

# Case Report Rapport de cas

## Accidental salinomycin intoxication in calves

Arash Omid, Mohammad R. Aslani, Ahmad R. Movassaghi, Mehrdad Mohri, Mohammad Dadfar

**Abstract** – Twenty-four 10- to 16-week-old calves in a dairy herd in Birjand, Iran, inadvertently received an excessive dose of salinomycin mixed with barley grain. There was 58% mortality within 10 d. The calves had high serum AST, LDH, and CK activities; histopathologic lesions in myocardium, liver, and kidneys; and clinical signs associated with acute and congestive heart failure.

**Résumé** – Intoxication accidentelle à la salinomycine chez des veaux. Vingt-quatre veaux âgés de 10 à 16 semaines faisant partie d'un troupeau laitier de Birjand, en Iran, ont reçu par inadvertance une dose excessive de salinomycine mélangée avec du grain d'orge. Il s'est produit une mortalité de 58 % dans un délai de 10 jours. Les veaux présentaient des activités sériques SGOT, LDH et CK élevées, des lésions histopathologiques du myocarde, du foie et des reins et des signes cliniques associés à une insuffisance cardiaque congestive.

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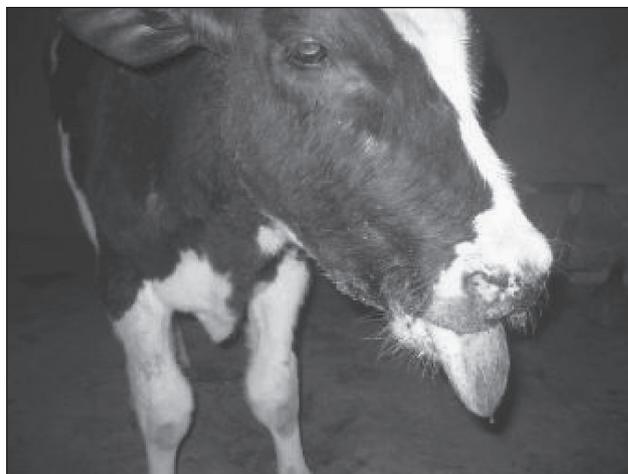
**S**alinomycin, monensin, lasalocid, narasin, and maduramicin are carboxylic ionophores intended for use as anticoccidial drugs for poultry and with a secondary role as growth promotants in ruminants (1–3). Ionophores are used to increase feed efficiency and milk production in dairy cattle (4). Minor benefits of ionophore use are prevention of acute pulmonary edema and emphysema, decreased incidence of bloat, prevention of ruminal lactic acidosis, and amelioration of ketosis in lactating cattle (3,5). However, because of a narrow safety margin and careless use, ionophores have been associated with major losses (3). Toxicity of these compounds varies with the particular ionophore compound and the species and age of animals (6–8). Salinomycin is approved as a coccidiostat for chickens and overdosage or use in non-target animal species can result in toxicosis (9).

Salinomycin intoxication has been described in turkeys (10–13), horses (14–16), pigs (17,18) and cats (19); however, it is rarely reported in cattle (20). This short communication describes a case of accidental salinomycin intoxication in calves.

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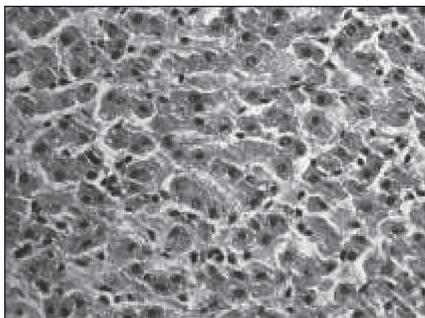


**Figure 1.** Tongue paralysis, facial edema, and sunken eyes in case of salinomycin poisoning.

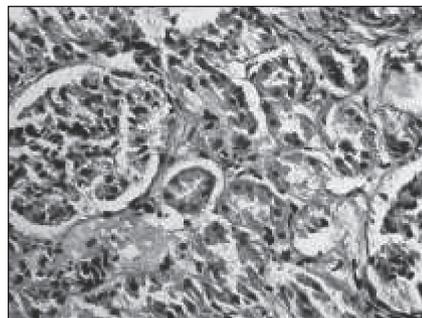
### Case description

In September 2008, salinomycin intoxication was observed on a farm with 120 Holstein-Friesian cattle located in Birjand, Iran. Twenty-four 10- to 16-week-old calves of both sexes had been fed a ration containing a high concentration of salinomycin. In this case, 1400 g of salinomycin (Salinomycin 12% Premix; Science Laboratories, Iran) had inadvertently been mixed with 20 kg of concentrate (70 g/kg) for prophylaxis against diarrhea. The ration of the calves included a mixture of concentrate with alfalfa hay and wheat straw.

