Hypomagnesemia among cows in a confinement-housed dairy herd

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- ➤ Hypomagnesemia occurs most often in older cows in early lactation that are grazing lush-growing, fertilized grasses in temperate regions.
- ➤ Confinement-housed dairy cows on a controlled feeding program can also develop hypomagnesemia.
- ➤ Cows with hypomagnesemia that do not have concurrent hypocalcemia may not develop episodic tetany, and the only clinical sign in such cows may be sudden death.

Beginning on January 16, 2002, a 1,200-cow dairy herd in south Florida began to experience an increase in the mortality rate of adult cows (**Fig 1**). Cows that died had few, if any, clinical signs of disease prior to death. Cows in the herd were milked twice a day, and mean daily milk production was 31 to 33 kg/d (68 to 72 lb/d). In terms of production, the herd ranked in the top 15th percentile in the state and was the highest producing herd in south Florida. Cows were grouped (n = 8) and fed according to production and parity and housed in drylots with a feeding barn. The 2 diets fed to the lactating cows were designed to meet or exceed the requirements for cows producing 41 kg of milk/d (90 lb of milk/d; high-producing groups) and 27 kg of milk/d (60 lb of milk/d; low-producing groups). Methods for decreasing heat stress included the use of forced air ventilation and sprinklers in the feeding barns, as well as a cooling pond in each drylot. Cows were fed in 2 areas of the farm. Immediately after each milking, cows in the 4 highest production groups had access to a high-fiber grain mix for 45 to 60 minutes; cows in the lower production groups did not receive this feed. Additionally, all cows were fed a total mixed ration in the drylot feed barn 3 times a day.

Many of the cows found dead in the drylot during this period had no clinical signs of disease prior to death. Affected cows that were seen antemortem had vague clinical signs of short duration that included stiff-legged gait and hyperexcitability. The case definition for a dead cow was a cow that died acutely in the absence of any identifiable disease processes. A case definition for cows that were still alive was difficult to establish; therefore, any cow with abnormal behavior was suspected to be a case. Initial diagnostic testing included physical examination of suspect animals, necropsy of 4 of the first 10 cows that died, inspection of premises and evaluation of potential risk factors, review of feeding management and general cow management practices, inspection of cow housing and feeding facilities, and collection of feed and water samples.

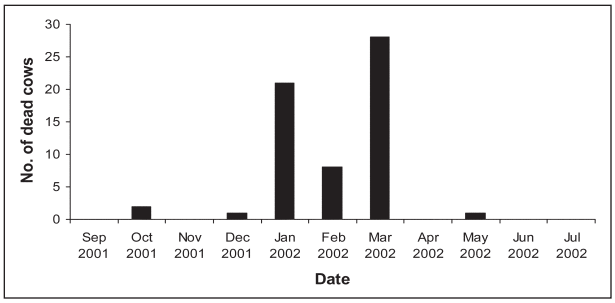

Figure 1—Temporal distribution of unexplained, sudden deaths of cows during an outbreak of hypomagnesemia in a confinement-housed dairy herd in south Florida.

All of the first 10 cows that were affected were from the 4 highest production groups. Factors common to these groups, other than the high milk production, were stage of lactation, water source, and exposure to the high-fiber grain mix. Older animals did not appear to be at any higher risk than young animals. A review of the herd history and feeding practices revealed that herd milk production was 1.8 to 2.3 kg/cow/d (4 to 5 lb/cow/d) lower than it was during the same period in 2001. In addition, 2 feed changes had been made during the first and second weeks of January. A mycotoxin binder had been added to the grain mix on January 8. Around January 12, the forage source was changed from mixed stargrass (*Cynodon nlemfuensis*) and limpograss (*Hermathria altissima*) silage that had been harvested in July 2001 and stored in bags[a] to silage that had been harvested in September 2001. Farm managers reported that fecal consistency was not uniform during these changes, but the change in fecal consistency was attributed to feeding of poorer quality silage from the ends of the storage bags.

