Urinary Excretion of Magnesium in Man Following the Ingestion of Ethanol

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CERTAIN clinical situations including chronic alcoholism,[1] pancreatitis,[2] the effect of prolonged administration of parenteral fluids without magnesium supplements,[1,3] the recovery phase of diabetic acidosis,[4] hyperparathyroidism,[5,6] the malabsorption syndrome,[7] ulcerative colitis,[8] malacic bone disease,[8] renal disease,[3,9] infantile protein malnutrition[10,11] and the result of prolonged use of chlorothiazide or mercurial diuretics[3] may be associated with a low serum magnesium value and sometimes with the magnesium deficiency syndrome. The syndrome includes a coarse tremor of the hands and tongue, athetoid movements of the extremities, convulsions and mental clouding of varying degree in association with sweating and facial flushing. Tetany is not a usual feature of magnesium depletion but has been reported particularly in intestinal malabsorption,[12] in kwashiorkor[11] and in a child with osteochondritis.[13]

The evidence relating some manifestations of chronic alcoholism to a lack of magnesium includes the low serum magnesium value found in alcoholics, the favorable response of alcoholic subjects to magnesium administration, the positive magnesium balance evident during the recovery phase of chronic alcoholism[14] and a resemblance of manifestations of chronic alcoholism to the cutaneous and neuromuscular manifestations of magnesium deficiency induced in animals.[15]

The etiology of magnesium depletion in alcoholism is unknown. Many alcoholic subjects have the magnesium deficiency state with only moderate dietary restriction during prolonged drinking bouts. One possibility is that alcohol interferes with the absorption of magnesium in the gut. Gottlieb et al.[16] showed that by an unknown mechanism the magnesium requirement was increased significantly in the diet of rats given alcohol. The absorption of xylose is depressed by alcohol ingestion, both during acute experiments in rats[17] and in chronic alcoholic subjects.[18]

Renal conservation of magnesium in man is ordinarily fairly efficient.[14] It would take many weeks to produce symptomatic magnesium deficiency experimentally in man solely by means of restricted intake of magnesium, judging from the experiments of Fitzgerald and Fourman.[19] However, alcohol may adversely affect magnesium conservation by the kidney and lead to accelerated magnesium losses by the renal route.

The following studies were carried out to evaluate urinary excretion of magnesium following ethanol ingestion. An abstract of preliminary findings has been published.[20]

METHOD

All of the subjects in this study were normal human beings, either volunteer nonhospitalized subjects or hospitalized men convalescing from pulmonary tuberculosis.

All of the subjects gave negative histories for urinary tract disease. Among the hospitalized subjects, histories of renal disease were negative, and blood urea nitrogen determinations were within normal limits.

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This study was supported in part by grant No. B1036 (C) of the U. S. Public Health Service.

TABLE I
Urinary Excretion of Magnesium in Normal Men

Subject*	Excretion of Magnesium (mEq./hr.)		
	9:00–12:00	12:00–15:00	15:00–18:00
J. V.	0.32	0.56	0.27
J. S.	0.13	0.22	0.22
E. F.	0.48	0.40	0.25
D. Q.	0.53	0.48	0.72
H. Q.	0.41	0.43	0.79
H. J.	0.36	0.29	0.41
A. E.	0.56	0.61	0.57
D. L.	0.47	0.35	0.26
Mean	0.407	0.413	0.436

* These subjects were fed identical amounts of liquid diet every three hours during this study.

