Consideration of Evidence for Therapeutic Interventions in Bovine Polioencephalomalacia

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KEYWORDS

• Polioencephalomalacia • Bovine • Thiamine • Dexamethasone • Furosemide
• Mannitol • Dimethyl sulfoxide • Nonsteroidal anti-inflammatory drugs

KEY POINTS

- Randomized, masked, prospective clinical trial evidence for therapeutic intervention in naturally occurring bovine polioencephalomalacia is nonexistent.
- Mechanistic, physiologic, and induced model data support the use of thiamine in the therapy of bovine polio.
- The use of nonsteroidal anti-inflammatory drugs and dexamethasone in the therapy of bovine polio are not supported by available induced model data and literature reviews of human data.
- Dimethyl sulfoxide has demonstrated efficacy against cerebral edema in induced models in laboratory animals, but lack of clinical trial confirmation in bovine polio and issues with legality of many of the available formulations call for caution in clinical use at this time.
- There are no clinical trial data to support the use of the diuretics furosemide or mannitol for bovine polioencephalomalacia; research data for mannitol demonstrate varying efficacy and potential adverse reactions depending on the mechanism of cerebral edema and status of the blood-brain barrier.

INTRODUCTION

In contrast to other articles in this issue, the volume of clinical outcome data for bovine polioencephalomalacia therapy borders on nonexistent. This article evaluates the use of thiamine and anti-inflammatories in the therapy of polioencephalomalacia based on available information related to the pathophysiology of the disease, induced models, disease outcome in other species (sheep), and parallels in similar disease in humans.

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POLIO PATHOPHYSIOLOGY

In 1956, Jensen and colleagues[1] described the neuropathology of widespread polio cases in cattle located in Colorado, Wyoming, western Kansas, and western Nebraska, mentioning a clinical similarity to blind staggers thought at that time to be associated with selenium toxicity. In 1969, Little and Sorenson described polio in feedlot cattle in Minnesota, referencing a relationship to thiamine deficiency, but recognizing the lack of clarity as to the cause of this deficiency in the face of adequate dietary thiamine.[2] By 1997, there were 13 articles demonstrating the association of excess sulfur in the ration and/or water with polio.[3]

In a 1998 review, Gould[4] pointed out that there is confusion in the literature as to how the term "polioencephalomalacia" is used. It can be used in reference to a softening of the gray matter of the brain (cerebrocortical necrosis), which may be attributed to altered thiamine status, water deprivation–sodium ion toxicosis, lead poisoning, or high sulfur intake. Polioencephalomalacia also may be used in reference to a neurologic disease syndrome associated with an altered thiamine status.

The reader is directed to Gould's review[4] for an in-depth discussion of the different etiologies of polio, but for the purposes of this article, it should be noted that the relationship of thiamine deficiency and polio is uncertain. In contrast, the association of sulfur-associated polio with excessive ruminal sulfide production has been demonstrated; more specifically, the production of abnormal quantities of hydrogen sulfide gas.[5] A review of thiamine status in the blood and sulfide in rumen fluid in steers with acute signs of polio as compared with normal steers revealed no alterations in thiamine status but significant alterations in ruminal sulfide concentrations during the time of highest polio occurrence at approximately 3 weeks on feed.[6]

In a 2013 publication, Amat and colleagues[7] conducted an induced model study and a field investigation of a field polio outbreak, along with an extensive literature review. In an induced polio model, these investigators evaluated rumen, blood, and brain concentrations of thiamine and the active metabolites thiamine monophosphate (TMP) and thiamine diphosphate (TDP). The 35-day study treatments consisted of a 2 $\times$ 2 factorial design incorporating low (0.3% dry matter) and high (0.67% dry matter) sulfur rations, and 2 differing concentrate-containing rations (4 heifers for each treatment combination). Thiamine was added to all diets at a low level, although the method of reporting in the article does not allow reporting of mg/kg body weight intake. No heifers displayed signs of polio during the study or histologic lesions of polio at necropsy. Results indicated that dietary sulfur had no effect on total thiamine and esters in the rumen fluid or blood. However, the heifers receiving high-sulfur ration had higher total thiamine concentrations in the brain compared with those on low-sulfur diets ($P<.01$), with a numerical decrease in free thiamine ($P = .35$) and numerical increase in TDP ($P = .10$).

Amat and colleagues[7] also reported on an outbreak of naturally occurring polio in feedlot heifers that occurred in close temporal proximity to the induced model study. Eighteen heifers were affected in the outbreak. The calculated total sulfur intake of the heifers in the natural outbreak was close to the high-sulfur intake group in the induced model; the feed was tested and found to contain 0.34% sulfur and the water contained 1755 ppm sulfate. Total sulfur intake from feed and water was estimated to be 47 g per head per day. Treatment consisted of 20 mg dexamethasone intravenously (IV) (Dexamethasone 5, 5 mg/mL; Vetquinol, Lavaltries, Quebec, Canada) and a combination of florfenicol and flunixin meglumine (Resflor, 6 mL/45 kg subcutaneously (SC); Merck Animal Health, Kirkland, Quebec, Canada), and later treated with trimethoprim-sulfamethazine and thiamine (Thiamine Hydrochloride Injection USP, 100 mg/mL