Novel treatment (new drug/intervention; established drug/procedure in new situation)

Antifreeze on a freezing morning: ethylene glycol poisoning in a 2-year-old

Gayle Hann,¹ Dana Duncan,² Gopakumar Sudhir,³ Peter West,⁴ Dalbir Sohi¹¹Paediatrics Department, North Middlesex Hospital, London, UK;²Medical Department, St George's University, Grenada, West Indies, Grenada;³Anaesthetics Department, North Middlesex Hospital, London, UK;⁴Biochemistry Department, North Middlesex Hospital, London, UK**Correspondence to** Dr Gayle Hann, gaylehann@yahoo.com**Summary**

This case report describes the presentation and management of a 2-year-old child who ingested a potentially fatal amount of ethylene glycol (EG). There are few published cases worldwide of EG poisoning in children managed with fomepizole. All cases described in the literature were managed in a paediatric intensive care unit. In this case, the child presented irritable, pale and confused with high anion gap metabolic acidosis. As there were no paediatric intensive care beds available in the region, the child was successfully managed in a high dependency area in our district general hospital. The child fully recovered and was discharged home in 7 days. The authors believe that multi-disciplinary team management and the use of fomepizole contributed to the positive outcome and this case raised many useful learning points.

BACKGROUND

Approximately 40 000 children each year attend emergency departments in the UK for suspected poisoning.¹ Health professionals turn to the National Poisons Information Service (NPIS), which provides evidence based information by telephone and online (TOXBASE). In 2007/8, the NPIS received over 525 000 poisons related enquiries.² 89.1% of telephone enquiries involved children under 5 years of age, reflecting the patterns of accidental childhood exposures in the general population.² Toxic alcohols were the second most commonly implicated products in referrals to NPIS consultants. Significant ethylene glycol (EG) poisoning is rare with only four cases recorded by NPIS in children under 5 years of age in 2007/8.² In USA in 2002, EG poisoning resulted in 40 deaths and 254 near-fatalities.³ There is very little published data on the outcome of EG poisoning in the UK.

The effects of ethylene glycol

EG is used in automotive antifreeze, engine coolants and hydraulic brake fluids.⁴ Due to its sweet taste, it poses a particular risk to children. Effects may be seen within minutes manifesting as inebriation, nystagmus, seizures, paralysis and coma. Sequelae include tachycardia, hypertension, calcium oxalate crystal formation in the urine and an anion gap metabolic acidosis. Hypoxia, congestive heart failure and acute respiratory distress syndrome can occur. After 24 h, renal symptoms typically predominate, which if left untreated, can lead to death from multi-organ failure.

CASE PRESENTATION

A 2-year-old boy was brought to the emergency department in the early morning hours, after his parents discovered he had accidentally drunk antifreeze. His father had diluted the antifreeze into a bottle of mineral water and stored it next to other bottles of mineral water. The

family reported he had been pale and lethargic associated with bouts of vomiting immediately after consumption of formula milk. In the morning, when another bottle was being prepared, the mistake was discovered. On arrival to the accident and emergency department of our hospital, he was noted to be ashen, irritable and confused. He was tachycardic with a heart rate of 170 per min and had deep sighing respiration. His initial capillary blood gas showed a high anion gap metabolic acidosis with a pH 7.24, pCO₂ 2.92 kPa, bicarbonate 9.1 mmol/l, base excess -16.7 and a lactate of 20 mmol/l.

It was estimated that he had ingested approximately 17 ml of pure EG. With 90 ml being the estimated fatal dose for a 70 kg adult, our 2-year-old patient had consumed a potentially fatal quantity of EG. Based on this information, his clinical status and the severe metabolic acidosis, the paediatric and anaesthetic team were involved in the management of this child. The Children's Acute Transport Service (CATS) was contacted, as it was predicted that this child would require transfer to a paediatric intensive care unit (PICU). The on-site clinicians were informed there were no PICU beds in London, the nearest PICU bed being 87 miles away. A continuous infusion of sodium bicarbonate was started as well as maintenance intravenous fluids. The on call pharmacist managed to locate a stock of fomepizole, with the aid of the NPIS team, at a hospital 15 miles away.

For the first 2 h, the child was managed by a multi-disciplinary team of seven doctors and nurses. As the child was supporting his own airway, the decision not to intubate was made. The capillary blood gas at 1 h showed an initial deterioration in pH but a small improvement in the base excess and lactate; pH 7.195, pCO₂ 3.78, HCO₃ 10.6 mmol/l, base excess -16.3, lactate 18 mmol/l. Four hours after the child's arrival, an initial infusion of fomepizole was started. One hour after the first dose of fomepizole

the pH, lactate and base excess had improved to pH 7.24, $p\text{CO}_2$ 3.36 kPa, HCO_3^- 10.7 mmol/l, base excess -15.2, lactate 13.1 mmol/l. Hourly blood gases were performed and the child was monitored for 11 h in the resuscitation area. During the first 11 h, the child remained pale, lethargic and had intermittent bouts of vomiting. At 24 h post-ingestion, he was suspected to have had a seizure with an episode of unresponsiveness associated with desaturation and bradycardia.