The collection of all urine specimens was timed, and voiding was carried out into clean jars or waxed cardboard containers. All studies were started between 6:00 and 9:00 a.m. and ran for variable lengths of time. There is a diurnal variation in magnesium excretion as indicated by the mean excretion value of a group of normal subjects.[21] Table I records previously unpublished data on the variations among the individual normal subjects of this group.[21] Although there are exceptions, the time periods 9:00 to 12:00 and 12:00 to 15:00 are stable. There is more variation in the time period from 15:00 to 18:00. After the volumes were measured, aliquots were frozen, and the magnesium determination was carried out later by a modification of the titan yellow method of Garner.[22]

RESULTS

The response of urinary magnesium to ethanol ingestion was studied in three experiments. The amount and type of ethanol ingested, the frequency and time span of urine specimen collections, as well as the nutritional state of the subjects, whether fasting or nonfasting, were slightly different in each experiment. Serum magnesium levels were normal in the nine subjects from whom blood was taken, both before and after the ingestion of alcohol.

Experiment 1

In this study, the acute response of urinary magnesium to treatment with a moderate dose of ethyl alcohol was measured in four healthy young adults (one man and three women). The subjects fasted during the morning on the first day (control day). Each subject received 150 ml. of water every hour to assure adequate urine volume. Urine specimens were collected hourly for six hours. After the collection of three specimens (three hours)* the subjects were given 150 ml. of orange juice. On the second day the experiment was duplicated exactly except that after the third hour,* 1 ml. of 95 per cent alcohol per kilogram body weight was substituted for an equal volume of orange juice. In two of the subjects (R. M. and M. L.), there was a parallel rise in urine volume and magnesium, but in subject P. J. the urine volume decreased while the amount of magnesium excreted increased. In Subject B. M. there was no change in volume but an increase in magnesium.

In Figure 1, the amount of magnesium excreted during the three periods before the administration of alcohol is compared to the amount excreted during the period after alcohol ingestion in each of the subjects. Depending on the control period used for reference, a twofold to fourfold increase in magnesium excretion occurred.

Experiment 2

In this study, three hospitalized adult men in the healing phase of pulmonary tuberculosis were evaluated. Again, the plan of a control day and a day for alcohol ingestion was utilized, and the conditions on the two days were made identical insofar as possible. The test regimen consisted of a breakfast of eggs, bacon, toast and milk, followed by the hourly ingestion of water. The study differed basically from the previous one in that these subjects were not fasting, the baseline excretion of magnesium was higher than in subjects studied in experiment 1, and the study was carried on for a longer period of time. At 11:00 on the control day, the subjects were given water and orange juice. On the following day in each study, alcohol was substituted for the water. Urine specimens were collected hourly from 8:00 through 14:00 and every three hours from

* Time in subject B. M. was divided into a two hour and a four hour period both days.

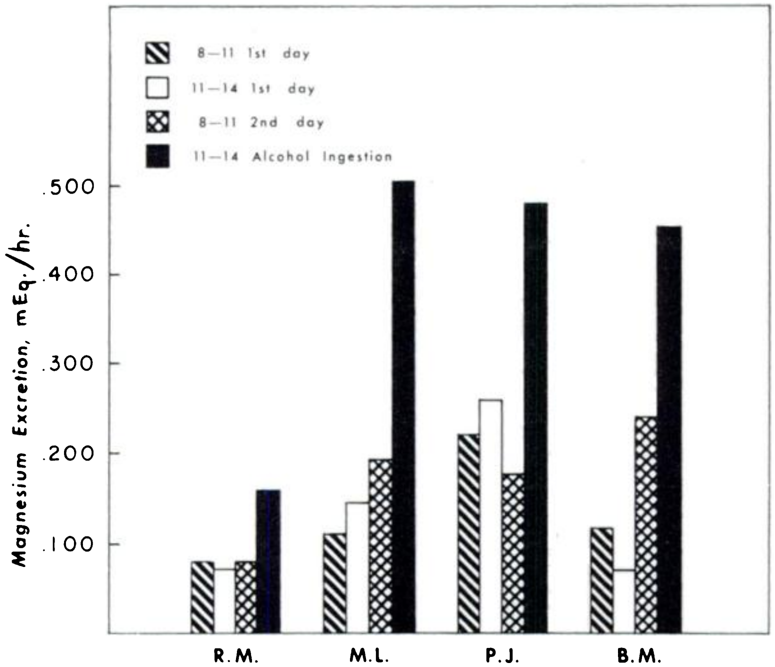

FIG. 1. Comparison of per hour urinary excretion of magnesium before and after control fluid or alcohol ingestion in four normal fasting subjects.

