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Nutritional and food aspects related to polioencephalomalacy in ruminant

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Abstract. Polioencephalomalacia (PEM) is a nervous disease with neuronal necrosis. He previously believed that this condition was related to thiamine deficiency, but studies suggest that it can be determined by different nutritional and dietary factors. In this context, objectified to perform a literature review on the main causes of polioencephalomalacia caused by nutritional and dietary factors as well as the appropriate treatment and prevention in ruminants. Therefore, PEM disease can be caused by the classic thiamine deficiency, lead poisoning, sulfur and salt associated with drinking water deprivation. To prevent PEM, avoid contaminated material in pastures (avoid lead and sulfur), invasive plants (avoid thiaminases) and nutritional management of dietary thiamine concentrations and sulfur levels in water and diet. For treatment it is recommended to identify the source that causes the disease, deprivation of contaminated material and use of food management techniques, drugs needed to restore the metabolic parameters.
Keywords: Ruminants diseases, Neuropathology, Cerebrocortical necrosis

Introduction

Polioencephalomalacia (PEM) is a designative term for the morphological diagnosis of softening necrosis (malacia) of the brain gray matter (polio) and cerebrocortical necrosis is the term used to designate the same pathological condition in Europe (MARKSON et al., 1972; EDWIN et al., 1979; JEFFREY et al., 1994).

The term “polioencephalomalacia” was first used in Colorado in the United States in 1956 to denote not only an injury, but a specific ruminant disease, primarily caused by thiamine deficiency and characterized by necrosis of the telencephalic cortex (JENSEN et al., 1956).

However, it is now known that not all cases associated with polioencephalotomalacia (PEM) in ruminants are related to thiamine deficiency. Thus, various nutritional etiologies are implicated in the appearance of the lesion. Usually cases of polioencephalomalacia are related to disturbances of the ruminal and intestinal ecosystem, due to intensive breeding practices and supplies by supplying large amounts of carbohydrates (SANTOS, 2005) or by contamination of certain substances in the diet or water of animals.

When affected, the animals present prodomic signs, leading to isolation and anorexia, where clinical signs: sudden depression, ruminal hypoactivity, dorsal medial strabismus, moderate opistoton, gait disturbance, cortical blindness and reserved pupillary reflex (SANTOS et al., 2005).

In this context, PEM is a non-infectious nervous disease that affects cattle (BARROS et al., 2006, RADOSTITS et al., 2007), sheep (LIMA et al., 2005, RADOSTITS et al., 2007), goats (COLODEL et al., 1998; LIMA et al., 2005; RADOSTITS et al., 2007) and buffalo (GUIMARÃES et al., 2008), which may be responsible for substantial economic losses in the productive sector.

Therefore, objectified to conduct a literature review on the main nutritional and dietary factors that influence the etiology of PEM as well as the appropriate interventions to treat the diseas.

Contextualization and Analysis

Tiamine deficiency

Thiamine is a necessary compound for several metabolic pathways (NADH and NADPH), its deficiency results in changes in carbohydrate metabolism (RADOSTITS et al., 2007) and consequently in energy metabolism.

In several pathways of metabolism thiamine is present, including the glycolytic pathway, which is the main pathway of carbohydrate metabolism directed to energy production in the Krebs Cycle. Thiamine is of great relevance in the intermediate pathway to the glycolytic pathway, called the pentose phosphate pathway, in which thiamine is responsible for the transketolases reactions. This pathway responds in potential for NADPH production, which is employed for the cell biosynthesis process. In this context, glial cells, which are cells responsible for the protection and maintenance of neurons, are dependent on the pentose phosphate pathway, thus thiamine becomes intermediate for neuronal maintenance and protection (SANT'ANA et al., 2009b).

However, thiamine still acts as a cofactor for several Krebs Cycle enzymes (CEBRA; CEBRA, 2004), such as the reaction of isocitrate dehydrogenase, α-ketoglutarto dehydrogenase, malate dehydrogenase, the conversion of pyruvate and lactate and ethanol to acetyl-coa (KANEKO et al., 1997) and pyruvate in acetyl-coa for entry into mitochondria. In this context, by directly interfering with ATP synthesis, there is a decrease in sodium and potassium pump efficiency, reflecting sodium retention, increasing osmotic pressure inside the cell and consequently changing cell volume due to greater water attraction. These disorders are responsible for the initial morphological changes observed in the Central Nervous System (CNS) affected by Polioencephalomalacia (PEM). Usually these lesions occur when erythrocyte transketolase concentrations decrease by about 50% in the brain and thiamine concentrations in the brain are below 20% of normal (DREYFUS, 1965).

