

LETTER TO THE EDITOR

A possible anaphylactoid reaction in a cow after intravenous meloxicam

We wish to report a fatal, possibly anaphylactoid reaction in a cow that occurred shortly after the intravenous (IV) injection of meloxicam.

A 3.5 year old pregnant female Ayrshire cow, weighing approximately 500 kg was referred to the Royal (Dick) School of Veterinary Studies' Farm Animal Hospital for lateral (left pelvic limb) digit amputation. The animal's severe lameness was thought to result from a septic digital arthritis. The cow appeared to be nervous but was not sedated before being restrained in a foot-trimming crush. The affected leg was hoisted with rope for foot examination and radiography. Meloxicam (Metacam 20 mg/mL Solution for Injection for Cattle, Pigs and Horses; BoehringerIngelheimVetmedica, UK) 250 mg was administered IV 'off the needle' into the left jugular vein. Intravenous injection was confirmed by intermittently aspirating blood during injection.

Approximately 10 minutes later, the cow became agitated. Profuse lacrimation was observed and coincided with a rapidly progressing bilateral periorcular oedema and chemosis. Hypersalivation progressed to blood-tinged foaming at the mouth. There was a marked tachypnoea and dyspnoea and the cow adopted an extended neck posture. Thoracic auscultation revealed tachycardia (heart rate 120 beats minute⁻¹) and pulmonary crackles. The oral, nasal and vulvar mucous membranes and the udder became cyanotic. When released from the crush, the cow was markedly ataxic and within seconds became recumbent, gasping for air. Considering the poor medical and economical prognosis the cow was euthanased with 8 g of pentobarbital sodium injected IV. Post mortem examination findings were consistent with the presumptive diagnosis of an anaphylactoid reaction. Significant findings included diffuse laryngeal oedema and numerous petechial to echymotic haemorrhages on the tongue, larynx and tracheal mucosa.

Anaphylaxis is an immunoglobulin E mediated reaction while anaphylactoid reactions involve antibody-independent mechanisms. Clinical signs are indistinguishable between the two (Armitage-Chan 2010). Cases in cattle have been described after antibiotic and vaccine injection with an estimated occurrence of less than one animal per 10,000 (Berrier 2003). Clinical signs vary between species and depend on the tissue distribution of mast cells. However, there is evidence that mediators other than histamine, i.e., 5-hydroxytryptamine, are important in bovine anaphylaxis (Eyre et al. 1973). In cattle, respiratory signs are most prominent with severe cases progressing rapidly to ventilatory failure and death (Berrier 2003). The signs observed in the reported case, i.e. acute, severe dyspnoea, anxiety and profuse salivation progressing to collapse appear to be typical.

A definitive diagnosis of anaphylaxis or anaphylactoid reaction is seldom possible and is usually based on clinical signs, responses to treatment, necropsy findings and the exclusion of other possibilities. Polypharmacy often hinders identification of the precipitating agent although in the case reported here, the brief interval between meloxicam injection and the onset of clinical signs, and the fact that the cow had received no other drug since admission (18 hours previously) strongly implicates a causal relationship between the meloxicam and the observed anaphylactoid signs.

Hypersensitivity to non-steroidal anti-inflammatory drugs (NSAIDs) is the second-most frequent cause of drug-induced hypersensitivity in human beings (Kowalski et al. 2011). Most of these are non-immune mediated and are associated with cyclooxygenase (COX)-1 enzyme inhibition. Proposed mechanism in humans involves deprivation of prostaglandin E2 following COX-1 inhibition leading to activation of inflammatory pathways, as well as abnormalities in the lipoyxygenase pathways causing mast cell and basophil degranulation (Kowalski et al. 2011). This probably explains why hypersensitivity to COX-2 compared with COX-1 inhibitors is extremely rare. Preferential COX-2 inhibitors are able to induce IgE mediated anaphylactic reaction following prior sensitization in people (Stevenson 2004). However, the COX selectivity ratio of

meloxicam has not been established in cattle and previous exposure to meloxicam could not be verified in the animal described here. Both patho-physiological mechanisms may have contributed to the signs observed.

To our knowledge, no previous report of an anaphylactoid reaction to meloxicam in animals has been described. The Metacam 20 mg/mL Solution for Injection for Cattle, Pigs and Horses data sheet mentions a very low risk of anaphylactoid reaction that may be serious and fatal. Figures of the frequency of anaphylactoid reactions to meloxicam are difficult to establish and may be underreported by practicing veterinarians. However, meloxicam's manufacturers report that the frequency of all suspected adverse reactions (fatal, non-fatal, anaphylactoid and non-anaphylactoid) is <1 per 30,000 administrations which indicates a very low risk.

Treatment of an anaphylactic reaction usually involves cardiovascular support with epinephrine. In the reported case the decision of euthanasia was made on humane and economical grounds without attempting treatment, given the severity of clinical signs and the poor prognosis for the dam and the foetus.

Whilst adverse reactions are rare, we believe their severity justifies that the possibility is appreciated and that steps are taken for early recognition and treatment (epinephrine) whenever meloxicam is used in cattle. However, the major benefits of

NSAIDs and other analgesics in the management of painful conditions in cattle must not be overlooked, and analgesics should not be withheld because of concerns with extremely rare adverse drug reactions.

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