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CASE REPORT

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Survival of formalin intoxication in a 13-year-old Thoroughbred gelding

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[Correction added on 25 August 2023, after first online publication: The headings in the Abstract section have been corrected in this version.]

Abstract

Background: Formalin intoxication via the gastrointestinal route has not been previously reported in the horse. Whereas ingestion of formalin in humans, although rare, is well documented. Majority of human cases are either accidental, suicidal or homicidal and often lead to fatality, with a reported lethal formaldehyde dose equating to 0.12 – 0.16 g/kg bwt.

Objectives: To describe a single case report of the clinical management of an adult horse referred to a veterinary teaching hospital following accidental administration of 10% formalin via nasogastric tube.

Methods: A 13-year-old Thoroughbred gelding originally presented to the referring veterinarian for colic where 1.8 L of 10% formalin was accidentally administered instead of mineral oil via nasogastric intubation, a potentially lethal dose of formaldehyde (0.12 g/kg bwt). Approximately 20-hours following 10% formalin administration the horse was admitted to the referral hospital with moderate tachycardia, occasional ectopic beats, tacky and hyperaemic mucous membranes, delayed capillary refill time, reduced borborygmi, and pronounced digital pulses. Diagnostic investigations included laboratory blood analysis, urinalysis, electrocardiogram, abdominal ultrasound, palpation per rectum and gastroscopy.

Results: Patient assessment found evidence of toxicity to the gastrointestinal tract, hypovolaemia and risk for laminitis. Intensive care included fluid and electrolyte therapy, anti-inflammatories and analgesia, continuous digital cryotherapy, gastro-protectants and other methods of gastrointestinal support. The horse was discharged from hospital on day 14 with no long-term complications and the client-veterinarian relationship was preserved.

Discussion: In human cases of ingestion, gastrointestinal injury is typically accompanied by severe metabolic acidosis and multiple organ dysfunction syndrome due to toxicity of other body systems that can contribute to non-survival. Formaldehyde toxicity in the present case predominantly affected the gastrointestinal tract, most likely a direct result of the route of administration. Aside from gastrointestinal injury, primary toxicity of other body systems was not confirmed. To prevent this medical

error recurring, the referring veterinary clinic revised their labelling and storage of 10% formalin.

Conclusion: This is the first report of systemic formalin intoxication in the horse. Following a high dose of 10% formalin (0.12 g/kg bwt formaldehyde) enterally, the horse survived having received intensive supportive care based on human guidelines for ingested formalin.

KEYWORDS
formaldehyde, formate, horse, medical error, toxicity

1 | INTRODUCTION

Formalin is the term used for a 40% solution of formaldehyde in water. Formaldehyde is a colourless, water-soluble, reactive gas known to have irritant, corrosive and toxic properties. Common medical uses of formalin include tissue preservation ('fixative'), as a disinfecting agent and for treatment of haemorrhage-related conditions in both human and veterinary medicine. In equine practice, formalin is used in vivo as a principal treatment of ethmoid haematomas.[1–4] The composition of formalin most commonly used in veterinary medicine is 10% formalin (10% of a 40% formaldehyde solution) which is equivalent to a 4% formaldehyde solution.[5]

Formaldehyde toxicity can occur with ingestion, inhalation or absorption of formalin via any surface of the body.[5] Formaldehyde ingestion at high doses is extremely corrosive to the gastrointestinal tract and toxic to body tissues, often leading to fatality. Local necrosis of the alimentary epithelium leads to mucosal injury, inflammation and potential ulceration and perforation.[5] Following systemic absorption, formaldehyde is oxidised to formic acid (formate) by the enzyme formaldehyde dehydrogenase produced by hepatocytes and by erythrocytes, myocytes and neurons to a lesser degree.[5,6] This can cause metabolic acidosis and necrosis of many cell types, resulting in multiple organ dysfunction syndrome (MODS). As such, formalin ingestion in humans leads to gastrointestinal disease (abdominal pain, vomiting, diarrhoea, haematemesis, melena), cardiovascular compromise (severe tachycardia, arrhythmias), abnormal mentation (including seizures) and acute renal tubular necrosis leading to acute renal failure.[5]