Adult ruminant animals synthesize sufficient amounts of this vitamin (GOONERATNE et al., 1989b) because the rumen microbiota accounts for large amounts of B-complex vitamin synthesis. Primary thiamine deficiency mainly affects young ruminants (no stabilized rumen microbiome), which are unable to synthesize the vitamin and ingest low amounts of this nutrient in the diet. Secondary deficiency is due to the production of substances that inactivate or compete with thiamine in the rumen or intestine (FERREIRA et al., 1986).

Diets high in soluble carbohydrates and low in fiber and sudden feeding changes, especially in the transfer of poor pastures to good pastures (JENSEN et al., 1956; MORO et al., 1994) may favor the occurrence of PEM. However, diets rich in soluble carbohydrates are easily fermentable, reducing rumen pH leading to rumen lactic acidosis, which inhibits the development of thiamine producing microorganisms and favors the multiplication of some thiamine degrading bacteria by thiaminase enzymes such as Clostridium sporogenes and Bacillus thiaminollyticus (MORGAN & LAWSON, 1974; SHREEVE & EDWIN, 1974; HAVEN et al., 1983).

Microorganisms responsible for producing thiaminases have been demonstrated in hay, silage, concentrate and forage samples (EDWIN & JACKMAN 1973). Thus, the proliferation of these agents in the rumen may occur after ingestion of these foods or conditions such as cobalt deficiency, administration of anthelmintics or oral antibiotics (RIET-CORREA et al., 2006) and ruminal acidosis (LEMOS, 2005). Thiaminase enzymes can also occur in plants, such as Amaranthus blitoides, Malva parviflora, Pteridium aquilinum, Marsilea drummondii, Cheilanthes sieberi and Equisetum arvense (MEYER, 1989; RAMOS et al., 2005), but they are rare and isolated. Other conditions that may lead to thiamine deficiency are the administration of vitamin B1 antimetabolic substances, such as piritiamine, oxytiamine and amprolium (LOEW & DUNLOP, 1972; MARKSON et al., 1972; MORGAN, 1974; SANT'ANA et al., 2009b) and also the use of some anthelmintics, such as levaisol and thiabendazole (LINKLATER et al., 1977).

For a long time it has been maintained that thiamine deficiency was the only cause of PEM, this is due to the constant recovery of cattle affected by the disease after treatment with vitamin thiamine (BARROS et al., 2006; RADOSTITS et al., 2007). However, attempts at experimental reproduction of the disease by inducing thiamine deficiency were not always satisfactory (RADOSTITS et al., 2007). Because low thiamine concentrations are not always detected in all natural cases of PEM in ruminants (MCALLISTER et al., 1997). Thiaminases also occur in clinically normal sheep feces (LINKLATER et al., 1977), which demonstrates that thiamine deficiency cannot be confirmed by this method.

Clinical signs observed in PEM are associated with primary lesions of the telencephalon, as well as secondary lesions in the cerebellum and brainstem. The latter occur as a result of the compression exerted by swollen telencephalon with edema (RIET-CORREA et al., 2002). The main signs are blindness of central origin, tournament, walking aimlessly, involuntary movements, head pressure against obstacles, depression, incoordination, muscle tremors, ataxia, bruxism, sialorrhea, opisthotonus, nystagmus, strabismus, withdrawal from the herd, decubitus, convulsions, decreased tongue tone and pedaling movements. At the onset of disease, animals may exhibit excitement and aggression (RIET-CORREA et al., 2007).

And the clinical course varies on average from two to four days (SANT'ANA et al. 2009a), but acute 12 hour evolution is described (NAKAZATO et al., 2000; SANT'ANA et al., 2009a) or chronic 22 days in sheep (VIEIRA et al., 2007) or 25 days in cattle (GONÇALVES et al., 2001).

The diagnosis of polioencephalomalacia is based on epidemiological, clinical necropsy and histopathological data. An important tool in the diagnosis of the disease is fluorescence visualization of the affected areas of the brain (mainly telencephalic cortex) when exposed to ultraviolet light (JACKMAN & EDWIN, 1983; GONÇALVES et al., 2001). Therapeutic diagnosis can also be made from the recovery of cattle in response to treatment with thiamine and corticosteroids (NAKAZATO et al., 2000). However, it is noteworthy that thiamine is efficient in the treatment of other central bovine neuropathies (COPPOCK et al., 1991).

