MAGNESIUM TOLERANCE IN GOATS FED TWO LEVELS OF POTASSIUM

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SUMMARY

Magnesium tolerance tests were conducted in five female goats to determine the effect of increasing dietary potassium level from .9% (basal diet) to 4.0% (high-K diet) on an animal's capacity for disposing of an intravenous load of magnesium. Both diets contained about .07% magnesium, .91% calcium and .56% phosphorus.

Following intravenous injections of magnesium acetate (.5 mEq of Mg/kg body weight), the time required for plasma magnesium concentration to decline to within 10% of the preinjection level averaged 239 and 176 min (P<.05) when the goats were fed the basal and high-K diet, respectively. Analysis of urine collected from two goats indicated that urinary magnesium excretion could account for all of the magnesium disappearing from plasma for 4 hr after magnesium loading when the goats were fed the basal diet but only about 80% of the magnesium when they were fed the high-K diet. It is postulated that supplementary potassium may have enhanced the disappearance of magnesium from plasma and decreased urinary magnesium excretion by increasing the cellular uptake and retention of magnesium because of increased cellular potassium levels.

Regardless of diet, intravenous magnesium loading produced transitory decreases in plasma levels of calcium, potassium and phosphorus. The mechanism(s) responsible for the responses in plasma calcium, phosphorus and potassium cannot be determined from the study reported here.

INTRODUCTION

Increased potassium intake by ruminants has been observed to decrease blood serum magnesium concentration (Kunkel et al., 1953; de Groot, 1962; Suttle and Field, 1969). The hypomagnesemic response to excess dietary potassium was attributed to either decreased food consumption, reduced magnesium absorption, or both. In addition, Suttle and Field (1969) suggested that potassium directly depressed the circulating level of magnesium. In this respect, de Groot (1962) postulated that there was increased cellular uptake and retention of magnesium in potassium-supplemented animals because of increased cellular potassium levels.

If potassium alters the cellular uptake of magnesium from plasma, then an animal's capacity for disposing of an intravenous load of magnesium should be altered by increasing potassium intake. To test this hypothesis, the plasma magnesium response to intravenous loading of magnesium was determined in female goats fed semipurified diets that contained low and high levels of potassium. Effects of magnesium loading and dietary potassium on plasma levels of calcium, potassium and inorganic phosphorus were also determined.

EXPERIMENTAL PROCEDURE

Five crossbred female goats were used to study the effect of increased potassium intake on intravenous magnesium tolerance. Initially, the goats were fed for 10 days a basal, semipurified diet that contained about .9% potassium. The goats were then fed for 6 days a diet that contained about 4.0% potassium (high-K). Composition of the basal diet is shown in table 1; the high-K diet was formed by adding potassium chloride to the basal diet.

1 The authors wish to thank Dr. Ruth Schwartz, Cornell University, for her helpful review of the manuscript.

(Key Words: Magnesium Tolerance, Dietary Potassium, Goats, Plasma Minerals.)
TABLE 1. COMPOSITION OF BASAL DIET

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Content (g/kg diet)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Timothy hay</td>
<td>400</td>
</tr>
<tr>
<td>Cellulose</td>
<td>287</td>
</tr>
<tr>
<td>Soy protein</td>
<td>130</td>
</tr>
<tr>
<td>Glucose monohydrate</td>
<td>80</td>
</tr>
<tr>
<td>Corn oil</td>
<td>40</td>
</tr>
<tr>
<td>Cane molasses</td>
<td>40</td>
</tr>
<tr>
<td>Mineral mixture</td>
<td>23</td>
</tr>
<tr>
<td>Vitamins</td>
<td>+</td>
</tr>
</tbody>
</table>

- *Timothy hay, s-c, over ripe, (1) IRN 1-04-889; finely chopped.
- *Assay Protein C-1, Skidmore Enterprises, Cincinnati, Ohio.
- *Sugarcane, molasses, mn 48% invert sugar, mn 79.5 degrees brix, (4) IRN 4-04-696.
- *Composition: CaHPO₄, 17.34 g; NaCl, 4.83 g; FeSO₄•7H₂O, .5 g; MnSO₄•H₂O, 160 mg; ZnCO₃, 113 mg; CuSO₄•5H₂O, 36 mg; KI, 20 mg; CoCl₂•6H₂O, 1 mg.
- *By analysis, diet contained: Mg, .07%; Ca, .91%; P, .56%; K, .90%.
- *Added per kilogram diet: retinyl acetate, 1,200 IU; cholecalciferol, 300 IU; DL-α-tocopheryl acetate, 50 IU.

