COPPER TOXICITY IN SHEEP

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Text:

Copper poisoning is one of the most important toxicities in the sheep industry, principally in housed lambs and rams fed large amounts of concentrates rich in copper. A Brazilian survey indicated that the occurrence rose steadily during 1970 to 2010 from 0.5 to 6.6 %.

The disease can occur as an acute or an accumulative (chronic) form, being the last the most prevalent.

Etiopathogenesis: The acute poisoning is caused by a large amount of copper ingested in a short period. Basically, the copper causes an intense gastroentenitis although a small quantity of this metal is absorbed (Radostits et al 2007, Ortolani et al 2004). The accumulative poisoning has two distinctive phases: the pre-hemolytic and hemolytic. In the first copper accumulates in the tissues over a period of weeks to months causing different degree of liver injury. Thereafter, in the hemolytic phase, ionized copper is suddenly released from the main hepatic storage sites into the bloodstream (Soares 2004, Oruc et al 2009). An intense hemolysis begins when glutathione concentration is lowered in the erythrocyte. Copper can also combines with sulfidryl producing in the process free radical. In approximately 30 % of the surviving erythrocytes, copper also oxidizes temporarily the iron in the hemoglobin interfering with the process of carrying oxygen to the organism (Machado 1998). Hemoglobin, free radicals, ionized copper and iron generated in the hemolysis cause intense renal insufficiency by glomerular and tubular necrosis (Machado 1998). Death is frequent within 4 d of the onset of the crisis, which is caused by renal insufficiency (Machado 1998). Few sheep survive the process and present temporarily jaundice and anemia until plenty recovery, even though they are in risk to present recurrent episode of hemolytic crisis (Antonelli 2007, Radostits et al 2007, Oruc et al 2009).

Epidemiology: The acute copper poisoning is rarer than the accumulative form and occurs in sporadic outbreaks. An outbreak of acute toxicosis was described in thirsty sheep treated for foot rot that drank footbath solution of copper sulfate (5%). The morbidity, mortality and lethality rates were 74 %: 44.5 % and 60 %, respectively (Ortolani et al 2004). Single ingestion of at least 50 mg/kg BW of copper can cause acute copper poisoning (Radostits et al 2007). Usually, less than 5 % of the herd is affected by the accumulative form, but more than 80% of these animals die if they are not treated adequately. Some breeds such as Texel and Ile-de-Franc are the most susceptible (Underwood and Suttle 1999). It is frequently observed in lambs fed on high concentrates where copper present in this rations more than double its availability as compare to the grass. Sheep fed complete diets containing over 15 mg Cu/ kg DM may be in risk, principally when the level of copper-antagonist elements are low (> 0.12 % sulfur and 0.2 ppm of molybdenum) in the diet. It is also described the toxicity in sheep grazing in orchards previously treated with copper fungicides, which contaminates the underlavered pastures, or in pastures deeply fertilized with poultry or swine manure (Oruc et al 2009, Underwood and Suttle 1999). Diet supplementation with monensin can predispose the toxicity by increasing dietary copper availability (Underwood and Suttle 1999).

Clinical picture: The Acute poisoning is characterized by intense and sudden apathy, dullness, weakness, sternal recumbency, head turned to the flank, anorexia, increased heart and respiratory rates, rumen atony, dehydration, hypertermia, diarrhea with mucous and dark blue-green feces, congested mucoza, grinding teeth and moaning (Ortolani et al 2004, Radostits et al 2007).

The clinical picture of Accumulative poisoning is unapparent in the prehemolytic phase. Nevertheless, some clinical evidences were recorded in this first phase 2. A decrease in the feed intake (25 %) was found on the 7th d, before hemolysis started, which dropped sharply on the 3rd d (75 %) and turn out to anorexia on day one. The appetite became selective with the refusing of concentrates on the 7th d, and gradual decreasing in the intake of hay from the 5th d on. No other changes were seen, but the lambs became very depressed and lethargic and lay down in sternal recumbency on the day previous to hemolytic crisis (Machado 1998).