Serum hematological and biochemical evaluations do not present consistent results and contribute little to the diagnosis of the disease (OLKOWSKI, 1997). However, increases in pyruvate, lactate, oxyglutarate and thiamine pyrophosphate (TPP) activity and decreased erythrocyte trancetolase activity are described in associated polioencephalomalacia and thiamine deficiency (RAMMELL & HILL, 1986; RADOSTITS et al., 2007). The activity of TPP in healthy cattle and sheep varies from 30 to 50%, while in the cases of PEM it can reach from 70 to 80% (RADOSTITS et al., 2007).

Serum urea and creatinine concentrations may be moderately increased in some cases and the activities of aspartate aminotransferase and creatinine phosphokinase are substantially increased in severely affected animals (OLKOWSKI, 1997). Analysis of the cerebrospinal fluid may reveal slight increase in protein content and mononuclear cells, which may be vacuolated. These changes in cerebrospinal fluid also occur in cases of polioencephalomalacia caused by lead poisoning (CEBRA & CEBRA, 2004).

Treatment and control may be effective when animals are treated early in the disease, slow intramuscular or intravenous administration of 10-20 mg thiamine/kg and 0.2 mg dexamethasone/kg animal weight is recommended. This treatment should be performed every 4-6 hours for three consecutive days (LEMOS & RIET-CORREA, 2007). This treatment was not effective in some cases of polioencephalomalacia associated with molasses (MELLA et al., 1976) or sulfur poisoning (BULGIN et al., 1996). Return of attitude and muscle control can be seen within 12 hours of treatment, as well as improved visual acuity that can be completed within 48 hours (CEBRA & CEBRA, 2004). In severely affected and recovered animals, blindness and other cranial nerve deficits are common.

Sulfur intoxication

In the literature there are incidences of PEM outbreaks associated with high sulfur levels (sulfates, sulfites or sulfides) in the diet (MELLA et al., 1976; RAISBECK, 1982; JEFFREY et al., 1994; BULGIN et al., 1996; LOW et al., 1996; HILL; EBBETT, 1997; NILES et al., 2000; TRAVERSO et al., 2001) or in water (HARRIES, 1987; GOONERATNE et al., 1989b; HAMLEM et al., 1993; GOULD , 2000) ingested by ruminants and the ruminal content of these animals (MCALLISTER et al., 1997). Sulphate intake favors sulfide reduction due to the rumen microbiota and binds to bivalent (mineral) cations. Sulphides prove to be the toxic form of sulfur (GOULD, 1998) and are found more in the rumen gas layer than in the rumen fluid (GOULD et al., 1997).

Ruminal microbiota adapted to sulfate-rich diets produces high concentrations of hydrogen sulfide, part of which is detoxified by bacterial sulfur amino acid production and the other part absorbed by the ruminal and intestinal mucosa or can be eructated (CEBRA & CEBRA, 2004, RADOSTITS et al., 2007). However, toxic anions derived from this gas inhibit the electron transport chain cytochrome oxidase enzyme, which lowers ATP production (MCALLISTER et al., 1997). Under these conditions, it interrupts cellular respiration and causes hypoxia, with consequent neuronal necrosis (MCALLISTER et al., 1992; RADOSTITS et al., 2007). However, other mechanisms of action may also be involved, with sulfur binding to hemoglobin forming sulfemoglobin, which in turn reduces blood oxygenation capacity (BULGIN et al., 1996).

Sulfites have the ability to cleave thiamine, however thiamine reduction has not been observed in sheep fed a sulphate-rich, thiamine-free semi-synthetic diet (OLIVEIRA et al., 1996).

The recommended dietary sulfur concentration for ruminants is at most 0.3% and the tolerable limit is 0.4% (NRC, 1996). Excessive rumen sulfide production and accumulation could be caused by the predominance of dissimilatory bacteria or the insufficient assimilation capacity of the bacteria (GOULD, 2000). Two dissimilatory bacteria isolated from ruminal fluid from sheep and cattle, Desulfovibrio spp. and Desulfotomaculum spp., are the main rumen sulfide producing microorganisms (CUMMINGS et al., 1995).

Ruminal H_2S production can also be affected by the amount, type of carbohydrate ingested, and ruminal fluid pH. Carbohydrate type and availability may affect the number and metabolism of sulfate-reducing bacteria (GOULD, 2000). Possible acid conditions favor an increased H_2S concentration in the gum layer of the rumen and inhalation of this eructated gas could serve as a route of absorption of sulfides. Although the main route of sulphide absorption is not known, there is evidence that the respiratory system serves as the primary entrance route (GOULD, 1998).

