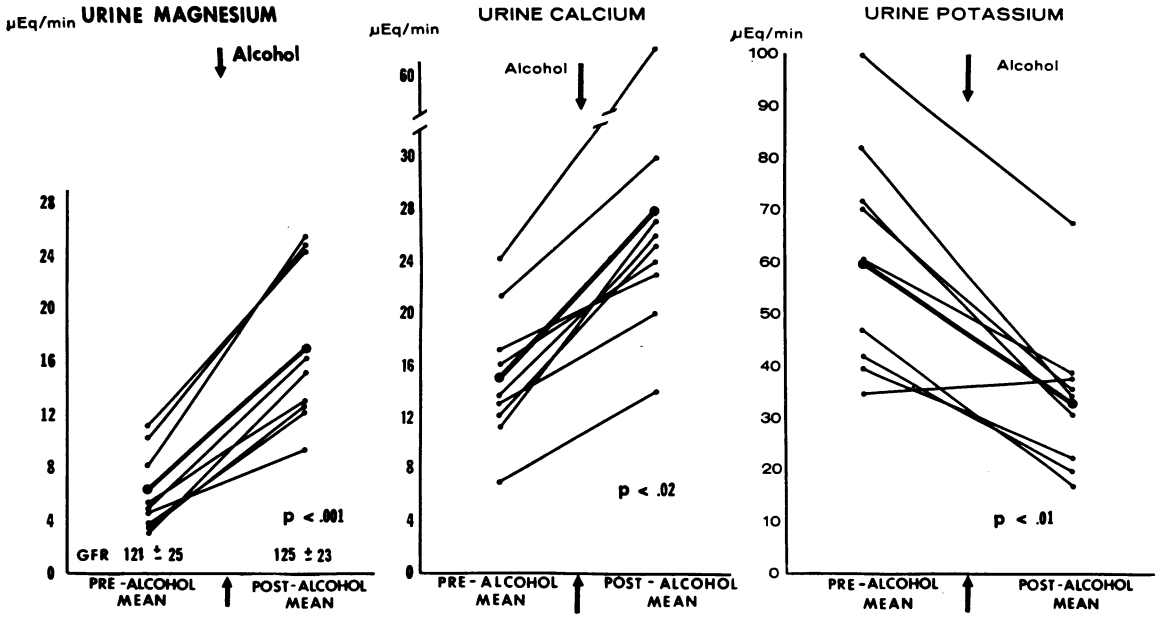

FIG. 1. MEAN URINE ELECTROLYTE EXCRETION BEFORE AND AFTER ETHANOL ADMINISTRATION.

anol administration cannot be attributed to changes in glomerular filtration or renal blood flow.

Urinary and blood lactate and citrate and urinary total organic acids were measured in four studies (Table I). The changes were small, amounting to an 37% increase in total organic acids after ethanol.

Changes in magnesium, calcium, and potassium excretion were invariably observed within 20 minutes after the administration of ethanol. The maximal effect, however, was generally seen at 60 to 80 minutes, and some effect persisted for 100 to 140 minutes. The results of a typical study are shown in Figure 2.

All subjects received 30 ml of 100% ethanol except one (Table I, Subject 11), who was given 60 ml. In this study, increasing the dosage of ethanol did not result in a greater rise in urinary magnesium excretion.

Although PAH saturation alone has been shown to cause an increased urinary magnesium excretion (15), this was not a factor in these studies because PAH was given before the control periods with the maintenance infusion held constant during both control and test periods, and plasma PAH concentration did not exceed 0.03 mg per ml. No ethanol was given in three control experiments to examine the effect of diurnal variation (Table I). No significant changes in urinary magnesium, calcium, or potassium occurred during the relatively short period of these studies. Lactate, citrate, and total organic acids showed no consistent alterations.

TABLE II

Mean plasma concentrations and inulin and para-aminohippurate (PAH) clearances before and after ethanol

Subjects	Period	P_{Na}	P_K	P_{Ca}	P_{Mg}	P_{Cl}	P_{Phos}	$P_{Lactate}$	$P_{Citrate}$	C_{In}	C_{PAH}
		mEq/L	*mEq/L*	*mEq/L*	*mEq/L*	*mEq/L*	*mg/100 ml*	*μg/100 ml*	*μg/100 ml*	*ml/min*	*ml/min*
Controls	Before	138 ± 4	4.1 ±.3	4.6 ±.3	1.7 ±.1	101 ±4	2.7 ±.3	147 ± 73	15 ±3	129 ±20	639 ±55
	After	139 ± 9	4.2 ±.2	4.5 ±.3	1.7 ±.1	101 ±3	2.9 ±.4	138 ± 73	11 ±2	112 ±13	624 ±25
Ethanol-loaded*	Before	137 ±10	3.2 ±.3	5.1 ±.6	1.3 ±.4	104 ±6	3.3 ±.6	195 ± 97	9 ±2	121 ±29	663 ±95
	After	136 ±12	3.2 ±.3	5.0 ±.4	1.4 ±.2	101 ±6	3.3 ±.5	206 ±101	8 ±1	123 ±34	694 ±35

* Includes four alcoholic subjects.

