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Selected Topics: Toxicology

ACUTE ENCEPHALOPATHY WITH CONCURRENT RESPIRATORY AND METABOLIC DISTURBANCES IN FIRST KNOWN PARENTERAL HUMAN ADMINISTRATION OF FLUNIXIN MEGLUMINE AND ACEPROMAZINE MALEATE

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□ **Abstract—Background: Flunexin is a nonsteroidal anti-inflammatory drug approved for veterinary use in horses and cattle. Acepromazine is a phenothiazine derivative used in horses, dogs, and cats. Human exposure to these substances is rare. Case Report: We report a case of a human injection of two equine medications, flunixin and acepromazine, which resulted in altered mental status, respiratory alkalosis, gastrointestinal bleeding, and elevation of liver transaminases in a 43-year-old woman who worked as a horse trainer. The patient intentionally self-injected these medications and subsequently presented to the Emergency Department with altered mental status and lethargy. The patient required hospitalization for metabolic abnormalities, including respiratory alkalosis, and suffered a gastrointestinal bleed requiring blood transfusion. The patient ultimately recovered with supportive measures. We believe this to be the first case of concomitant injection of flunixin and acepromazine in a human. Conclusions: This report explains a case of parenteral administration of two equine medications and the subsequent complications in a patient that presented to the Emergency Department. Human exposure to veterinary medications cannot be predicted by their effect in animals due to variations in absorption, distribution, and metabolism. Physicians should be aware that individuals who work with animals may have access to large quantities of veterinary medicine. This case also exemplifies the challenges that Emergency Physicians face on a daily basis, and generates additional consideration for overdoses and intoxications from medications that are not considered commonplace in humans.** © **2013 Elsevier Inc.**

□ **Keywords—Banamine; flunixin; acepromazine; equine; veterinary; nonsteroidal anti-inflammatory drug; human**

INTRODUCTION

Flunixin meglumine (Banamine®; Intervet/Schering-Plough, Kenilworth, NJ) is a nonsteroidal anti-inflammatory drug (NSAID) that has analgesic and antipyretic properties for use in horses and beef and dairy cattle (1). It can only be prescribed by a licensed veterinarian and is regulated by the United States Food and Drug Administration. Flunixin is dosed at 0.5 mg/lb once daily and is given intravenously or intramuscularly for a maximum of 5 days. Flunixin can also be prepared in a granular form to be used after the first intravenous or intramuscular dose by placing it into the animal feed. The pharmacokinetics of flunixin have been studied in the cow, showing extensive distribution of the drug in tissues and less so in the milk of dairy cattle (2–4). However, when used in cattle or horses, precautions must be made with regard to human consumption of milk or meat from those cattle or horses; specifically 36 h from last administration of flunixin for milk use

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and 4 days from last administration for use of meat from the slaughtered animal (1).

Flunixin is considered a potent NSAID that should not be combined with other NSAIDs or steroid agents due to its potential adverse effects. The risk and adverse effect profile is similar to that of other NSAIDs and includes gastrointestinal ulceration due to inhibition of the cyclooxygenase-2 enzymes and prostaglandins, and bleeding due to the reduction in platelet aggregation and renal toxicity. Although this drug is designed for animals, there have been reports of human oral ingestion with gastrointestinal bleeding (5).

Acepromazine maleate (Atravet®; Boehringer Ingelheim Vetmedica, St Joseph, MO) is a medication used primarily in horses, dogs, and cats (6). It is a derivative of phenothiazine and was initially used in humans for treatment of chronic schizophrenia (7). Acepromazine maleate is not currently intended for use in humans and is used as an animal sedative or tranquilizer, often concomitantly with other medications as a preanesthetic (8). As a sedative, oversedation and hypotension are the major risks and bradycardia is seen rarely (8). There have been reports of sedation and hypotension with human oral ingestion requiring hospitalization (9). Dosing varies by animal species, but is 2–4 mg/100 lb in horses given intravenously, intramuscularly, or subcutaneously. There is a tablet form for use in dogs.