In Brazil, there were two outbreaks of PEM described in sheep (LIMA et al., 2005) and cattle (TRAVERSO et al., 2001) ingesting diets with high sulfur levels. To diagnose, one must analyze the sulfur concentration in water, feed, roughage, protein-energy and mineral supplement that animals had access to (RIET-CORREA et al., 2007). The maximum tolerated dietary sulfur concentration is

0.4% based on dry matter (NRC, 1996). Another important finding to confirm the diagnosis is the detection of high concentrations of hydrogen sulfide in the rumen gas layer of diseased animals (GOULD et al., 1997).

As H_2S concentrations decrease markedly in anorexia animals, cattle from the same herd that did not fall ill should also be examined (GOULD, 1998). Sulfur concentrations in water, diet and hydrogen sulfide in the rumen gas layer greater than 1.000 ppm, 4.000 ppm and 1.000 ppm, respectively, are suggestive of toxicosis (CEBRA & CEBRA, 2004). Values of 2.000 ppm of ruminal H_2S may precede the development of PEM in cattle (GOULD et al., 1997). The presence of sulfemoglobin in the blood can also be investigated, which may be used to estimate ruminal sulfide absorption, although this substance is not detected in some situations of dietary sulfur excess (GOULD et al., 1997).

In the treatment of PEM associated with sulfur toxicosis, there is no specific treatment. The recommendation is to look for the probable source of the mineral and eliminate it from animal feed, thus providing low sulfur feed. It is not known whether the addition of thiamine to the diet can prevent sulfur-related PEM (OLKOWSKI et al., 1992). Generally, when there is recovery within hours of thiamine treatment, the condition is suggestive of thiamine deficiency-related PEM; failure of this treatment is indicative of sulfur toxicosis (RADOSTITS et al., 2007).

Lead intoxication

Lead poisoning occurs by accidental ingestion of lead-containing products or by ingesting pastures contaminated with lead (DRIEMEIER & BARROS, 2007). Cases of poisoning are often associated with exposure of herds such as waste batteries, paint, lubricants, motor oils, industrial fumes, herbicides, insecticides and pastures contaminated by industrial waste (CEBRA & CEBRA, 2004; LEMOS et al., 2004; TRAVERSO et al., 2004).

Nervous changes are undoubtedly due to lead deposition in the capillary endothelium, on the other hand digestive lesions occur by caustic action of lead salts in the gastric mucosa. In some animals, normochromic normocytic anemia may develop due to chronic poisoning due to reductions in erythrocyte life and the synthesis of the heme portion of hemoglobin. This mechanism occurs by increasing protoporphyrin by inhibiting the enzyme hemessynthetase, which makes it impossible to bind iron to protoporphyrin (RADOSTITS et al., 2007).

Lead toxicity varies according to the species and chemical composition in which it is carried, and the metal and sulfitic forms are poorly absorbed, while acetate, phosphate, carbonate and hydroxide salts are readily assimilated (CEBRA & CEBRA, 2004). For cattle the toxic doses range from 600-800 mg/kg in adult cattle and from 220-600 mg/kg for calves and goats are 400 mg/kg; Daily doses of 6-7 mg/kg may cause chronic intoxication (RADOSTITS et al., 2007).]

Clinical signs in lead-poisoned cattle are similar to those described in PEM for other causes, evolution is approximately 2-7 days (LEMOS et al., 2004; TRAVERSO et al., 2004) and rarely can affected cattle survive longer time (LEMOS et al., 2004).

In its acute form, lead PEM in cattle may be sudden in death and no clinical signs are usually observed, in the subacute form with ataxia, muscle fasciculations, hyperesthesia, depression, central blindness, salivation, head pressure against objects and walking without course (SUMMERS et al., 1995; CEBRA & CEBRA, 2004). Although in some animals they may have tournament, rumen atony, colic and fetid diarrhea, chronically intoxicated cattle have anemia, melena and abdominal pain (DONAWICK, 1966), but this form is not common in cattle (SUMMERS et al., 1995).

At diagnosis, normal blood concentrations are 0.05-0.25 ppm, to 0.35 ppm are already considered toxic and concentrations above 1 ppm the death of the animal is certain (RADOSTITS et al., 2007). Some hematological tests include regenerative anemia, presence of erythrocyte basophilic stippling (SUMMERS et al., 1995) and in some cases increased blood erythrocyte porphyrin concentration (CHRISTIAN & TRYPHONAS, 1971).

