Sunflower meal as cause of chronic copper poisoning in lambs in southeastern Spain

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Abstract — Sunflower meal with a copper/molybdenum ratio of 10 caused copper toxicosis in lambs. Copper must be analyzed on a dry matter basis in liver and renal cortex. Oral administration of molybdenum and thiosulfate had a certain effectiveness in sick animals. Care must be taken with feedstuffs made from copper-dependent plants.

Résumé — Empoisonnement chronique par le cuivre chez des agneaux du sud-est de l'Espagne associé à un aliment à base de tournesol. Un aliment à base de tournesol ayant un ratio cuivre/molybdène de 10 a été à l'origine d'un cas d'empoisonnement par le cuivre chez des agneaux. Le cuivre doit être analysé sur une base de poids sec dans le foie et le cortex rénal. L'administration orale de molybdène et de thiosulfate a eu un effet positif sur les animaux malades. La prudence est de mise lors d'une alimentation avec des plantes à haute teneur en cuivre.

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Copper (Cu) is both an essential nutrient and a toxic element for all domestic animals; however, sheep differ from other species in their susceptibility to chronic Cu poisoning because of the small difference between required and toxic concentrations (1). In 1995, Cu poisoning was diagnosed in several lambs in southeastern Spain. Although no investigations into the source of the Cu were carried out, all the lambs had consumed a diet composed principally of sunflower meal.

This paper describes the clinical, pathological, analytical, and epidemiological investigations of an outbreak of Cu poisoning in sheep during the following year caused by the consumption of sunflower meal manufactured from plants grown in soils fertilized with Cu.

In March 1996, a veterinary practitioner reported that a number of lambs had died or were showing signs of hemolytic crisis suggestive of Cu toxicosis. Retrospective information about feeding and production management was obtained from the owner of the affected farm and his veterinarian. Segureña sheep and Murciano-Granadina goats constituted the animal population on the farm. The sheep flock consisted of 110 lambs, 106 ewes, and 8 rams, which were divided into 2 groups, based on feeding practices. Group A was composed exclusively of lambs ($n = 110$) weaned at different times and placed in a feedlot for finishing. They were fed exclusively sunflower meal from September 7 until February 20, the last group being weaned on December 5. Group B was composed of adult animals (ewes, rams, and goats) and these grazed with no supplementary feeding. Within the 48-day period prior to treatment (January 3 to February 20), 24 lambs died and 11 showed signs of Cu intoxication. On and after February 20, 100 mg of ammonium molybdate and 1 g of thiosulfate were administrated daily, PO, for 3 wk, as recommended by Osweiler et al (1). Two days after the treatment began, 3 animals showed signs of hemolytic crisis. The treatment period lasted until March 12, during which 7 lambs died and 7 sick animals recovered.

The sick animals were anorectic and showed weakness, icterus, and hemoglobinuria, followed by collapse and death. Occasionally, they showed nervous symptoms (incoordination, obnubilation, ptyalorrhea) and blackish diarrhea. One animal had a high temperature, 40°C. Gross pathological changes were recorded in 5 dead lambs necropsied before the treatment began and in 3 after the beginning of treatment (Table 1). Postmortem changes were typical of Cu toxicosis in sheep. These changes included severe icterus in all the carcasses examined; hemorrhages in the heart; hydropericardium; hemorrhagic lymph nodes; enlarged and friable liver and spleen; enlarged and distended gallbladders containing dense, dark bile; and enlarged, friable, hemorrhagic, and blackish kidneys. Histopathological findings in the kidneys from 3 lambs were typical of hemoglobinuric nephrosis and included severe vascular congestion, vacuolar tumefaction of the tubular cells, hyaline degeneration, fibrosis of the Bowman's capsule, and severe interstitial fibrosis in the renal medulla. No morphopathological differences were found between the groups of lambs necropsied before and after the beginning of the treatment.