Cow management practices had not changed during this period, except that multivalent *Clostridium* vaccines that were routinely administered on a semiannual basis had not been given in November as scheduled. In feeding areas, feedbunks and water troughs were clean, and feed was uniformly mixed. Cow comfort was assessed as good. A pinkish, foamy film was observed in the cooling ponds.

Because most affected cows were found dead, physical examinations could not be performed on many of them. Two that were examined had normal rectal temperatures, but had tachycardia (90 to 110 beats/min) and reduced rumen motility. These cows, and others

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observed by farm managers, had a glassy-eyed appearance. Dipstick analysis of urine from 2 cows did not reveal any ketones or glucosuria. One cow had signs of severe agitation and aggression.

Gross lesions consistently found at necropsy included ecchymotic hemorrhages of the epicardium and endocardium and pulmonary emphysema with or without edema. The rumen was full of grossly normal ingesta; the small intestine was relatively empty, containing only a milky, mucoid material; and the colon was full of grossly normal feces. Some cows had mild to moderate enteritis with a blood-tinged, watery, small intestinal content. All other tissues were grossly normal.

On the basis of these findings, differential diagnoses that were considered included *Clostridium perfringens* enterotoxemia, blue-green algae toxicosis, and mycotoxicosis. Other possibilities that were thought of but considered less likely included polioencephalomalacia secondary to high concentrate intake, hypomagnesemia, nitrate or nitrite toxicosis, and heavy metal poisoning. Initial responses were to restrict access to the cooling ponds (January 18), vaccinate the herd (January 19) against *C perfringens* with a multivalent clostridial toxoid-bacterin,[b] and reduce the carbohydrate portion of the high-fiber grain mix (January 24). Blood samples were collected from 40 randomly selected cows in the 4 highest production groups (January 22) and submitted for CBCs and serum biochemical testing.

Samples of the high-fiber grain mix, the concentrate portion of the total mix ration, the silage harvested in July 2001, and the silage harvested in September 2001 were submitted for routine nutrient analysis and mycotoxin screening. Water samples were submitted for chemical analysis, and tissue and ocular fluid samples from dead cows and pond water samples were submitted for analysis for blue-green algae.

Histologically, the lungs of affected cows had evidence of congestion, edema, and emphysema, and the heart had signs of myocardial congestion and epicardial and endocardial hemorrhage, but did not have any myofiber lesions. Evidence of past hepatic lesions was present (ie, mild fibrosis, biliary hyperplasia, and lipidosis). Mucosal congestion and hemorrhage and mild acute mucosal inflammation were found in the small intestines of 3 cows; in addition, rod bacteria resembling *Clostridium* spp were seen along the mucosal surface and in midlevel glands. No lesions were seen in the adrenal glands, kidneys, spleen, or brain. *Salmonella* organisms (types C and E) were isolated from 2 of the first 6 cows that underwent a necropsy. Ocular fluid from the first cow that underwent a necropsy was negative for nitrates; because of the lack of clinical signs and the fact that there was no evidence of antemortem convulsive activity near the carcass, no other tests were performed on this sample.

Nutrient analysis of feed samples included determination of moisture, protein, energy, fiber, macromineral, and micromineral contents. Water was tested for macrominerals, microminerals, sulfates, sulfites, and nitrates. Results for all feed and water samples were within reference limits. Results of mycotoxin analyses of feedstuffs were negative. Pond water was negative for blue-green algae toxins, and because there was no evidence of hepatic lesions, blue-green algae toxicosis was eliminated from consideration. Complete blood counts performed on the 40 randomly selected cows revealed leukocytosis in 13 cows (> 12,000 cells/mL; reference range, 4,000 to 12,000 cells/mL) and neutrophilia in 17 cows. Results of serum biochemical tests of hepatic and renal function were within reference limits. Serum magnesium concentration was low in 7 cows (0.1 to 1.4 mg/dL; reference range, > 1.5 mg/dL) with 4 cows having concentrations < 0.9 mg/dL. There did not appear to be an association between low serum magnesium concentration and milk production or days in lactation. Serum sodium concentration was high and serum chloride concentration was low in most cows that were tested. Serum potassium concentration was within reference limits. Because of the high proportion of clinically normal cows with abnormal serum sodium, chloride, and magnesium concentrations, laboratory error was suspected.