The first (pretreatment) EG level was 84.624 mg/l, demonstrating significant ingestion, yet below the 500 mg/l level recommended for haemodialysis. After the second dose of fomepizole, the EG level fell to 31 mg/l. The child continued to improve clinically. A further two doses of fomepizole were given over the next 24 h, making a total of four doses, until the EG level was undetectable. Urine output was monitored for calcium oxalate crystal formation and remained clear over the next 72 h. Urea and electrolyte estimations revealed no abnormality apart from hypokalaemia, which was likely as a result of alkalinisation therapy. The child was discharged after 7 days, having fully recovered with no sequelae to EG poisoning and no adverse effects of fomepizole.

DIFFERENTIAL DIAGNOSIS

It is important to state that where the poison is not known, a high anion gap metabolic acidosis, can guide the physician towards diagnosis.⁵

Other drugs that can cause a high-anion gap metabolic acidosis include:

- ▶ Methanol
- ▶ Salicylates

Other toxins that can cause a high-anion gap metabolic acidosis are:

- ▶ Isopropyl alcohol
- ▶ Butoxyethanol

TREATMENT

There are currently three treatment options for EG poisoning; fomepizole, alcohol and haemodialysis. Fomepizole, is a competitive inhibitor of alcohol dehydrogenase (ADH), the enzyme responsible for the oxidation of ethanol to acetaldehyde. ADH also catalyses the initial steps in the oxidative metabolism of EG to its toxic metabolites. Alcohol can therefore be used as an antidote, and the affinity of ethanol for ADH is 100 times that of EG. However, the dose is hard to calculate and its effect unpredictable. Haemodialysis is recommended for severe metabolic acidosis, very high EG concentrations, renal failure, deteriorating condition despite supportive measures and severe electrolyte imbalance.

OUTCOME AND FOLLOW-UP

The child was reviewed 4 months after the incident and continued to remain well.

DISCUSSION

To our knowledge, this is the first documented case of severe EG poisoning managed outside an ITU setting with the use of fomepizole and alkalinisation therapy. The case presented us with various management issues in a busy

district general hospital. The child presented out of hours on a weekend requiring continuous monitoring and treatment, the closest laboratory able to process EG levels 119 miles away, and there was a time lag between availability of the previous EG level and the timing of the antidote. This meant that the last dose may have been given when the EG level was already undetectable. This has financial and patient safety implications, as fomepizole is a costly drug at an estimated £2500 per dose and is only stocked in a few centres.

Evidence

There is only anecdotal evidence on the management of EG poisoning in children. A literature review of Medline, Mbase, PubMed, AMED, evidence based reviews, Cochrane Database of Systematic Reviews and NHS guidance (1966–2010) using the following search terms (ethylene and glycol and poisoning and paediatric). ti,ab found 15 papers in the English language. This included a review article,⁶ a case series⁷ and 13 case presentations. The review article⁶ described 10 published cases of children who had ingested EG and were treated with fomepizole. The median age of the children was 5.5 years and the mean recorded arterial pH was 7.27 (range 7.03–7.38), serum bicarbonate concentration was 13 mEq/l (range 2–25) and EG concentration was 2140 mg/l (range 130–3840). Only two patients were haemodialysed. Two further cases were originally treated with ethanol but switched to fomepizole because of adverse effects.⁸ The only adverse reaction to fomepizole reported was transient nystagmus in a 6-year-old with a serum EG concentration of 130 mg/l.⁹

CONCLUSION

Our case report suggests that it is possible to manage a child with a potentially fatal EG poisoning outside the ITU setting with multi-disciplinary team work in a district general hospital. However, there are logistical, resource and expertise implications in managing such a case in a district general hospital setting. The main learning point from this case is that multi-disciplinary team management is essential with good communication between paediatrics, CATS, anaesthetics, pharmacy, biochemistry teams and the National Poisons Information Service. Our case also has important lessons for public health regarding the safe storage of household chemicals which are potentially lethal poisons.

Learning points

- ▶ Fomepizole, when available, is a safe alternative to ethanol in the treatment of children with EG poisoning.
- ▶ If the poison taken is not known, the anion gap may help narrow down the potential drug or toxin ingested.
- ▶ It is possible to manage a child with a potentially fatal EG poisoning outside the ITU setting with multi-disciplinary team work in a district general hospital.

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Competing interests None.

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