During the onset of the hemolytic crisis sheep present the following clinical symptoms: hemoglobinuria, intense apathy, dullness, jaundice, dehydration, mild diarrhea and oliguria (Soares 2004, Radostits et al 2007). Elevated heart rates and rectal temperature, and reduced respiratory and ruminal movement rates were recorded at the first days of the onset of the poisoning. The sheep may develop mild alkalosis caused by lower urinary bicarbonate excretion 2. The increasing in the heart rate was directly proportional to the degree of anemia, while the reduced respiratory rate was inversely proportional to the level of alkalosis. Further, there was a positive relationship between plasma free hemoglobin and rectal temperature. The mucous membranes color changes according to the evolution of the metabolic status of the disease. In the first 30 h the mucous membranes are dark brown, as influence by the level of metahemoglobinemia, following to yellow yolk that remains for the next six days caused by the high plasmatic levels; thereafter they became pale for the next 10 d until anemia is corrected (Machado 1998).

An atypical clinical manifestation of accumulative copper poisoning was seen in sheep, goat, cattle and buffalo (Minervino et al 2009, Soares 2004). These animals did not present hemoglobinuria and jaundice, but showed the following signs: dehydration, reduced rumen movements, oliguria and severe and progressive apathy. Additionally, these animals demonstrated progressive hyporexia, followed by anorexia and rapid loss of body condition followed by death.

Diagnostic: The gold standard method for diagnosis is the copper concentration in the liver 5. While normal hepatic copper levels remains on 30 - 400 ppm (DM basis), sheep with the toxicity may present 1500 to 5000 ppm. Usually, animals may be in risk when the liver concentration is higher than 1000 ppm (Underwood and Suttle 1999). Plasma or serum copper is increased only during the first days of the hemolytic phase (Minervino et al 2009, Underwood and Suttle 1999). The best early diagnosis in the prehemolytic phase is the increase of liver enzymes activity in serum, especially γ-glutamyltransferase (γGT), followed by aspartate
aminotransferase and glutamate dehidrogenase. An experimental study detected high serum γGT activity as early as 28 d before the presence of hemoglobinuria (Machado 1998).

Gross and histopathological manifestations: Animals with clinical signs of Cu toxicosis demonstrated icteric mucosal and serosal membranes; yellow and severely enlarged liver; severely darkened kidneys, dark urine; discrete edematous fluid within the trachea; severe congestion and small ulcers at the abomasal mucosa (Minervino et al. 2009, Radostits et al. 2007). The histological hepatic alteration commonly found are moderate to severe diffuse portal fibrosis, centrilobular hepatocellular necrosis, biliary and intracanalicular cholestasis, mild multifocal hepatitis, and microvesicular lipidosis. Renal lesions were characterized by tubular necrosis (Machado 1998, Soares 2004, Radostits et al. 2007).

TREATMENT: Although copper poisoning is highly lethal, early medicated animals with 3.7 mg/kg BW ammonium tetrathiomolybdate (ATM), (IV) once a day for the next 5 d, may have a high recovery rate (85%). The ATM is a specific chelate that firmly binds different forms of copper from the bloodstream and liver enhancing the excretion of the complex in the urine (Underwood and Suttle 1999). Supportive treatment can also be used, for correction of dehydration and anemia.

Prevention: The level of copper and its antagonists in the diet must be analyzed. When diet copper levels are higher than 15 ppm and the levels of molybdenum and sulfur lower than 0.2 ppm and 0.15 %, respectively, preventive measures must be adopted (Underwood and Suttle 1999). Special attention should be considered to more susceptible breeds and animals on intensive system with high concentrate on diet. For these breeds the maximum level of copper in the diet must not exceed 12 ppm (Underwood and Suttle 1999).

A commercial mineral salt containing 300 ppm of molybdenum was tested to prevent the occurrence of copper cumulative poisoning in sheep that received high copper levels in the diet (150 mg Cu/head/d). We found 40 % less hepatic copper accumulation in sheep that received high Mo and this supplementation reduce the mortality rate, but fail to prevent 100% of copper poisoning in high copper intake (Antonelli 2007). Another possibility is the supplementation with high levels (200 mg/head/d) of zinc. This microelement increases the metallothionein concentration in the liver and improves the copper excretion to the bile (Minervino et al. 2009).

Key words: copper, poisoning, sheep, clinical aspects.

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