Sheep store Cu in liver more readily than do other animal species and a Cu concentration of 10 to 50 mg/kg on a wet matter basis is normal. Copper toxicosis may be associated with hepatic and renal concentrations of Cu greater than 150 and 15 mg/kg on a wet matter basis, or 500 and 100 mg/kg on a dry matter basis, respectively (1–3). Mean concentrations in the liver and renal cortex of the sheep in this study were higher than these values, though the mean renal medullary concentration was below that. Causes of Cu intoxication include the consumption of complete feeds containing Cu levels above the dietary requirement or with a Cu/molybdenum (Mo)

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Table 1. Copper concentrations (mg/kg, wet weight and dry weight) in liver and kidneys at necropsy of lambs showing signs of copper intoxication

Lamb	Date of the sampling	Liver		Renal cortex		Renal medulla	
		Wet wt	Dry wt	Wet wt	Dry wt	Wet wt	Dry wt
1	February 14	230	691	—	—	—	—
2	February 16	172	1029	11	74	7	61
3	February 19	194	990	104	402	31	127
4	February 20	302	877	9	77	3	20
5	February 20 (date Tx began)	252	1513	52	213	6	35
6	February 21	122	967	6	68	2	13
7	February 25	132	960	51	277	26	177
8	February 26	—	—	9	48	3	13
	Mean	200.57	1003.86	34.57	165.57	11.14	63.71

wt — weight; Tx — treatment
Normal values: liver, < 50 mg/kg; renal cortex, < 5 mg/kg; renal medulla, < 3 mg/kg

Table 2. Copper (Cu) and molybdenum (Mo) concentrations (mg/kg) in feedstuffs consumed by lambs during different time periods[a]

	Feedstuffs	Cu	Mo	Cu/Mo
September 7–October 1, 1995	Sunflower meal	10	1.25	8.00
October 2–November 15, 1995	Sunflower meal	8.5	1.21	7.02
November 16, 1995–February 19, 1996[b]	Sunflower meal	14	1.10	12.73
February 20, 1996–March 12, 1996[c]	Grains of barley	2	0.5	4.00

[a]Each time period represent one batch of feed
[b]January 3 — beginning of the outbreak
[c]February 20 — beginning of treatment

imbalance, the consumption of plants contaminated by Cu-containing pesticides, soils and vegetation contaminated by mining and industrial activities, and no access to green forage (1,4).

Because no animals from group B were affected, we took group A (all lambs) as the total population for the epidemiological investigation. A third of the lambs (35%) showed clinical signs of Cu toxicosis and 82% of these died. Since the drinking water supply was the same for both groups, we investigated the feedstuffs consumed by group A from September 1995 to March 1996.

The farmer had put away samples of each batch of feed consumed by the lambs, so they could be analyzed. One sample from each batch was analyzed. The Cu and Mo concentrations and the Cu/Mo ratio in the feedstuffs are shown in Table 2. The sunflower meals consumed over the 4 mo prior to the start of the outbreak contained Cu concentrations slightly below those associated with Cu toxicosis (8.5–14 mg/kg) (1,2). However, the Cu/Mo ratios higher than 6 to 10 meant that toxicosis was extremely likely (1). Furthermore, the lambs were confined with no access to green forage and, therefore, with insufficient Mo to prevent excessive accumulation of Cu in the liver (4).

The referring veterinarian had made the presumptive diagnosis of Cu toxicosis on the basis of the clinical signs and his pathological findings. Diseases such as leptospirosis, eperythrozoonosis, babesiosis, and others are also known to cause icterus and hemoglobinuria in sheep, but, in this case, chronic Cu poisoning had been diagnosed in nearby farms in recent months. The sheep's response to the treatment and the high liver and kidney concentrations of Cu confirmed the diagnosis of chronic Cu poisoning. However, veterinary practitioners and toxicologists may like to consider a number of noteworthy points that emerge from this case in relation to the analytical diagnosis and treatment of Cu toxicosis, and to the consumption of sunflower meals.