Reports of enteral formalin intoxication in veterinary species are primarily limited to rodents in a research setting.[7–10] Two equine case reports describe severe neurologic toxicity following intralesional formalin of an ethmoid haematoma and an ethmoid adenocarcinoma (due to diffusion of formalin through the cribriform plate), but there are no equine reports on formalin intoxication by gastrointestinal route.[11,12] Hence, the pathophysiological effect of formaldehyde toxicity on horses is not well understood. In both human and veterinary scientific literature, precise lethal doses remain undetermined. However, ingestion of >10 g of formaldehyde by an adult human is known to be fatal, and fatal doses less than this have also been reported across the world.[5,13–17] Ten grams of formaldehyde would equate to a lethal dose of 0.12–0.16 g/kg in an average adult human.[18] This report describes the successful medical management of formalin intoxication in an adult horse after accidental administration via nasogastric intubation.

2 | CASE DESCRIPTION

2.1 | History

A 13-year-old Thoroughbred gelding was presented to Massey University Equine Veterinary Clinic (MU-EVC) due to accidental administration of 1.8 L of 10% formalin via nasogastric tube by the referring veterinarian approximately 20 h previously. The day before, the horse was presumptively diagnosed and medically managed for a large intestinal impaction. This included three farm visits to administer intravenous (IV) analgesia (flunixin meglumine, xylazine, dipyrone), anti-spasmodic therapy (*N*-butyl-scopolamine IV), IV fluids, and enteral fluid with electrolyte therapy via nasogastric intubation. In the evening, 1.8 L of 10% formalin was accidentally administered by nasogastric tube instead of mineral oil. This accident was identified the following morning by the veterinarian while the work vehicle was prepared for the day. Mineral oil and 10% formalin were stored in identically coloured (white with a red lid) generic 2-L containers, as both of these liquids were bought in bulk and decanted into smaller containers for ambulatory use (clinical cases and post-mortem cases, respectively). However, these containers were usually kept in separate locations within the vehicle and on this day for unknown reasons the 10% formalin container was in a different location. Furthermore, the original hand-written label on the 10% formalin container was worn. The call was end of day around a completely booked schedule with more farm visits remaining, so the veterinarian was under time pressure and had not taken any breaks. Following consultation with MU-EVC, referral was recommended due to concerns that a potentially lethal dose of formaldehyde was administered, based on extrapolations from the human literature. The client was notified, reassured that all costs pertaining to the 10% formalin administration would be covered by the referring practice and the veterinarian re-evaluated the horse on-farm prior to referral. Prior to transport (2 h travel time), the horse was quiet, alert, responsive, tachycardic (60 bpm) and normothermic (37.7°C). Analgesia

(butorphanol 40 mg subcutaneously) and IV fluids (5 L Hartmann's solution) were administered.

2.2 | Case presentation

On presentation to MU-EVC the horse weighed 596 kg, and a formaldehyde dose was calculated: 0.12 g/kg. He had generalised sweating, was quiet, alert and responsive, tachycardic (72 bpm) with an irregularly irregular rhythm, normopnoeic (20 bpm) and normothermic (38.1°C), with hyperaemic and tacky mucous membranes. Capillary refill time (CRT) was 2.5 s, borborygmi were markedly reduced in all quadrants, extremities were normothermic on palpation, and digital pulses were pronounced in all limbs. No cranial nerve deficits or other neurologic abnormalities were appreciated. Electrocardiography (ECG) showed sinus tachycardia and infrequent (~1 per 5–10 min) ectopic P-QRS-T complexes (shortened R-R interval with normal QRS morphology) suggestive of supraventricular premature complexes (SVPC). The ECG was obtained during initial case evaluation (<1 h), 24-h telemetric ECG was not conducted. Serum cardiac troponin I was not evaluated as this laboratory test had a 3–4 day turn around.

