Maximum Safe Dietary Magnesium and Effects of High Dietary Magnesium on Zinc Metabolism in Holstein Calves

E. R. QUILLIAN, W. J. MILLER, R. P. GENTRY, S. R. HEINMILLER, and M. W. NEATHERY
Department of Animal and Dairy Science
University of Georgia
Athens 30602

ABSTRACT
Fifteen male Holstein calves were fed diets containing .25 (control), .7, or 1.15% magnesium (from supplemental magnesium oxide) for 28 days. Feed consumption and growth rate were not affected adversely by .7% magnesium but were depressed with 1.15% magnesium. Fecal dry matter percentage was reduced slightly with .7% magnesium and substantially decreased with 1.15% magnesium. However, feces from calves fed .7% magnesium were more fluid in consistency. Urinary and fecal magnesium content increased in calves fed .7 and 1.15% magnesium, with changes closely related to dietary magnesium. Magnesium in plasma increased slightly with .7% magnesium and materially with 1.15%. Magnesium in liver, kidney, and heart was not affected by diets. Apparently calves can tolerate safely .7% magnesium, but 1.15% is detrimental.

On day 21 of treatment, all calves received zinc-65 orally and were killed 7 days later. Calves fed .7 and 1.15% magnesium excreted less zinc-65 and retained more, especially in liver and large intestine. Liver and kidney of calves receiving higher percents magnesium had elevated stable zinc. Calcium and copper in tissue were not elevated. The effect of high dietary magnesium on zinc metabolism appears to be systemic in tissues.

INTRODUCTION
In cattle, excessive dietary Mg reduces feed consumption, weight gain, and milk production and causes diarrhea (8, 25). However, the minimum Mg necessary to produce adverse effects had not been established. Since grass tetany is a serious problem of cattle (15) and because high dietary Mg is used often to combat this condition, it is important to know maximum amount of dietary Mg that can be fed without deleterious effects. One of the objectives of this study was to establish more accurately the maximum safe percent of dietary Mg for calves.

Little is known of the effect of high dietary Mg on Zn metabolism of cattle. An important interrelationship exists between Ca and Zn in animals (14). Magnesium has many similarities to calcium with both being divalent cations in group II A of the periodic chart. The possible existence of a Zn-Mg interrelationship is evident. A second objective of this study was to determine the effect of high dietary Mg on Zn metabolism in calves.

METHODS AND MATERIALS
Fifteen 4-mo-old male Holstein calves averaging 103 kg when the experiment was initiated were divided into three comparable groups of five calves each, balanced for body weight. One group was fed a control diet (.25% Mg), and the others were fed the control diet plus sufficient supplemental MgO to bring total Mg content of the diet to .7% and 1.15%. By analyses the control diet contained 10.4% moisture and (of dry matter) 5.3% ash, 17.6% protein, 1.5% ether extract, 7.5% crude fiber, .51% P, 1.0% K, .92% Ca, .25% Mg, and 57 ppm Zn.

Calves were placed in wooden metabolism stalls and fed a control diet (Table 1) for 7 days to establish baselines for feed consumption, fecal dry matter percentage, and plasma, fecal, and urinary Mg. They were fed whole milk for 2 wk after birth, followed by milk replacer
TABLE 1. Composition of control diet.

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(kg/100 kg)</td>
</tr>
<tr>
<td>Ground corn meal</td>
<td>60</td>
</tr>
<tr>
<td>Soybean oil meal (44%)</td>
<td>22</td>
</tr>
<tr>
<td>Cottonseed hulls</td>
<td>15</td>
</tr>
<tr>
<td></td>
<td>(g/100 kg)</td>
</tr>
<tr>
<td>Vitamin A (30,000 IU/g)</td>
<td>22</td>
</tr>
<tr>
<td>Vitamin D (15,000 IU/g)</td>
<td>4</td>
</tr>
<tr>
<td>Auromycin (chlortetracycline 50 g/454 g)</td>
<td>80</td>
</tr>
<tr>
<td>CaCO₃ (marble dust)</td>
<td>1,444</td>
</tr>
<tr>
<td>Dicalcium phosphate</td>
<td>1,008</td>
</tr>
<tr>
<td>Salt-trace mineral mixa</td>
<td>1,000</td>
</tr>
</tbody>
</table>

Salt-trace mineral mix contained (g/100 kg of diet): NaCl 967.48; (Fe₂)₂(SO₄)₃ • H₂O 19.10; MnSO₄ • H₂O 6.30; ZnO 4.90; CuSO₄ • 5H₂O 2.10; CoCO₃ (45% Co by assay) .02; KI .10.

and grain until 8 wk of age, and then a diet similar to the control diet until initiation of the experiment.