The concentration of inorganic phosphorus in plasma was determined by a colorimetric procedure (Chen et al., 1956). Urinary magnesium concentration and plasma levels of magnesium, calcium and potassium were determined by atomic absorption spectrometry in the presence of lanthanum chloride. The data were analyzed statistically by a t-test (Steel and Torrie, 1960); statements of significance are based on a probability level of at least 95%.

After injecting magnesium acetate, changes in excess plasma magnesium concentration (absolute minus preinjection level) with time were described by an exponential function of the form:

\[ G_t = G_1 e^{g_1 t} + G_2 e^{g_2 t} \]  

(1)

where \( G_t \) represents excess plasma magnesium concentration at time \( t \), \( G_1 \) and \( G_2 \) represent the zero-time intercepts and \( g_1 \) and \( g_2 \) the slopes of the two exponential components. The slopes were determined by the method of least squares. Equation 1 was used to calculate the time required for excess plasma magnesium to return to within 10% of the preinjection level.

The amount of magnesium disappearing from plasma after intravenous magnesium loading was calculated by multiplying the fractional rate of loss of magnesium from the system by the theoretical pool size. The fractional rate of magnesium loss was estimated by normalizing equation 1 and evaluating the first derivative of the normalized equation at time zero. Pool size was calculated by multiplying magnesium distri-
TABLE 2. DIETS AND BODY WEIGHTS OF GOATS USED IN MAGNESIUM TOLERANCE STUDIES

<table>
<thead>
<tr>
<th>Diet&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Days fed&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Goat&lt;sup&gt;c&lt;/sup&gt;</th>
<th>Body weight&lt;sup&gt;d&lt;/sup&gt; kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basal</td>
<td>1 to 10</td>
<td>FF</td>
<td>54</td>
</tr>
<tr>
<td>High-K</td>
<td>11 to 16</td>
<td>CC</td>
<td>51</td>
</tr>
<tr>
<td></td>
<td></td>
<td>LF</td>
<td>36</td>
</tr>
<tr>
<td></td>
<td></td>
<td>LW</td>
<td>29</td>
</tr>
<tr>
<td></td>
<td></td>
<td>BW</td>
<td>40</td>
</tr>
</tbody>
</table>

<sup>a</sup>Basal and high-K diet contained .9 and 4.0% potassium, respectively. Both diets contained about .07% magnesium, .91% calcium and .56% phosphorus.

<sup>b</sup>Inclusively, days of experiment that the respective diets were fed. Exogenous magnesium was injected intravenously on the last day each diet was fed.

<sup>c</sup>Goats FF and CC were estimated to be 4 years old; the other goats were 10 months old. Goat FF was the dam of LF, and CC was the dam of LW and BW. Neither of the dams was lactating at the time of the experiment.

<sup>d</sup>Body weight determined, after an overnight fast, on the last day each diet was fed.

...distribution volume by the absolute concentration of magnesium at time zero. The distribution volume (V) was calculated by the equation:

\[ V = \frac{D}{G_{10}} \]  

where D equals the dose of exogenous magnesium and \( G_{10} \) represents excess plasma magnesium concentration at time zero as calculated from equation 1.

RESULTS

The goats refused about half their feed the first day they were fed the high-K diet, and each of the last 2 days the diet was fed each animal refused about 100 g per day. No feed refusals occurred when the goats were fed the basal diet.

Table 3 shows the plasma concentrations of magnesium, calcium, phosphorus and potassium before magnesium loading. Plasma mineral levels were similar in all goats regardless of age. Potassium levels increased (\( P<.05 \)) with increased intake of potassium. Dietary potassium had no effect (\( P>.05 \)) on plasma magnesium, calcium or phosphorus.

Only minor side effects accompanied the injection of magnesium acetate. Immediately after the injection, the animals would grind their teeth, lick their lips, and swallow repeatedly for 10 to 30 seconds. On several occasions these signs were observed before the entire dose of exogenous magnesium had been injected. No other pathophysiological signs were noticed.