During the week following the initial responses, 6 more cows died under similar circumstances, but no more cows died during the subsequent 10 days. This pattern of deaths was believed to be consistent with a response to clostridial vaccination in a herd with *C perfringens* enterotoxemia, and a presumptive diagnosis was made. During the second week of February, however, 4 more cows died, so further testing was warranted. Tissue and rumen fluid samples were obtained from cows that underwent a necropsy, and feed samples were collected and submitted for further analysis. To validate results of earlier serum biochemical testing, blood samples were collected from an additional 11 high-producing cows. Because some response to clostridial vaccination had been seen, the herd was again vaccinated with the multivalent clostridial bacterin-toxoid. It was further recommended that cows observed to be sick be treated with *C perfringens* CD antitoxin,[c] magnesium sulfate IV and PO, thiamine, and ceftiofur sodium.

Additional recommendations at this time were to improve feed management by eliminating the 2-feed system and feed a total mixed ration to all cows. In the interim, the concentration of soluble carbohydrates in the high-fiber grain mix was reduced and that in the total mixed ration increased.

During the next 4 weeks (February 8 to March 7), few cows died. Sick cows that were treated as recommended tended to become more alert and responsive, and farm managers reported that after administration of the *Clostridium* antitoxin, many cows would sweat. However, all cows that were treated as described died within 24 hours after the initiation of treatment. Results of tests performed on samples taken in early February were within reference limits or negative, with the exception of serum magnesium concentrations.

The low serum magnesium concentrations that had been observed earlier and attributed to laboratory error were now considered valid, and a working diagnosis of hypomagnesemia without tetany was made. On February 25, magnesium concentration of the diet was increased from 0.28%, on a dry matter basis, to

0.35%. On March 6, the facilities were reconfigured so that a true total mixed ration balanced for 3 production groups (> 41 kg of milk/d, 27 to 41 kg of milk/d, and < 27 kg of milk/d) could be fed. On March 8, some mold was noticed in the silage being fed, and farm managers immediately switched to another bag of silage.

Beginning on March 8, 2 to 3 cows died each day. Vitreous humor was collected from 3 cows within 3 to 4 hours after death and submitted for determination of magnesium and potassium concentrations. Magnesium concentration was < 1.1 mg/dL, and potassium concentration ranged from 5.9 to 12.3 mEq/L, supporting the earlier diagnosis of hypomagnesemia. On March 20, magnesium concentration in the diet was increased further to 0.42%, on a dry matter basis, and possible causes of the hypomagnesemia were investigated. Because problems had become apparent after switching from silage harvested in July 2001 to silage harvested in September 2001, the September silage was removed from the diet of all cows on March 21 and replaced with silage that had been harvested in December. Two cows died after this change, 1 on March 21 and 1 on March 22. After that time, however, no additional animals died. A total of 55 cows died during the period of this investigation.

To our knowledge, outbreaks of sudden death secondary to hypomagnesemia in confinement-housed dairy cows on a controlled feeding program have not been reported previously. Hypomagnesemia is typically a disease of pastured cattle.[1-3] In particular, it occurs most often in older cows in early lactation grazing lush-growing, fertilized grasses in temperate regions.[1] Cows in the herd described in the present report were high producers, by comparison with other herds in the area, and the forages from which silage was obtained had had standard amounts and proportions of fertilizer applied. The diet of these cows was formulated to contain 0.28% magnesium on a dry matter basis, which complies with National Research Council's recommendations,[4] and nutrient analysis of the diet confirmed that it contained this proportion of magnesium. Sources of magnesium in the diet were naturally occurring magnesium in forages used for silage and grains supplemented with magnesium oxide. Availability of magnesium from magnesium oxide is highly variable and dependent on factors such as particle size and particle surface area.[5] According to the feed mill supplying the mineral portion of the diet, there had been no change in the source of magnesium oxide.