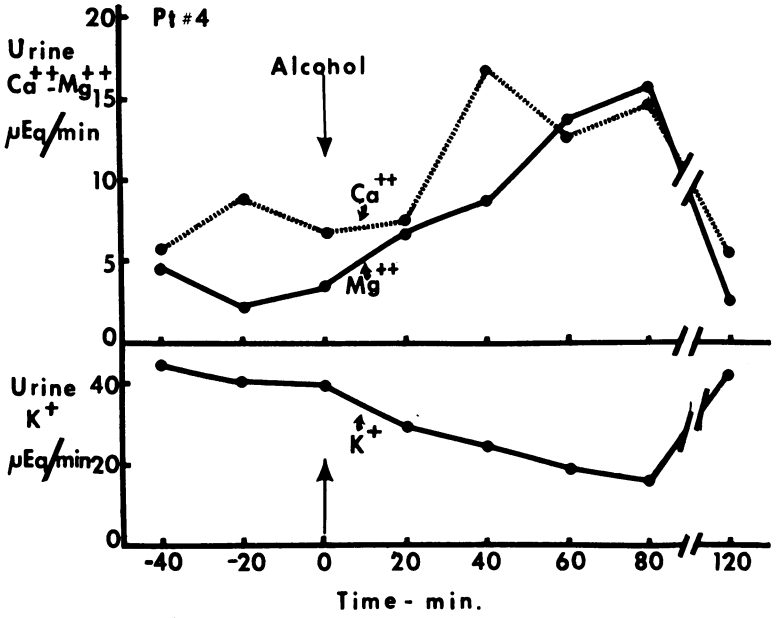

FIG. 2. RESULTS OF A TYPICAL ETHANOL-LOADING STUDY.

DISCUSSION

The consistent, prompt increases of urinary magnesium and calcium and decrease of urinary potassium after an acute ethanol load were independent of glomerular filtration rate, renal plasma flow, or rate of urine flow. These changes were unrelated to water diuresis or PAH administration, and could not be attributed to diurnal variation (16).

There was no significant difference in the ethanol-induced magnesium diuresis in normal and alcoholic subjects. Previous studies have shown that hypomagnesemic subjects have a markedly positive magnesium balance during the repletion period (3). Ethanol administration apparently interferes with this renal conservation mechanism, however, as increased magnesium excretion after ethanol occurred in two hypomagnesemic subjects.

The mechanism by which ethanol produces these changes is not clear. Barker, Elkinton, and Clark (15) have previously demonstrated that lactate administration results in an increased urinary excretion of magnesium. It has also been shown that the administration of ethanol results in increased levels of blood lactate (13, 17), introducing the possibility that the increased renal excretion of magnesium after ethanol might be related to an increased lactate production and excretion. The small changes observed in urinary lactate excretion alone in four studies were not sufficient to account for the magnesium diuresis after ethanol. Likewise, only small increases in urinary citrate were observed. The increase in total organic acids was more substantial. The usual metabolic pathway for ethanol includes oxidation to acetaldehyde and conversion to acetyl coenzyme A with complete combustion in the citrate acid cycle (18). It is possible that certain organic acids accumulating after ethanol ingestion may form magnesium organic acid complexes that are not readily absorbed in the renal tubules. Citrate is more important than lactate in its complexing properties (19), but the small changes observed in citrate excretion alone could not account for the marked increase in magnesium or calcium excretion.

The possibility that ethanol or one of its intermediate metabolites exerts a direct renal tubular effect on a cation-exchange mechanism must be considered, since increases in total excretion of calcium and magnesium approximated the decrease in potassium excretion. A simple ion-exchange mechanism for magnesium, however, has not been demonstrated satisfactorily (15).

SUMMARY

The administration of ethanol to normal and alcoholic subjects induced an acute urinary diuresis of magnesium (167% of control values) and calcium (89%) and a decreased excretion of potassium (44%). These changes occurred in two hypomagnesemic subjects despite renal conservation mechanisms. The onset of the effect was within 20 minutes, reaching a maximum in 60 to 80 minutes and returning to control levels in 100 to 140 minutes.

The increased excretion of magnesium was independent of water diuresis or para-aminohippurate administration, and was not due to changes in renal blood flow or glomerular filtration. These excessive urinary magnesium losses after ethanol ingestion undoubtedly contribute to the magnesium depletion often seen in alcoholics.

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