Clinical communication — Kliniese mededeling

First report of suspected ethylene glycol poisoning in 2 dogs in South Africa

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INTRODUCTION

Ethylene glycol (E/G) is a serious emergency in both veterinary and human medicine. Ethylene glycol (E/G) is the active anti-freeze principle in radiator water additives. It is odourless, colourless and has a sweet taste. As little as 5 ml or 20 ml is sufficient to kill a cat or a dog, respectively. Ethylene glycol is rapidly absorbed and metabolised in the liver to oxalate, which is deposited as calcium oxalate in the kidneys causing irreversible damage. This report describes 2 dogs that were suspected to have ingested ethylene glycol. The report contains a description of the 3 stages of ethylene glycol toxicity as well as a short discussion of the treatment. Public awareness about the dangers of anti-freeze will help in limiting exposure of pets and humans to this potentially fatal toxin. Veterinarians need to be aware of anti-freeze toxicity as delayed recognition and treatment will lead to the death of the patient.

Key words: acute renal failure, ethanol, ethylene glycol, 4-methylpyrazole.

Fig. 1: Ethanol and ethylene glycol metabolic pathways.6

ABSTRACT

Ethylene glycol (anti-freeze) toxicity is a serious emergency in both veterinary and human medicine. Ethylene glycol (E/G) is the active anti-freeze principle in radiator water additives. It is odourless, colourless and has a sweet taste. As little as 5 ml or 20 ml is sufficient to kill a cat or a dog, respectively. Ethylene glycol is rapidly absorbed and metabolised in the liver to oxalate, which is deposited as calcium oxalate in the kidneys causing irreversible damage. This report describes 2 dogs that were suspected to have ingested ethylene glycol. The report contains a description of the 3 stages of ethylene glycol toxicity as well as a short discussion of the treatment. Public awareness about the dangers of anti-freeze will help in limiting exposure of pets and humans to this potentially fatal toxin. Veterinarians need to be aware of anti-freeze toxicity as delayed recognition and treatment will lead to the death of the patient.

Key words: acute renal failure, ethanol, ethylene glycol, 4-methylpyrazole.

never been reported in South Africa. The aim of this case report is to inform South African veterinarians of the clinical signs and treatment of anti-freeze toxicity. This case report also describes the clinical signs, treatment and outcome of 2 dogs in South Africa that were suspected to have ingested anti-freeze.

CASE HISTORY

A 3-year-old, intact female Labrador retriever was referred to the Onderstepoort Veterinary Academic Hospital due to severe, uncontrollable seizures.

The previous morning the animal appeared ataxic and was vocalising. She was also vomiting and polyuric. The owner took her to a veterinarian where the dog was treated with amoxycillin/clavulanic acid (Clavumox RTU, Pfizer, Sandton) (20 mg/kg), prochlorperazine (Stemetil, Aventis Pharma, Midrand) (0.5 mg/kg) and metoclopramide (Clopamon, PharmaCare, Port Elizabeth) (0.2 mg/kg). Later that evening the dog appeared disoriented and was still vomiting. The owner returned the dog to the veterinarian. The animal was hospitalised and placed on Lactated Ringers (Lactate Ringer’s, Fresenius Kabi, Port Elizabeth). She was also treated with morphine (Micro Morphine, Micro HealthCare, Bethlehem) (0.2 mg/kg), trimethoprim/sulphonamide (Norotrim 24, Pharmacia Animal Health, Craigall) (20 mg/kg) and metoclopramide (see above). During the night the dog had haematemesis and started having seizures. She was treated with diazepam (Pax, PharmaCare, Port Elizabeth) (0.5 mg/kg), but it only controlled the seizures for a short period. The dog was then referred to the Onderstepoort Veterinary Academic Hospital.