Gastric lavage obtained 2 L of net gastric reflux, which was bile-coloured and smelt of formaldehyde. Gastroscopy revealed no overt lesions of the squamous mucosa, but it was diffusely wrinkled and shiny. Examination per rectum returned dry, dark faeces within the rectum, a normal pelvic flexure, and a suspected small colon impaction. Transcutaneous ultrasonography of the abdomen demonstrated normal appearance and thickness of the stomach wall, normal appearance of large intestinal structures, but mildly thickened (6 mm; normal reference 0.3 ± 0.02 cm)[19] and hypomotile loops of small intestine were present diffusely, including the duodenum.

Haematology (Table 1) and biochemistry (Table 2) on admission identified leukopaenia characterised by neutropaenia with a left shift, normocythaemia, hypoproteinaemia due to hypoalbuminaemia, mildly increased urea, hyperglycaemia, hyperlactataemia, mild hypochloraemia and marked hypocalcaemia (total and ionised). Venous blood gas analysis (VBGA; Table 3) on admission identified a mildly increased

TABLE 1 Haematology results during hospitalisation in a case of formalin intoxication.

	Day 1	Day 3	Day 5	Day 11	Units	Reference range
RBC	8.98	8.7	8.8	8.7	$\times 10^{12}$/L	7.0–11.8
HCT	37.9	39.0	39.0	38.0	%	30.0–47.0
WBC	3.82	2.5	6.3	9.8	$\times 10^{9}$/L	5.7–12.0
Lymphocytes	1.6	1.8	0.8	2.5	$\times 10^{9}$/L	1.5–6.3
Neutrophils-segmented	2.03	0.4	4.3	6.5	$\times 10^{9}$/L	2.9–6.9
Neutrophils-band	Suspected	0.1	0	0	$\times 10^{9}$/L	0
Monocytes	0.19	0.2	0.8	0.5	$\times 10^{9}$/L	0.15–0.7
Fibrinogen		4.0	3.4	5.8	g/L	1.5–5.0
Serum amyloid A				<1	mg/L	0–8.0

TABLE 2 Biochemistry results during hospitalisation in a case of formalin intoxication.

	Day 1	Day 3	Day 11	Units	Reference range
Total protein	49	42	52	g/L	52–72
Albumin	21	22	25	g/L	28–38
Globulin	29	20	27	g/L	21–39
Urea	12.5	4.5	5.8	mmol/L	3.3–8.7
Creatinine	128	103	116	μmol/L	81–164
Calcium (total)	1.54	2.03	2.47	mmol/L	2.9–3.3
Calculated corrected calcium[a]	1.92	2.39	2.77		
Magnesium (total)		0.66	0.66	mmol/L	0.68–0.9
Calculated corrected magnesium[b]		0.71	0.7		
Phosphate		1.07	1.09	mmol/L	0.7–1.7
Sodium		136	141	mmol/L	131–141
Potassium		3.3	3.6	mmol/L	3.0–4.6
Chloride		103	99	mmol/L	93–105
Bilirubin	37	77	38	μmol/L	13–39

Note: The following values remained within reference range: creatinine kinase (CK), aspartate aminotransferase (AST), gamma-glutamyl transferase (GGT), glutamate dehydrogenase (GLDH).
[a]Calcium correction calculated using https://www.omnicalculator.com/health/corrected-calcium.
[b]Magnesium correction calculated using https://www.omnicalculator.com/health/corrected-mg.

TABLE 3 Venous blood gas analysis results during hospitalisation in a case of formalin intoxication.