Percentage changes in plasma magnesium concentration after intravenous magnesium loading are shown in figure 1. Table 4 shows plasma magnesium levels at selected times after the injection. Changes in excess plasma magnesium concentration (absolute minus preinjection level) with time could be described by a second-order exponential function (equation...
TABLE 3. EFFECT OF DIETARY POTASSIUM ON PLASMA CONCENTRATIONS OF MAGNESIUM, CALCIUM, POTASSIUM AND INORGANIC PHOSPHORUS IN GOATS PRIOR TO MAGNESIUM LOADING

<table>
<thead>
<tr>
<th>Diet</th>
<th>Mg</th>
<th>Ca</th>
<th>K</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basal</td>
<td>1.9 ± .06</td>
<td>10.4 ± .08</td>
<td>16.0 ± .84</td>
<td>6.6 ± .53</td>
</tr>
<tr>
<td>High-K</td>
<td>1.8 ± .07</td>
<td>10.9 ± .25</td>
<td>18.4 ± .88</td>
<td>6.8 ± .73</td>
</tr>
</tbody>
</table>

aBasal and high-K diet contained .9 and 4.0% potassium, respectively. Both diets contained about .07% magnesium, .91% calcium and .56% phosphorus.

bPlasma concentration immediately prior to magnesium loading. Values are means ± SE; five observations per treatment.

c,dMeans in same columns not followed by the same superscript differ significantly (P<.05).

1). The predicted curves agreed well with the experimentally determined points (R² values exceeded .9). An intravenous injection of 6 ml of physiological saline followed by repeated blood sampling had no significant effect on plasma magnesium concentration (figure 1).

Table 5 shows the effect of increased potassium intake on magnesium tolerance time, the time required for plasma magnesium concentration to decline to within 10% of the preinjection level. Magnesium tolerance time was lower (P<.05) when the goats were fed the high-K diet than when they were fed the basal ration.

Following intravenous magnesium loading, plasma calcium and phosphorus concentrations declined for about 30 min and then increased. The initial response in plasma potassium to exogenous magnesium was similar to that observed for calcium but plasma potassium concentration was greater than the preinjection level for the period 90 to 240 min after magnesium loading. Moreover, the responses in plasma calcium, potassium and phosphorus were similar in all animals regardless of diet or age. Therefore, the results from both trials were pooled and figure 2 shows the percentage changes in plasma calcium, potassium and phosphorus after magnesium loading.

In the two goats tested, urinary magnesium excretion after magnesium loading decreased with increased dietary potassium intake (table 5). The amount of magnesium disappearing from plasma was greater than the amount excreted in urine when the goats were fed the high-K diet; urinary magnesium excretion could account for all of the magnesium disappearing from plasma when the goats were fed the basal diet.

Discussion

Development of hypomagnesemic tetany in ruminants has been associated with a sudden increase in potassium intake (Fontenot et al., 1973). Investigators reporting a pronounced hypomagnesemic response to dietary potassium observed minimum plasma magnesium levels
Figure 2. Changes in plasma concentrations of potassium, calcium and inorganic phosphorus after intravenous injections of magnesium acetate (.5 mEq of Mg/kg body weight) in goats. Concentration is expressed as percent of the preinjection level (solid symbol) and each value is the mean ± SE of 10 observations.

Table 5. Magnesium tolerance time and urinary magnesium excretion after intravenous magnesium loading in goats.

<table>
<thead>
<tr>
<th>Item</th>
<th>Basal</th>
<th>High-K</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tolerance time, b min</td>
<td>239 ± 28f</td>
<td>176 ± 16f</td>
</tr>
<tr>
<td>Observed urinary Mg, c mg</td>
<td>372 ± 3</td>
<td>256 ± 9</td>
</tr>
<tr>
<td>Theoretical urinary Mg, d mg</td>
<td>319 ± 11</td>
<td>323 ± 15</td>
</tr>
<tr>
<td>Urinary Mg ratio e</td>
<td>1.17</td>
<td>.79</td>
</tr>
</tbody>
</table>

aBasal and high-K diet contained .9 and 4.0% potassium, respectively. Both diets contained about .07% magnesium, .91% calcium and .56% phosphorus.

bTime required after magnesium loading for plasma magnesium concentration to decline to within 10% of the preinjection concentration. Values are means ± SE; five observations per treatment.

cMagnesium excreted in urine for 4 hr after magnesium loading in goats FF and CC. Values are means ± range for the two animals in each of the treatments.

dAmount of magnesium expected if all of the magnesium disappearing from plasma during the observation period were excreted in the urine. Values are means ± range for goats FF and CC in each of the treatments.

eRatio of observed to theoretical urinary magnesium excretion.

f,gMeans in same row not followed by the same superscript differ significantly (P<.05).

After 5 to 7 days of potassium supplementation (Suttle and Field, 1969). Consequently, the diets were fed to the goats in the order reported, and magnesium tolerance tests were conducted on the days reported, so that plasma magnesium would be near a minimum level if there was a magnesium response to increased potassium intake.