The treatment diets were fed for 28 days after which the calves were killed. Feed and water were provided ad libitum throughout the experiment with feed refusals weighed daily. Total daily excretions of urine were collected with 1% of the total collection retained each day and composited into weekly samples for Mg analysis. Total daily fecal excretions were collected with dry matter determined daily. The dried fecal samples were ground and combined into a weekly composite for Mg analysis. Blood samples were drawn from the jugular vein into heparinized tubes after 1, 3, 7, 14, 21, and 28 days on treatment. Plasma was recovered and stored. Plasma, fecal, and urine samples were wet-ashed by placing samples in a 50-ml Erlenmeyer flask and refluxing with a 70:21:9 mixture of nitric-perchloric-sulfuric acid until a clear liquid was obtained. Samples then were made up to volume with .1 N hydrochloric acid and analyzed for Mg by atomic absorption spectrophotometry.

All calves were given an oral dose via gelation capsule of 500 μCi of ⁶⁵Zn (specific activity of 3.45 mCi/mg) on day 21 of treatment. Seven days later the calves were anesthetized by injection of sodium pentobarbital and killed by cannulation of the carotid artery to remove blood from the tissues. Tissue samples taken included the heart, lung, liver, kidney, semitendinosus muscle, 12th rib, pancreas, spleen, whole blood, small intestine (first .9 m, middle .9 m, and last .9 m), and a section of the large intestine. These samples were frozen and later ground and subsampled for analyses.

Determination of ⁶⁵Zn activity in fecal and tissue samples were with an automatic gamma test tube changer system with a 7.62 cm NaI (TI) well-type crystal. Portions of the dosing solution were used for making counting standards, eliminating the need to correct for radioactive decay. The ⁶⁵Zn tissue data were expressed as a percentage of administered dose per kilogram of fresh tissue. These percents were adjusted to mean body weight for all animals, which has the effect of calculating the data to uniform dosing per kg of body weight (16). The ⁶⁵Zn activity of the liver, kidney, heart, lung, and spleen also was expressed as a percentage of the administered dose per whole organ. Tissue samples were analyzed for stable Zn, Mg, Ca, and Cu by atomic absorption spectroscopy with nitric-perchloric-sulfuric acid wet-ashing of samples.

The data were subjected to analysis of variance according to procedures outlined by Snedecor and Cochran (23).

RESULTS AND DISCUSSION

Feed consumption was not affected by .7% Mg in the diet but was significantly reduced with 1.15% Mg (Figure 1). Likewise, growth was not affected adversely by .7% Mg but was depressed with 1.15% Mg (Figure 1). The reduction in weight gain appeared to be related partially to reduction in feed consumption.

Fecal dry matter percentage was measured to quantitate the effect on diarrhea produced by high Mg intake (Figure 2). There was a slight, nonsignificant decrease in percentage of fecal dry matter with .7% Mg, while reduction was substantial with 1.15% Mg. This decrease in percentage of fecal dry matter began 1 day after administration of the Mg supplement.
after initiation of treatment and leveled off after 4 days, with little subsequent change for the remainder of the experiment. Although there was only a small effect on dry matter percentage, feces of calves fed the .7% Mg were more fluid in consistency (as determined visually) than those of controls. This indicates that this Mg diet had a physical effect by means other than just the change in water content. High dietary magnesium has produced diarrhea in calves (8) and sheep (19). Fecal excretions from Mg-supplemented calves also deviated from the control group by containing mucous material which was excreted in tubular strands up to .5 m long. Feces of all calves fed 1.15% Mg contained mucus. Four of the five calves fed .7% Mg voided mucus in feces, but amounts excreted and frequency of occurrence were considerably less than with calves fed more magnesium. Tubular mucus in feces has been noted before in calves fed high dietary Mg (8).

Concentrations of Mg in plasma were increased slightly but nonsignificantly with .7% Mg. Three days after initiation of treatments, the Mg of plasma from calves fed 1.15% Mg was significantly increased (P<.05) (Figure 3). These concentrations continued to increase for approximately 2 wk, after which there was a leveling off with little further change. Concentrations of urinary and fecal Mg increased in calves fed .7% and 1.15% Mg (Figure 3). Magnesium peaked in urine at 1 wk and in feces at 2 wk posttreatment after which it remained relatively constant. The increased Mg in urine and feces was closely related to Mg in the diet. The relatively steady state of fecal and urinary excretions in control calves suggests that Mg excretion was in equilibrium with dietary Mg intake.

The Mg contents of liver, kidney, and heart are in Table 2. No treatment difference was significant in Mg content of these tissues. These soft tissues were well protected from excess Mg deposition even when dietary Mg was fed in toxic amounts.

At necropsy, the kidney and bladder of each calf was examined for evidence of urinary calculi formation. Four of five calves fed .7% Mg had small crystals in bladder or kidney. In calves fed 1.15% Mg, crystal formation was in four of five calves with one calf having a blockage which resulted in a ruptured urethra. Two of the five control calves had urinary calculi formed in the bladder, but the other three animals did not. High dietary Mg has been implicated in urinary calculi formation in rats (12, 27), and high serum Mg has been associated
with urinary calculi formation in sheep (5).