In cattle, magnesium is primarily absorbed from the rumen.[6] Magnesium absorption is linked to absorption of sodium and not under hormonal control, and several factors in the rumen may lead to reduced magnesium absorption. A high forage concentration of potassium will inhibit magnesium absorption, as will a high rumen ammonia concentration.[6] However, in the herd described in the present report, forage potassium concentration and rumen ammonia concentration were measured multiple times and fell within expected ranges, given the types of grasses fed, each time.

On occasion, abnormal fermentation in the rumen will result in high concentrations of tricarballylic acid, a possible intermediary in the pathogenesis of hypomagnesemia.[7] In a previous study,[8] rats fed tricarballylate had lower blood magnesium, calcium, and zinc concentrations than did rats fed citrate, a metabolizable analog. This reduction in serum magnesium concentration was related to increased renal excretion of magnesium. However, analysis of rumen fluid from 1 dead cow from the herd described in the present report did not reveal any detectable concentrations of tricarballylic acid.

A diagnosis of hypomagnesemia is usually made on the basis of serum magnesium concentrations in cows with typical clinical signs.[3] However, only 1 cow early in the course of the outbreak described in the present report had classic clinical signs of hypomagnesemia. Seven of 40 clinically normal cows in the herd tested early during the outbreak had low serum magnesium concentrations, and serum magnesium concentration did not appear to be associated with production, age, or stage of lactation. It is possible that the variability in serum magnesium concentration among cows in the herd was a result of the method of feeding on this farm. Cows in the high-production groups had access to a high-fiber grain mix for 45 minutes immediately after milking, as well as to the total mixed ration fed in the drylot. Some cows may preferentially have eaten more or less of the silage-based total mixed ration, thus resulting in variable serum magnesium concentrations.

Several aspects of this outbreak caused some confusion and a delay in final diagnosis. One of the classic signs of hypomagnesemia is episodic tetany,[3] but only 1 of the 55 cows in this herd that died had evidence of tetany. This cow was treated with magnesium salts, *C perfringens* antitoxin, and antimicrobials and improved clinically, only to die 3 weeks later without any recurrence of clinical signs. Two previous reports[9,10] mentioned that cows with hypomagnesemia that did not have concurrent hypocalcemia do not exhibit tetany, but these observations were incidental findings and not emphasized. Although serum calcium concentrations were not measured in any of the cows that died, testing of 40 clinically normal cows from this herd revealed 7 with hypomagnesemia and none with hypocalcemia (calcium concentration < 8.0 mg/dL).

Complicating the investigation of the outbreak of hypomagnesemia described in the present report was the fact that results of all feed and water analyses were well within guidelines established by the National Research Council[4] for all factors known to play a role in magnesium metabolism. We speculate, therefore, that there was some as yet undetermined chemical in the ration, most likely in the silage harvested in September 2001, that chelated magnesium in the rumen, making it unavailable for absorption, or caused increased renal excretion of magnesium.

Finally, the authors may have been remiss in incorrectly interpreting the results of serum biochemical analyses. We had thought that cows with serum magnesium concentrations < 0.3 mg/dL were likely to have signs of clinical or subclinical disease, but these values were obtained from clinically normal cows. Later follow-up and analysis of laboratory records for samples

submitted from other cattle farms during the same period showed that laboratory error was not a likely explanation for the low serum magnesium concentrations.

[a]Ag-bag, Ag-bag Int, Warrenton, Ore.
[b]Ultrabac-8, Pfizer, Exeter, Pa.
[c]*Clostridium perfringens* types C & D antioxin, Colorado Serum Co, Fort Collins, Colo.

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