14:00 to 20:00. In Table II are charted hourly excretions of magnesium on both days in each subject before 1:00, from 11:00 to 14:00 and for the whole nine hour period from 11:00 to 20:00.

The results show that the subjects excreted more magnesium on the day when alcohol was ingested than on the control day. When considered from the standpoint of total magnesium excretion in the nine hour period following alcohol ingestion, the patients excreted 0.54 mEq., 0.56 mEq. and 1.03 mEq., respectively, more than on the control day for the same period. The results are less striking than in experiment 1, but these subjects had regular meals in contrast to subjects in experiment 1 who fasted.

Experiment 3

Two men and three women were studied in an attempt to simulate a day of chronic alcoholism. Two of the subjects (R. M. and M. L.) had participated in experiment 1. Fractional urine specimens were collected for two complete twenty-four hour periods separated by a one week interval. The first period is designated as control day; on the second day alcohol is ingested. During both days, the subjects were ambulatory or sitting, except for a six hour period of sleep between midnight and 6:00. The amount of physical activity was somewhat less on the second day. A light diet low in magnesium content was provided to prevent starvation ketosis. The diet and fluids were measured and were duplicated on the second day; alcohol was substituted for water, volume for volume. In this experiment, the alcohol was in the form of blended whiskey (45 per cent alcohol) taken at more or less regular intervals starting at 9:00 and ending before midnight in all cases except one (P. L.). The total amounts ingested ranged from 180 to 540 ml. of whiskey.

The results for the five subjects are represented graphically in Figure 2. The ordinate represents the cumulative difference in urinary magnesium in milliequivalents between the two days, and the abscissa depicts times of specimen collection. Points above the zero line show increases in magnesium excretion over the control day; points below the line represent decreases in excretion.

TABLE II
Data on Urinary Excretion of Magnesium in Experiment 2

Urinary Excretion of Magnesium	Control Day	Day of Alcohol Ingestion
Subject M. G.		
8:00–11:00 (mEq./hr.)	0.39	0.41
11:00–14:00 (mEq./hr.)	0.35	0.51
11:00–20:00 (mEq.)		
Total	3.206	3.760
Difference	...	+0.56
Subject M. L.		
8:00–11:00 (mEq./hr.)	0.34	0.37
11:00–14:00 (mEq./hr.)	0.22	0.24
11:00–20:00 (mEq.)		
Total	1.732	2.273
Difference	...	+0.54
Subject J. H.		
8:00–11:00 (mEq./hr.)	0.28	0.22
11:00–14:00 (mEq./hr.)	0.30	0.33
11:00–20:00 (mEq.)		
Total	1.882	2.891
Difference	...	+1.03

Three of the five subjects showed an increased output when alcohol was ingested (second day). During the hours when alcohol was not ingested, magnesium was retained by two subjects, and cumulative losses approached zero for the twenty-four hour period. One subject (V. M.) showed a decreased output when alcohol was ingested. Subject P. L. drank the most whiskey (540 ml.), consumed the most ethanol (expressed as milliliters per kilogram) and had the greatest net increase in magnesium excretion. It should be noted that this subject not only drank considerably more whiskey than the others, but in addition, continued to drink to 2:00, beyond the stop point of the others. His failure to show a decreased value for magnesium excretion late in the study period may well have been a result.

In Table III the magnesium excretion in the five subjects is compared to the net changes in urinary output and the alcohol ingested per kilogram. The subject with the greatest increase in magnesium excretion also has the largest increase in urine volume as well as the greatest value for alcohol ingestion. There is no correlation between increased urine volume and increased urine magnesium in the other subjects. This parallels the experience noted in experiment 1. The amount of alcohol consumed and the rate of ingestion may have influenced the result. Only subject P. L. drank an amount comparable to the consumption of many alcoholic patients.