Feeding supplementary potassium to goats did not significantly alter plasma magnesium concentration. A significant depression in plasma magnesium in response to supplementary potassium has been observed in sheep by some investigators (Kunkel et al., 1953; Suttle and Field, 1969) but not by others (Pearson et al., 1949; House and Van Campen, 1971). The differences in plasma magnesium concentration between experiments may be the result of differences in the potassium status of the animals. Those animals exhibiting a marked hypomagnesemic response to dietary potassium had higher levels of plasma potassium than the goats described here (about 25 vs 18 mg/100 ml). The potassium status of the goats may have been depressed because of decreased feed consumption.

Compared to when the goats were fed the basal diet, magnesium tolerance time was significantly lower when the goats were fed the high-K diet. Increased excretion of magnesium or increased cellular uptake of magnesium are possible factors that could account for the more rapid decrease in plasma magnesium concentration following magnesium loading when the goats were fed the high-K diet. However, urinary magnesium excretion in the two goats tested was lower when they were fed the high-K diet than when they were fed the basal diet. Although some of the magnesium disappearing from plasma may have been secreted into the gastrointestinal tract, this mechanism of magnesium disposal probably can be discounted since a similar level of dietary...
potassium (4%) depressed endogenous fecal magnesium excretion in sheep (House and Van Campen, 1971). Cellular uptake of magnesium could account for the magnesium disappearing from plasma that was not excreted. This explanation is consistent with de Groot's (1962) hypothesis that there is increased cellular uptake and retention of magnesium because of increased cellular potassium levels.

It is conceivable that the treatments imposed may have altered the distribution of body fluids and that such alterations affected plasma magnesium concentration. We observed that plasma volume, expressed in relation to body weight, was not affected significantly in sheep by feeding diets that contained high levels of potassium, citric acid, or both (unpublished observations). However, additional experiments are necessary to determine if dietary potassium, intravenous injection of magnesium acetate, or both, significantly alter the volumes of distribution of body fluids in goats. In addition, it is possible that magnesium tolerance time decreased when the goats were fed the high-K diet because of some carryover effect from the previous treatment. Such residual on carryover effects cannot be established or eliminated under the conditions reported here.

Previous studies have shown that magnesium loading leads to hypocalcemia in man (Womersley, 1956) and rats (Radde et al., 1968). Similarly, plasma calcium levels of the goats declined temporarily following administration of exogenous magnesium but the mechanism of hypocalcemia cannot be determined from the experiment reported here. Hypermagnesemia may inhibit parathyroid gland activity (Care et al., 1966) but not alter calcitonin secretion (Care et al., 1967). Radde et al. (1968) suggested that bone was the main site of alteration of calcium metabolism in rats after magnesium loading and that calcitonin was the principle hormone involved since it inhibits bone resorption. In addition, renal factors may be involved in the hypocalcemic response since administration of magnesium leads to an increase in urinary calcium excretion (Womersley, 1956; Chesley and Tepper, 1958). We suggest that the transitory decline in plasma calcium in response to magnesium loading in the goat may have resulted from increased urinary calcium excretion with a coincident decrease in calcium resorption from bone. Similar changes in phosphorus metabolism could account for the decrease in plasma phosphorus levels after magnesium loading.

The reason plasma potassium levels decreased temporarily following magnesium loading is not known. Similar responses in plasma potassium to intravenous infusions of magnesium have been observed in dairy calves (Bergman and Sellers, 1953) and dogs (Smith, 1949). It is not likely that the decline in plasma potassium resulted from increased urinary potassium excretion since the opposite has been shown to occur (Womersley, 1958; Wilson, 1964). The intracellular ratio of potassium to magnesium generally remains constant (de Groot, 1962). If cellular magnesium levels increased temporarily after magnesium loading, this may have initiated a transitory shift of potassium from plasma to cells.

Previous investigators have established that high dietary levels of potassium may adversely affect magnesium metabolism (Fontenot et al., 1973). In the study reported here, an intravenous tolerance test was used for comparative purposes to determine the effect of dietary potassium on an animal's capacity for disposing of an intravenous load of magnesium. Under the conditions reported here, increased potassium intake increased the rate of disappearance of magnesium from plasma but decreased urinary magnesium excretion. Moreover, the results reported here suggest that solutions injected intravenously to treat hypomagnesemia should contain both magnesium and calcium since injection of magnesium alone may confound the tetany problem by lowering plasma calcium levels.

**LITERATURE CITED**