Clinical examination revealed a semi-comatose dog with increased respiration (72 breaths/minute). She was well hydrated, but no bladder could be palpated. A bloody discharge was noted at the vulva. Abdominal ultrasound was performed to rule out a pyometra and to collect urine via cystocentesis. No bladder could be seen on ultrasound and no signs of a pyometra. Results of haematological analysis were normal. Serum chemistry revealed a 4 times normal elevation of urea (33.5 mmol/l, normal 3.6–8.9 mmol/l) and creatinine (704 µmol/l, normal 40–133 µmol/l). Potassium and blood glucose levels were normal, but the dog had severe hypocalcaemia (Ca²⁺ = 0.25 mmol/l, normal 1.25 mmol/l). Venous blood gas analysis indicated severe metabolic acidosis [pH = 7.143 (normal 7.35–7.45); HCO₃⁻ = 8.7 mEq/l (normal 18–24 mEq/l)]. Severe acute renal failure was suspected. A urinary catheter was placed – the dog was anuric and therefore no urinalysis could be performed.

The owners were contacted again for more information regarding medications given and whether their dog could have ingested any toxins. The owners searched their house and found an open container of radiator fluid in the garage. Their car broke down in the driveway and the tow truck company emptied the radiator fluid into this container prior to towing the car. The container was left open in the garage where the dogs had free access to it. There were signs that the dogs had drunk from the container. No further diagnostic tests were possible to confirm the E/G toxicity.

A commercial test kit (Allelic Biosystems Ethylene Glycol Test Kit, PRN Pharmacal, Inc., Pensacola) is available abroad. In South Africa, a mass spectrophotometry test is available that can be done on urine or plasma (Niehaus, Dyson and Lancet Laboratory). The test results however are only available after 3 days and cost about R400 per sample.

Treatment with an intravenous infusion of ethanol as a 20% solution (Ethanol 99.9%, Medicolab, Johannesburg) at 5 ml/kg every 4 hours was immediately instituted. Other medications to treat the acute renal failure were also given: Mannitol at 0.5 g/kg initially and thereafter 0.25 g/kg (Mannitol 20%, Fresenius Kabi, Port Elizabeth); furosemide (Salix, Intervet, Johannesburg) (4 mg/kg initially and then 2 mg/kg); sucralfate (Ulsanic, PharmaCare, Port Elizabeth) (5 ml/20 kg), cimetidine (Lenamet, PharmaCare, Port Elizabeth) (5 mg/kg) and a constant rate infusion of dobutamine at 5 µg/kg/min over 6 hours (Dobutrex, Fresenius Kabi, Port Elizabeth).
Intravenous calcium (Calcium gluconate, Fresenius Kabi, Port Elizabeth) (1 m/kg) was given to try and control the seizures and to correct the hypocalcaemia. The seizures continued and due to the poor prognosis the dog was euthanased 12 hours later. The owner declined a post mortem examination and took the dog home.

The owner was asked to bring in her other 2 Labrador Retrievers. The one, a 2-year-old male, had a history of vomiting the previous day, but appeared normal and alert at presentation. A urinalysis was performed. The urine had a lime green colour. Calcium oxalate crystals (mono-hydrate), renal tubular epithelial (RTE) cells and RTE cells were present in the urine. Serum urea and creatinine levels were both 3 times above normal (urea 30 mmol/l (normal 3.6–8.9 mmol/l); creatinine 600 µmol/l (normal 40–133 µmol/l)). The calcium levels however were normal (1.32 mmol/l, normal 1.25 mmol/l). The 3rd dog’s urinalysis and serum chemistry results were normal (urea 4.6 mmol/l (normal 3.6–8.9 mmol/l); creatinine 92 µmol/l (normal 40–133 µmol/l)).

The 2nd dog was admitted for treatment and observation. A urinary catheter was placed. The treatment was the same as for the 1st dog, except that no calcium was given. On day 1 this dog was still producing adequate amounts of urine. He became severely hyperactive during the ethanol infusion and was sedated with diazepam (Fpx, PharmaCare Ltd, Port Elizabeth – 0.5 mg/kg iv). Over the next 24 hours he deteriorated markedly and his urine production became minimal (<1 m/kg/hour). The dog died 36 hours after presentation. Again the owner declined a post mortem and took the dog home. The 3rd dog remained healthy throughout this period of time and received no treatment.

