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Ionophore Toxicity in Horses

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Introduction

Ionophores (e.g., Rumensin®) were first used in the diets of beef cattle in the United States in the 1970's. Shortly thereafter (1976), the first study of monensin (active ingredient in Rumensin®) toxicity in horses was reported. As I began my study of animal science in the late 1980's and early 1990's, I learned of the ionophore risk to horses. However, the way I learned it was "horses that consume ionophores suffer cardiac arrest (heart attack) and die." As my journey in animal science exposed me to the feedlot industry in West Texas in the mid-1990's, I heard many reports of working feedlot horses that occasionally consumed some of the cattle ration with no reports of ill effects. That was a "head-scratcher" for me that I filed away as one of many anomalies between "science" and the "real world."

For decades, equine experts have advised that ionophore ingestion causes death in horses. There have been infrequent, yet perennial, instances of ionophore poisoning in horses over this time with the most recent being reported in California in 2017. These cases always elicit heartache and concern from horse owners about the potential for ionophore contamination in commercial equine feeds, so much so that some equine feed manufacturers now use "ionophore free" facility references in their marketing materials.

Earlier this year, I had the chance to speak to an audience of working feedlot cowboys on proper nutrition for their working horses. As always, my most enjoyable part was visiting with the folks at the break following my talk. This is where I get to learn more about them and aid them in improving their horses' management. This time, I was confronted with the issue of a "poor doing" horse that "doesn't have the energy" and "is not as handy" (agile) as "when he came into the yard three years ago." This came up within the context of discussing the effect of high sulfate water on cattle performance in the yard. I told the gentleman that I did not have an answer "off the top of my head", but that I would get back to him after I did some review of the research available. This is what caused me to re-visit the effect of ionophores on horses, and I wanted to share with you what I found from that investigation as there has been more learned on the subject in the past 10 years.

Benefits of Ionophores

Presently, there are three ionophore products licensed in the US for use in beef cattle: Rumensin® (monensin; Elanco), Bovatec® (lasalocid; Zoetis), and Cattlyst® (laidlomycin propionate; Zoetis). In 2004, the FDA approved monensin to be fed to lactating and dry cows in the US dairy herd. Outside of these, there are many other ionophores used to control coccidiosis in poultry. While each of these ionophores are distinct chemical compounds, they have similar effects in terms of mode of action and effect on bacteria.

For simplicity's sake, I'll focus the remaining discussion on monensin as it is probably the most widely implicated in equine toxicity cases. Monensin is an antibiotic derived from the bacteria *Streptomyces cinnamonensis*. The use of monensin in beef cattle feeding has reported the following results: increased average daily gain and feed conversion and improved feed digestibility; decreased incidence of acidosis and methane production in the feedlot setting; and decreased incidence of bloat. In dairy cattle, the following improvements were noted: increased milk yield and milk protein content; improved feed conversion; reduced incidence of subacute rumen acidosis, ketosis, and displaced abomasum. Many of these observed benefits are due to the effect that ionophores have on the bacteria population in the rumen of the cow.

Mode of Action

In general, there are two main categories of bacteria: Gram (+) and Gram (-). This classification is based on how they take up Gram stain which indicates if they have a simple (Gram +) or complex (Gram -) membrane structure. Generally, most Gram (-) bacteria are more resistant to the effects of ionophores due to their more complex membrane structure.

Essentially, ionophores bind metal cations and help move them across bacterial membranes. This disrupts the ion gradients that bacteria use to take up nutrients, and the bacteria must expend energy to counteract the effect the ionophore and metal ions have on their membrane integrity. The net effect in the rumen is that the Gram (-) bacteria flourish while the Gram (+) do not. This is how ionophores create a rumen microbial environment that results in the beneficial effects reported above.