We report a case of intentional human exposure of parenteral flunixin meglumine and acepromazine maleate that resulted in altered mental status, respiratory alkalosis, metabolic acidosis, gastrointestinal bleeding, and an elevation of liver transaminases.

CASE REPORT

A 43-year-old woman who worked as a horse trainer presented to the Emergency Department by Emergency Medical Services. Two friends reported to providers that approximately 2 weeks earlier, she was kicked by a horse in several places on her body and had been complaining of total body pains. She has a history of alcohol abuse and had started binge drinking during the past few weeks. Her friend reported missing acepromazine and flunixin from the horse stable, and the patient was found wandering around barefoot in the snow, which prompted the call to Emergency Medical Services. The patient was confused on presentation, although admitted to injecting 15 mL flunixin and an unknown amount of acepromazine to help with her pain. It was estimated from this information that she was exposed to an NSAID dose 15 times the maximum human dose. Significant history included alcohol abuse and untreated bipolar disease. She was not on any prescription medication, but reported taking nutritional supplements, including a multivitamin, thiamine, and folic acid at home. On examination, the patient had altered mental status and was only oriented to person. She was awake but lethargic and confused. She was able to follow some commands. Her skin was slightly flush and dry. Her vital signs were temperature 36.3°C, respiratory rate 18 breaths/min, heart rate 102 beats/min, blood pressure 125/85 mm Hg, and room air oxygen saturation 99%. Her physical examination was otherwise unremarkable and included 3-mm pupils that were equal and reactive.

Initial laboratory data revealed a white blood cell count of 15.3 thousand/μL and hematocrit of 37%. Her sodium was 134 mEq/L, potassium was 3.2 mEq/L, chloride was 105 mEq/L, CO_2 was 15 mg/dL, and glucose was 217 mg/dL. Initial arterial blood gas, performed 14 h after arrival, revealed a pH 7.57, pCO_2 of 17 mm Hg, pO_2 of 126 mm Hg, base excess of -5 mEq/L. Initial liver transaminases and coagulation studies were in the normal range. Acetaminophen, salicylate, ethanol, ethylene glycol, isopropanol, acetone, and methanol blood levels were undetectable. A urine toxicology screen was positive for benzodiazepines; however, amphetamines, cocaine, opiates, and tetrahydrocannabinol were all negative. Testing for flunixin or acepromazine was not available through our laboratory resources and the manufacturer was not contacted to determine detection by further analytical testing. Initial and repeat electrocardiogram showed sinus tachycardia and borderline t wave abnormalities. A computed tomography scan of the head and a chest x-ray study were normal.

There was no treatment given to the patient in the prehospital setting. In the Emergency Department, the patient was given normal saline, potassium chloride supplementation, and multivitamins, thiamine, and folic acid. The patient was admitted to the intensive care unit for overdose of flunixin and acepromazine and worsening alkalemia. The inpatient course was complicated by recurrent respiratory alkalosis noted within 24 h of admission. The arterial pH increased to 7.6 and pCO_2 decreased to 14 mm Hg, all of which gradually resolved by day 4 of the hospital admission On day 2 of admission, the hematocrit decreased to 17% from 37%, the patient had guaiac-positive stools, and was thought to have an upper gastrointestinal bleed from the flunixin overdose and heavy alcohol use. She required a transfusion of packed red blood cells, was started on a proton-pump inhibitor, and was scheduled for an outpatient endoscopy. In addition, on day 2, elevation of liver transaminases were noted, which peaked later that day to , alanine aminotransferase 190 IU/L, aspartate aminotransferase 382 IU/L, total bilirubin 3.1 mg/dL, and direct bilirubin 2.4 mg/dL. Her coagulation studies became marginally elevated on day 2 with a prothrombin time of 15.3 s and an international normalized ratio of 1.2. Partial