**DISCUSSION**

**Ethylene glycol (E/G) toxicity in dogs** has never been reported in South Africa. In South Africa many people are unaware of the danger posed by anti-freeze in radiator fluid. People may also not know that radiators in South Africa contain anti-freeze. This lack of knowledge could lead to accidental poisoning of children and pets.

The owners of these 2 dogs were not aware of the danger of E/G. As mentioned before, the container with radiator fluid was inadvertently left open on the garage floor where the dogs had free access to it. This could have been the cause of losing 2 of their 3 pets.

Early diagnosis of E/G poisoning is essential for a favourable outcome. Often this is difficult due to inadequate history and non-specific clinical signs, which can mimic those of many other conditions, as seen in the cases described here.

Acute intoxication is a rapidly, progressive, life-threatening emergency with a variety of clinical signs and problems. Knowledge of the 3 different stages and presentation is important for quick and effective treatment.

Treatment involves preventing further absorption of ethylene glycol from the stomach, to increase secretion of both ethylene glycol and its metabolites and to prevent further metabolism of ethylene glycol2,3,4.

Further metabolism is prevented by inhibiting alcohol dehydrogenase (ADH), the enzyme responsible for the initial reaction in the metabolic pathway of ethylene glycol. (Fig. 1). Ethanol is the preferred substrate of ADH and therefore, by saturating the enzyme with its preferred substrate, less ethylene glycol is then metabolised and also at a lower rate and excreted unchanged by the kidneys5. Ethanol thus serves as an antidote for ethylene glycol toxicity. Ethanol itself can cause severe CNS and respiratory depression and can confuse the situation. The occurrence of hyperexercitability of the one dog during the ethanol treatment will need further investigation and is beyond the scope of this case report.

An alternative can be found in 4-methylpyrazole (fomepizole – Antizol, Orphan Medical) that has been shown to be a good substrate for ADH and is both safe and effective5,6.

Intensive monitoring is essential in these patients and early supportive intervention may lead to a favourable outcome. An indwelling urinary catheter should be placed to monitor urine output. Other treatments should include haemodynamic support and ventilatory support if needed. Sodium bicarbonate administration is controversial and should be based on determination of serial serum bicarbonate concentrations. The aim is to increase the patient’s pH to 7.2 to reduce the risk of life-threatening haemodynamic complications. Calcium gluconate may also be administered especially in animals showing seizures or tetanic spasms secondary to hypocalcaemia.

In animals that present with oliguric renal failure most of the ethylene glycol has already been metabolised, but there may still be some small benefit in trying 4-methylpyrazole or ethanol. Re-establishment of diuresis is of utmost importance for survival and where it is not possible, haemodialysis or peritoneal dialysis should be considered. It may take several weeks to months for the kidneys to heal and in some cases even kidney transplants were performed10.

Prognosis of ethylene glycol toxicity depends largely on the amount ingested and time since ingestion. Patients presenting less than 5 hours after ingestion have an excellent prognosis with 4-methylpyrazole (fomepizole) or ethanol treatment. Patients with oliguria and azotaemia have a very poor prognosis11. Unfortunately both cases discussed here arrived in Stage 3, i.e. azotaemia.

Fomepizole is currently not available in South Africa, but can be imported. Delivery takes 10–12 days, but fortunately the drug has a long shelf life (100 mg = R250; dose 20 mg/kg iv). Ethanol (which is readily available) has been shown to be as effective, but does have more side-effects. It is important to use absolute (medicinal) ethanol and not denatured (industrial) ethanol. The denaturing agent in industrial ethanol is toxic. There are also reports of using Vodka if medicinal ethanol is not available. Owing to the high alcohol contents it is relatively sterile and can be given intravenously, but it is still advised to administer both the ethanol and the vodka through an in-line filter12.

Some of the new radiator anti-freeze products that are available internationally contain propylene glycol, which has less toxic effects than ethylene glycol, and most products now also contain bittering agents to lessen accidental ingestion. Whether this is true for radiator anti-freeze products in South Africa is unknown and therefore public awareness about the dangers of anti-freeze will help with limiting exposure of pets as well as children to this potentially fatal toxin.

Veterinarians need to be aware of anti-freeze toxicity as delayed recognition and treatment could result in the death of the patient.

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