Ionophores are generally safe and effective when used as recommended by the label. However, toxicity can occur due to accidental overdose, misuse, and mixing errors in the ration. Horses are particularly susceptible when compared to other species due to their much lower LD_{50} (Figure 1). Also, remember that ionophores act on rumen microbes to exert positive effects in the rumen. In the absence of the rumen microbes (i.e., the horse is a hind-gut fermenter), the ingested ionophores are absorbed by the intestine and exert similar effects on cells of the animal. The normal ionic gradient of the cell is maintained and tightly controlled by specialized transport complexes found in cell membranes, and the ionophores disrupt these gradients which leads to cell death. Key tissues involved include cardiac and skeletal muscle, the kidneys, and nerves. In muscle tissue, ion flux across the membrane and the cell membrane potential is disrupted which alters muscle contraction and leads to cellular damage or death. In neural tissue, the ionophore effects the depolarization, or "firing", of the nerve cell and causes cellular damage and death. This cell death (necrosis) results an infiltration of macrophages and fibrosis in the surrounding tissue.

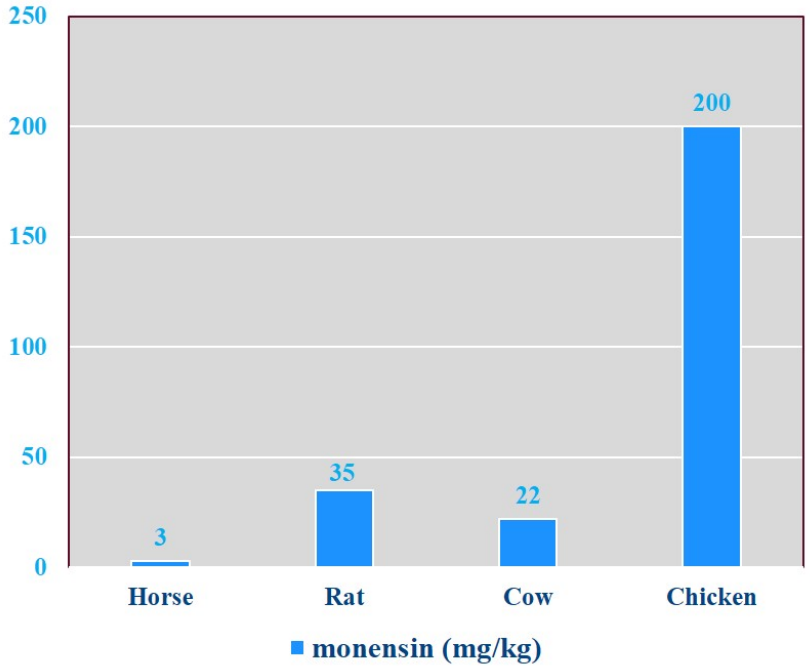

Figure 1. Lethal dose where 50% of test subjects die (LD_{50}) for monensin in various species.

Clinical Symptoms in the Equine

Given the effects of monensin at the cellular level, we can see corresponding impacts in the clinical symptoms observed in the diseased animal. In the short-term, the acute symptoms are likely dependent on the dose of monensin ingested, and include:

- Anorexia, or reduced appetite, and diarrhea
- Depression, incoordination, and ataxia
- Sweating
- Respiratory distress
- Cardiac arrhythmias (irregular heartbeat)
- Overly prominent jugular vein distension and pulsation
- DEATH within a few hours of ingesting a large dose of monensin

The chronic symptoms resulting from ingestion of sub-lethal dose(s) of monensin may include:

- Poor growth and/or weight gain
- Poor performance
- Muscular weakness
- Progressive signs of congestive heart failure due to irreparable damage to cardiac muscle
- DEATH

NOTE: A definitive diagnosis of monensin toxicity requires evidence of the equine consuming a monensin-tainted feed (as determined by analysis of feed samples and gut contents if available).