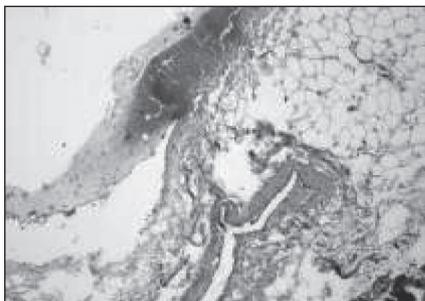
Four calves died within a short time after feeding. The affected calves were anorexic, depressed, weak, ataxic, and salivating; they had tachycardia, tachypnea, and ruminal atony. One calf displayed tongue protrusion and paralysis, pharyngeal paralysis, facial edema, and sunken eyes (Figure 1): this calf



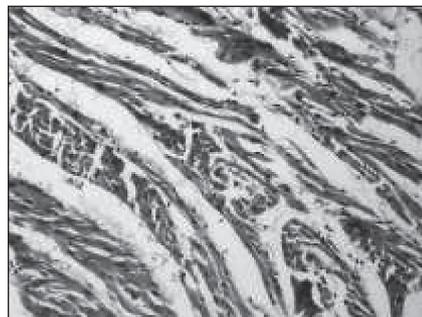
**Figure 2.** Hepatocytes showing fatty change and single cell necrosis. Hematoxylin and eosin, X640.



**Figure 3.** Renal tubules showing coagulative necrosis of the convoluted tubules. Hematoxylin and eosin, X640.



**Figure 4.** Severe epicardial hemorrhage. Hematoxylin and eosin, X160.



**Figure 5.** Focal necrosis of cardiac muscle cells. Hematoxylin and eosin, X320.

died 10 h after exposure to the salinomycin-containing ration. On the second day, other calves developed signs of intoxication including anorexia, marked engorgement of the jugular veins, severe dyspnea with crackles on auscultation of the lungs, diarrhea, and dehydration. No antidote or specific treatment is available for toxicoses induced by ionophores, thus the calves were treated symptomatically.

Venous blood samples were collected from the calves and serum aspartate aminotransferase (AST), creatine kinase (CK) and lactate dehydrogenase (LDH) activities were determined using commercial kits (Parsazmoon, Tehran, Iran) on a selective chemistry analyzer (Biotechnica; Targa, Rome, Italy).

Of 24 calves that had been exposed, 14 died within 10 d (58% mortality). Two calves died within the next 60 d (overall mortality 67%). Serum biochemical analysis revealed high activities (mean  $\pm$  standard deviation) of AST, CK, and LDH ( $626 \pm 666$  U/L,  $2902 \pm 4187$  U/L, and  $4243 \pm 2460$  U/L, respectively). At necropsy, the main gross findings were hydrothorax, hydropericardium, pulmonary congestion and edema, and swelling of the liver. Tissue samples of heart, liver, and kidneys were taken for histopathology.

Histopathological examination revealed sinusoidal hyperemia and degenerative changes especially fatty change in hepatocytes associated with single cell necrosis (Figure 2), and cell swelling and epithelial cell necrosis in renal tubules (Figure 3). There were also severe hemorrhage in the epicardium (Figure 4) and some foci of degenerate and necrotic cardiac muscle cells in the ventricular myocardium (Figure 5).

## Discussion

To our knowledge, this is the second report of salinomycin toxicosis in cattle. Salinomycin is a monovalent ionophore that

has higher affinity for  $K^+$  than  $Na^+$ . Binding to  $K^+$  can cause loss of intracellular potassium, which results in inhibition of ATP hydrolysis in the mitochondria with subsequent decreased cell energy production and death (16). In the present report, 4 calves died within 4 h after being fed grains mixed with salinomycin; these calves likely died from acute heart failure in the acute phase of the poisoning (3). Cardiac myocytes do not regenerate and fibrosis develops, predisposing the affected animals to congestive heart failure (CHF). Therefore, it is likely that deaths from CHF may occur in some animals that survive the acute toxic episode depending upon the affected area of the heart and the cardiac reserve (3,5).

The clinical and clinicopathological findings and the histopathological changes were consistent with previous reports of salinomycin and other ionophores toxicosis (3,5,21,22). Tongue and pharyngeal paralysis associated with ionophore intoxication have not previously been described in cattle (3,19).

Elevation of serum enzymes, CK, AST, and LDH may indicate damage to cardiac and skeletal muscles and has been reported in some ionophore intoxication (5). As in the present case in cattle, high mortality, ranging from 60% to 100% has been reported in horses intoxicated by ionophores (23). Sudden death within weeks or even months following ingestion of ionophores has been reported. In cattle, death occurs without struggle (24,25).

Although the primary target organ affected by toxic doses of ionophores are striated (cardiac and skeletal) muscles, degeneration of peripheral nerves and associated deficits have been reported in horses and cats, and in chickens due to salinomycin and lasalocid intoxication (16,19,26). Although all animal species are susceptible to the toxic effects of ionophores, horses and dogs are the species most severely affected (5,16).

Neonatal calves are much more susceptible to lasalocid than older calves, so that a single dose of 5 mg of lasalocid per kg bodyweight (BW) was fatal for 2 neonatal calves while daily doses of up to 15 mg/kg BW did not produce any toxic effect in calves over 7 d old (21). Salinomycin is more toxic than lasalocid. Feeding milk powder containing 420 to 810 ppm of salinomycin was fatal to 16-week-old calves (20). In the present case, 10- to 16-week-old calves, exposed to a concentration of salinomycin, estimated to be 70 000 ppm in the concentrate showed acute intoxication and mortality.

Care must be exercised in the diagnosis of ionophore toxicoses since clinical signs and lesions are not pathognomonic (2). Although a definitive diagnosis of salinomycin intoxication requires analysis of the feed for the presence and level of that compound, diagnosis in the present report was made on the basis of history of exposure and clinicopathological findings consistent with those previously reported.

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