Several factors must be taken into account to avoid an erroneous diagnosis based on tissue Cu concentrations. They include the time of the sampling of tissues in relation to the beginning of the treatment, the tissue type and the number of samples that must be sent to the laboratory, and whether the analysis is on a wet or dry matter basis. After comparing the Cu concentrations in the livers and kidneys analyzed (Table 1) with those levels described in the literature as being indicative of Cu poisoning, we observed some controversial facts. While all the hepatic Cu concentrations on a dry matter basis were greater than the 500 mg/kg, which is indicative of Cu poisoning, only 3 renal cortex (lambs 3, 5, 7) and 2 renal medulla (lambs 3, 7) samples contained Cu concentrations on a wet or dry matter basis of diagnostic value. According to the concentrations cited in the literature (1,2), lamb 8 did not die of Cu toxicosis, although it showed all clinical and pathological signs of Cu poisoning. Certainly, this lamb died 6 d after the beginning of the treatment, so the Cu concentrations should have fallen in response to the treatment. Lamb 4 died before treatment began and the Cu levels on a wet matter basis found in its renal cortex and medulla were very similar to those found in lamb 8. On the other hand, the "Cu on a dry matter basis/Cu on a wet matter basis" ratios varied widely in each tissue (2.9 to 7.93 in liver; 4.10 to 11.33 in renal cortex; 4.33 to 8.71 in renal medulla), which may be attributed to the state of dehydration in each animal, since several lambs had

diarrhea and were anorectic. In brief, we suggest it is necessary to analyze Cu concentrations in both liver and renal cortex on a dry matter basis for a reliable diagnosis of Cu poisoning. We also consider it necessary, when possible, to collect samples from several animals before and after the beginning of treatment in order to avoid errors in diagnosis.

The oral administration of 100 mg of Mo and 1 g of thiosulphate as a preventive treatment is recommended by Osweiler et al (1), to avoid the excessive storage of Cu in the liver and increased Cu elimination, thus reducing disease severity and minimizing tissue damage. It is the cheapest treatment for preventing Cu toxicosis in ruminants, although its therapeutic value has been considered poor or null in animals showing signs of hemolytic crisis (1,2). This affirmation could be misunderstood by practitioners and, given the low morbidity rate of Cu poisoning, it is possible that ill animals may not be treated. In our case, morbidity was high (35%) but after oral treatment to all the animals, 50% of the sick lambs recovered. Because this study is retrospective, important information about the response of individual animals is not available, so the effectiveness of this oral treatment is speculative. Treatments based on SC injection of tetrathiomolybdate have shown great effectiveness in animals with clinical signs of Cu toxicosis (5–7). For these reasons, we recommend treating all animals, including those that are sick.

Some plants growing in organic matter-rich or highly phosphated soils may have low levels of plant-available Cu. The Cu interacts with other compounds, mainly phosphates, and forms an insoluble Cu-complex that cannot be absorbed by plants. Copper is necessary for sunflower growth and a lack of this element produces important growth defects. For this reason, Cu is widely added without control to soils used for growing sunflowers (8), which is what occurred in this case. Under such conditions, sunflower meals will contain high levels of Cu or have a Cu/Mo ratio greater than 6 to 10. Furthermore, the availability of Cu in the diet should also be taken into account, because such availability is greater in feedstuffs that are low in fiber than in fresh herbage (9). It is possible that Cu availability in the sunflower meal used in this case was high. Many sheep producers and feed manufacturers are unaware of the catastrophic consequences that may result when feeds containing high concentrations of Cu combined with insufficient amounts of Mo are fed to sheep. In Spain, there are no regulations about Mo concentrations in animal feedstuffs and manufacturers often do not analyze the Cu/Mo ratio. Veterinarians must advise sheep producers about the consequences of a Cu/Mo imbalance in the diet, especially when animals are confined and consume feedstuffs with a high Cu availability (9), with no access to green forage during several months. It is necessary to take great care with feedstuffs originating from plants that require Cu, such as sunflower.

There are well recognized breed differences as regards the susceptibility of sheep to chronic Cu poisoning. Although there are no experimental studies that confirm the greater susceptibility of Segureña sheep, the high mortality observed and epidemiological data obtained are sufficient to suggest that this may be the case. As a safeguard, we think it necessary for farmers and veterinarians to monitor the diet and management of this breed in order to avoid similar cases of Cu poisoning. CVJ

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