COMMENTS

Kalbfleisch et al.[23] recently reported a striking increase in magnesium excretion during acute experiments in which alcohol was infused. The magnesium diuresis was independent of water diuresis and was not influenced by carbonic anhydrase inhibition. In our studies, there was also no consistent relationship between urine volume and magnesium excretion although water diuresis occurred shortly after alcohol ingestion. Heaton and co-workers[24] also have demonstrated increased magnesium excretion when alcohol is administered.

Our studies furnish evidence which suggests that alcohol exerts a direct effect on magnesium handling by the nephron. An additional explanation for magnesium deficiency in alcoholism is thereby possible. Not all subjects showed the same degree of magnesium excretion, and one subject actually had a negative

TABLE III
Data From Experiment 3

Subject	Whiskey Ingested (ml.)	Alcohol (ml./kg.)	Urinary Excretion of Magnesium* (mEq./24 hr.)	Net Excretion of Water* (ml./24 hr.)
P. L.	540	3.4	+3.92	+1,022
L. S.	180	1.3	+1.43	−879
M. L.	300	2.5	+0.25	+293
R. M.	300	1.7	−0.14	−832
V. M.	300	2.5	−1.46	−125

* Net excretion for both magnesium and water represents the quantity on the day alcohol was ingested minus that on the control day for a twenty-four hour period. Figure 2 depicts the course of magnesium excretion.

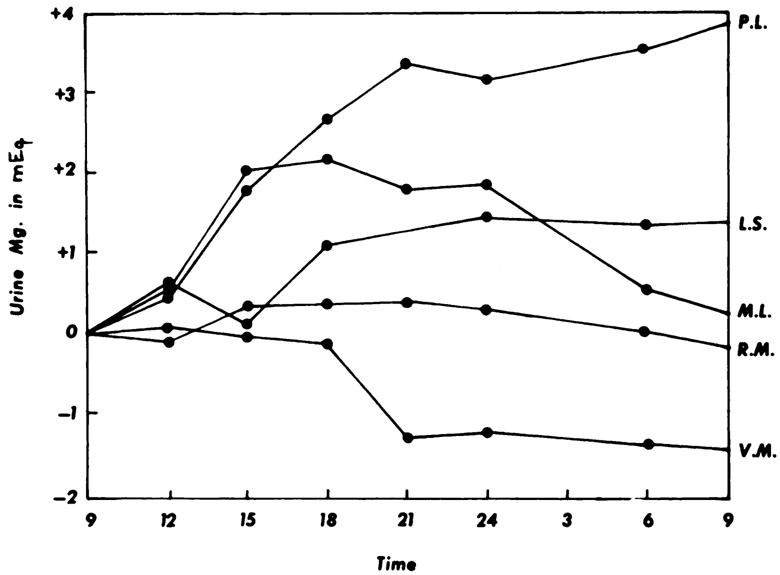

FIG. 2. Cumulative difference in urinary excretion of magnesium (expressed as milliequivalents) in five normal subjects for a twenty-four hour period. Each point in time is represented on the abscissa as the difference between total magnesium excretion up to that time on the alcohol day and the control day. See Table III for quantities of alcohol ingested and other data.

response. It should be noted in this regard that the response of alcoholic subjects was even greater than that of normal subjects in the study of Kalbfleisch et al.[23] Further studies of the specific biochemical effects of ethyl alcohol administration on the renal mechanism for excretion of electrolytes and particularly magnesium should be rewarding.

SUMMARY

Following alcohol ingestion under varying dietary conditions, the urinary excretion of magnesium increased strikingly in six of twelve subjects. In four of the remaining six a definite increase in the urinary excretion of magnesium occurred. The mechanism of this action is unknown. Magnesium excretion induced by alcohol ingestion as well as poor dietary intake probably contributes to magnesium deficiency in chronic alcoholism.

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