For the control and treatment in lead poisoning, there is no right treatment, one must remove the lead source from the animals, it is recommended to remove the material contaminated by ruminotomy in acute cases, use of cathartics such as salts of magnesium to decrease absorption and increase intestinal excretion and administration of thiamine hydrochloride to reduce neurological clinical signs (COPPOCK et al., 1991; CEBRA & CEBRA 2004).

Salt poisoning associated with water privacy

Salt poisoning can be caused by direct and immediate ingestion of high amounts of sodium chloride while indirect poisoning (most common) results from continuous salt intake associated with water deprivation (MAXIE & YOUSSEF, 2007).

In direct poisoning, it occurs in thirsty cattle that have access to a source of brackish water or sodium chloride supplementation after the restriction period of this mineral (MAXIE & YOUSSEF, 2007), although it is uncommon (SUMMERS et al., 1995).

However, in indirect intoxication in situations of high ambient temperature, animals can ingest large volumes of water after a long period of water restriction (LINDLEY, 1977). The pathogenesis of this intoxication has not been fully understood, but the influx of eosinophils into the perivascular space is related to the increase in sodium ions (Summers et al., 1995).

Sodium is the major determinant of extracellular osmolarity and slowly passes through the blood-brain barrier when blood sodium

concentrations are high in the blood (145-185 mE/L), and the brain also has high concentrations of this mineral, which inhibits anaerobic glycolysis. After access to water, blood sodium concentrations return to normal but in the brain remain high. Because anaerobic glycolysis is impaired, there is no active transport out of the nervous system. Thus, an osmotic gradient is created and water passes from the blood to the brain, leading to cerebral edema (CEBRA & CEBRA 2004).

In rapid rehydration, the flow of water to the erythrocytes often causes intravascular hemolysis, which can make the serum and urine red or brown (CEBRA & CEBRA 2004).

Ruminants can tolerate 13% salt with free access to clean water, but it is recommended not to exceed 4% in feed and 0.3% in water. Lower concentrations may be toxic if water is restricted or if the water contains 7.000 ppm (0.7%) salt or more. Chronic toxicosis can be caused by lower than acute amounts of salt, and acute toxic doses of approximately 2.2 mg/kg for cattle and 6 mg/kg for sheep (CEBRA & CEBRA, 2004).

Clinical signs in salt-poisoned cattle are usually developed after prolonged periods of water fasting or water restriction, followed by unrestricted access to water. The signs are similar to those described for PEM caused by other causes (Summers et al., 1995), but may also present vomiting, ruminal atony, diarrhea and abdominal pain, with clinical evolution of approximately one day (CEBRA & CEBRA, 2004).

Digestive signs are mainly observed in direct sodium chloride poisoning (MAXIE & YOUSSEF, 2007). Serum and urine with brown or red hue are useful in suspected salt poisoning (CEBRA & CEBRA, 2004). Diagnosis for PEM associated with salt poisoning or water deprivation requires determination of sodium concentrations in cerebrospinal fluid. Values above 160 mEq/L sodium in cerebrospinal fluid are suggestive of salt poisoning in cattle (LONERAGAN & GOULD, 2002) and sheep (KANEKO et al., 1997).

Treatment In case of salt poisoning or water deprivation, the water should be slowly returned to the animals. Initially, it is recommended to administer 7 or 10% of body weight in water to adult and newborn animals, respectively, four to six times a day and from the fourth day to provide water freely (ANGELOS et al., 1999).

In animals with clinical signs, water may be administered by nasogastric tube. In severely affected animals, cerebral edema may be reduced by intravenous administration of mannitol (0.5-2 mg/kg) in a 20% solution or oral glycerin (1 mL/kg) diluted 50% in water (ANGELOS et al. al., 1999). Corticosteroids may be used, but may promote sodium retention and hyperglycemia (CEBRA & CEBRA, 2004). It is not known whether thiamine is effective in cases of salt-related PEM (RIET-CORREA et al., 2007).

Final considerations

PEM is a multifactorial disease in relation to nutritional and dietary aspects, and can be determined by thiamine deficiency, lead, sulfur or salt poisoning associated with drinking water deprivation. The PEM can cause and great economic losses for the productive sector as well as be lethal for the animals affected by this metabolic disorder.

Therefore, to prevent PEM, contaminated material in pastures, weeds (possible sources of thiaminases) and management of thiamine concentrations in the diet and sulfur levels in water and diet should be avoided. For the treatment it is recommended to identify the source that causes the disease, deprivation of contaminated material and use of food management techniques according to intoxication, as well as to make use of drugs among the necessary to restore the metabolic parameters.

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