Recent advances in the area

Divers et al. (2009) investigated the use of blood serum levels of cardiac troponin-I (cTnI), a known biomarker of heart injury, in assessing the degree of cardiac disease caused by ingestion of sub-lethal doses of monensin in six adult horses (Table 1). They found that the feeding state of the horse (fed vs. fasted) and the monensin carrier (water vs. fat supplied as corn oil) influenced the severity of clinical symptoms and the degree of cardiac tissue damage as determined by cTnI. Ionophores are lipophilic molecules meaning they are more readily absorbed along with fats. Furthermore, previous studies have shown withholding feed prior to dosing antibiotics in the horse increased absorption in the gut. From a practical standpoint, this might suggest that "hungry" horses exposed to a fat-supplemented ration (containing monensin) might experience greater injury to the cardiac muscle, as measured by cTnI, over a previously fed horse consuming a monensin-containing supplement with a low fat content. This is speculation of course, given the study only observed a total of six horses. However, small sample size studies are an accepted norm in the equine research field, and they provide the only referenced information available on the subject. Divers et al. also suggested cTnI shows promise as a diagnostic tool. In the setting of a horse herd exposed to ionophore, cTnI could be used to differentiate individual horses that have ionophore-induced cardiac damage from those that do not. Also, cTnI might give veterinarians another decision tool when arriving at a prognosis for an ionophore-poisoned equine.

Table 1. Impact of monensin dose, carrier, and feeding status on disease progression in six adult horses.

Horse #	Monensin dose (mg/kg of body wt.)	Monensin dose carrier	Feeding status	Clinical signs	Effect on cardiac troponin-I level	Outcome
1	1.0	water	No feed withdrawal	Transient anorexia and diarrhea	normal	Survived; no disease
2	1.5	227g of corn oil	Fast for 6 hr prior to monensin	Transient anorexia and diarrhea, ataxia	increased	Died from cardiac failure
3	1.0	227g of corn oil	No feed withdrawal	Transient anorexia	normal	Survived; no disease
4	1.2	227g of corn oil	Fast for 6 hr prior to monensin	Transient anorexia and diarrhea; jugular vein distention	increased	Euthanized due to cardiac failure
5	1.0	227g of corn oil	Fast for 6 hr prior to monensin	Transient anorexia and diarrhea	increased	Survived with cardiac disease
6	1.0	227g of corn oil	Fast for 6 hr prior to monensin	Transient anorexia and diarrhea	increased	Euthanized with cardiac disease

Modified from Divers et al., 2009.

Prognosis for monensin-poisoned equines

If a veterinarian can initiate treatment immediately after ingestion of monensin, decontamination of the gut can be attempted. However, in most cases, exposure is not realized until clinical symptoms have developed. Although there is no known antidote for ionophore poisoning, a veterinarian can initiate symptomatic and supportive care. Some horses might die regardless of treatment, others might recover over days, weeks or months and return to performance, and some will develop permanent heart damage and never fully recover. In horses that survive initial exposure, cardiac evaluation is recommended. The final outcome will likely depend on the amount of monensin consumed as well as the degree of damage inflicted on the heart, kidneys, and neural tissue.

Summary

In closing, ionophores have been a valuable "game changer" in improving the efficiency of production for meat and poultry in America. Their use and place on the farm, ranch, and feeding operation are valid. However, the risk they pose to equines require diligent attention to good management practices that will insure horses are not exposed to ionophores. Isolated departures from these good management practices result in the headlines and heartache mentioned at the beginning of this article. **The key take-home message for all: keep ionophore treated feeds, mineral supplements, etc. away from equines.**

References

1. Divers, TJ, et al. 2009. Clinical findings and serum cardiac troponin I concentrations in horses after intragastric administration of sodium monensin. *J Vet Diag Invest* 21:338-343. Retrieved December 12, 2017 from: https://doi.org/10.1177/104063870902100305
2. Gaskill, C. Ionophore Intoxication in Horses. In *The Horse Magazine*. Retrieved December 12, 2017 from: http://www.thehorse.com/articles/28868/ionophore-intoxication-in-horses
3. House, AM. Monensin and Lasalocid Toxicity in Horses. Retrieved December 12, 2017 from: http://nwdistrict.ifas.ufl.edu/phag/files/2015/02/Monensin-and-Lasalocid-Toxicity-in-Horses.pdf
4. Hutjens, M. Use of Rumensin in Dairy Diets. Retrieved December 12, 2017 from: http://articles.extension.org/pages/11330/use-of-rumensin-in-dairy-diets
5. NRC. 2016. Nutrient requirements of beef cattle. 8th rev. ed. Natl. Acad. Press, Washington, DC.

From our staff to yours, may you all have a very Merry Christmas and a Happy & Prosperous New Year 2018