The reduction in feed intake with high dietary Mg has several possible explanations. Magnesium oxide is unpalatable. However, it has not been demonstrated clearly that MgO will decrease palatability of the feed when added to .45 to .9% of Mg of the diet. Another possibility is that appetite is affected by gastrointestinal disorders resulting from the diarrhea caused by high Mg. Humans receiving large oral doses of Mg have experienced nausea and abdominal pain (7). Possibly the same effect could occur in calves and might decrease feed consumption. It also has been suggested that increased dietary Mg, because of its effect on the central nervous system, may affect intestinal motility and appetite (6, 8, 10).

The reduction in feed consumption and weight gain and the diarrhea from feeding 1.15% Mg demonstrates its toxicity for calves. Calves receiving .7% Mg showed no effects other than the small decrease in percentage of fecal dry matter, more fluid feces, and possibly increased crystal formation in the bladder and kidney. Except for the possible effects on crystal formation, this indicates that .7% Mg in the diet was tolerated safely by the calves. Other dietary constituents may have an influence on the minimum toxic Mg content in calf diets. Several dietary components, especially Ca and K, can affect toxicity and metabolism of Mg (4, 17, 18, 27).

The percentage of the $^{65}$Zn dose excreted in the feces per day is in Figure 4. After the 1st day, both groups fed high Mg consistently excreted a smaller portion of the dose per day than did controls. The two groups of calves fed high Mg excreted less ($P<.01$) $^{65}$Zn over 7 days than controls (Figure 4). Control calves excreted 77.4% of the dose while those fed .7% and 1.15% Mg excreted 61.7% and 61.3% of the total dose. This suggests an increased body retention of $^{65}$Zn. A higher $^{65}$Zn retention also is indicated in those fed added Mg by the $^{65}$Zn content in most tissues (Tables 3 and 4). The increase was greater for those fed the most Mg. Calves fed 1.15% Mg retained more $^{65}$Zn ($P<.05$) in the liver and large intestine than controls. Even though other means were not

<table>
<thead>
<tr>
<th>Table 2. Magnesium content of body tissues in calves fed different percents of magnesium.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dietary magnesium</td>
</tr>
<tr>
<td>-------------------</td>
</tr>
<tr>
<td>Tissue</td>
</tr>
<tr>
<td>Liver</td>
</tr>
<tr>
<td>Kidney</td>
</tr>
<tr>
<td>Heart</td>
</tr>
</tbody>
</table>

$^a$Means on the same line not followed by same superscript are different ($P<.05$).

$^b$From error mean square with five calves per treatment.
significant, an overall trend was established in which calves receiving high Mg retained more 65Zn in the spleen, rib, pancreas, sections of the small intestine, and whole blood.

Both liver and kidney of calves fed added Mg had higher stable Zn contents (Table 5). The effect was significant (P<.05) for calves fed 1.15% Mg as compared with control animals.

The effect of high dietary Mg on Zn metabolism has received little study previously, especially with ruminants. An interrelationship between Mg and Zn has been noted in monogastric animals when either element is deficient in the diet (2, 9). A high Zn diet had an adverse effect on absorption and utilization of Mg in rats (24), and high dietary Mg decreased Zn utilization in chicks (11).

Unlike Zn, the Cu and Ca concentrations were not increased by high Mg (Table 6). There was no change in the Cu content of the liver or in the Ca content of the liver and kidney. These data suggest that the mechanism by which high Mg increases Zn content of liver and kidney does not affect Cu or Ca metabolism.

Calcium content of the heart decreased (P<.05) when supplemental Mg was fed (Table 6). Inadequate magnesium can result in cardiovascular calcification (1). Our control diet contained materially more Mg than is required by calves (13).

Zinc content of cattle tissues is controlled substantially by mechanisms of zinc homeostasis, of which changes in absorption percentage are the most important (13, 14). When zinc is in adequate supply, as in this study, changes in zinc availability or endogenous excretion would have little or no effect on tissue zinc contents. Thus, the influence of the high Mg must have been through some mechanism in the tissue. Also, it is unlikely that Mg had a direct effect at the tissue level, since Mg content of the heart, liver, or kidney was not increased. Cadmium has a similar effect on Zn metabolism; it is antagonistic to Zn absorption and yet causes an increase in Zn content of certain tissues (20, 21, 22). This results from Cd
stimulation of the production of metalloproteins which bind Zn (3, 26). Perhaps excess Mg also stimulates production of Zn binding proteins through some systemic mechanism, resulting in more Zn being deposited and bound in tissues. This effect on tissue demands for Zn probably was responsible for the decreased fecal excretion of $^{65}$Zn.

ACKNOWLEDGMENTS

The authors thank Gold Kist and Dawe’s Laboratories, Inc., for contributing some of the feedstuffs.

Appreciation is extended to R. H. Whitlock, Ruth Harris, Herbert Teague, Jim Jarrell, Mark Collier, Cathy Caputi, Shih-Yieh Ho, and Jonathan Allen for technical assistance.

REFERENCES


27 Watchorn, E. 1932. The effects of excessive intake of magnesium by the rat, especially concerning the factor relating to the production of renal calculi. J. Hyg. 32:156.