Value	Day 1 2 pm	Day 1 10 pm	Day 2 8 am	Day 2 8 pm	Unit	Reference range
pH	7.525	7.413	7.404	7.373		7.35–7.45
Partial pressure CO_2	30.5	44.9	49	43.7	mmHg	36–46
Partial pressure O_2	52.7	34.1	33.1	30.3	mmHg	n/a
Bicarbonate (HCO_3^-)	25.2	28.7	30.6	25.4	mmol/L	25–30
Sodium	137	137	139	138	mmol/L	128–142
Potassium	2.7	2.8	2.7	3	mmol/L	1.9–4.1
Calcium (ionised)	0.86	1.03	1.1	1.26	mmol/L	1.25–1.75
Chloride	96	96	97	99	mmol/L	100–111
Total CO_2	25.5	29.1	31	26.1	mmol/L	24–32
Anion gap including potassium	29	16	15	17	mmol/L	5–15
Base excess	2.9	3.6	5	−0.1	mmol/L	−5 to 5
Glucose	9.4	8.1	7.1	7.1	mmol/L	3.4–7.4
Lactate	2.54	1.35	0.86	0.85	mmol/L	0.3–1.5

pH, low partial pressure CO_2, normal base excess and bicarbonate, and markedly increased anion gap. Stall side urinalysis was performed 5 h after fluid therapy was initiated and identified renal glucosuria (3+) (concurrent blood glucose of 8.1 mmol/L), proteinuria (1+) (potentially spurious due to alkaline pH),[20] and a urine specific gravity (USG) of 1.022. Haematology, biochemistry and VBGA results over time are shown in Tables 1–3, respectively.

In accordance with the history, results of the initial examination and clinical pathology were consistent with what might be expected with formaldehyde toxicity: hypovolaemia, gastrointestinal disease (small intestinal thickening and hypomotility, abnormal gross appearance of gastric squamous mucosa, leukopaenia due to neutropaenia and left shift, hypoalbuminaemia (likely due to protein losing enteropathy [PLE]), systemic inflammatory response syndrome (SIRS) due to mucosal injury and early indicators of laminitis. Primary formaldehyde toxicity of other body systems was ambiguous: renal involvement (mildly increased urea with marked renal glucosuria), cardiac disease (inappropriate tachycardia and supraventricular premature beats) and quiet mentation could likely be secondary to the aforementioned systemic derangements (hypovolaemia, SIRS, electrolyte and acid/base derangements) and pain.

As the horse was admitted 20 h after being given 10% formalin, the benefit of an intestinal absorbent was considered questionable but activated charcoal (1 g/kg PO) was administered once on Day 1 of hospitalisation due to the formalin smell of the gastric contents.[5] IV fluid therapy (Hartmann's solution with magnesium sulphate added to achieve approximately 6 mg/kg/h IV supplementation) was started as a bolus until the horse urinated, then reduced to approximately 3 L/h (5 mL/kg/h) for 12 h, then 2.5 L/h (4 mL/kg/h) during Day 2, and maintained at 1.5 L/h (2.5 mL/kg/h) from Day 3 until fluids were discontinued Day 6. These fluid rates were guided by correction of hypovolaemia, improving urinary elimination of formic acid, and maintenance of renal diuresis (urination observed q1–3h and USG <1.015). Given initial hypovolaemia and renal concerns, non-steroidal anti-inflammatory drugs (NSAIDs) were considered contraindicated on Day 1. Instead, analgesia and anti-inflammatory treatment was limited to lidocaine continuous rate infusion (CRI) at 3 mg/kg/h IV, with the additional benefit of its antiarrhythmic properties. Trophic enteral nutrition (L-glutamine [0.3 g/kg/d PO][21] and molasses [1 mL/kg/d PO]), mucosal protection (sucralfate, 20 mg/kg q4h PO), gastric acid suppression (buffered omeprazole, 4 mg/kg q24h PO) and continuous digital cryotherapy were also commenced. Mentation, comfort, urination, defecation, heart rate and rhythm were monitored hourly for the first 24 h of hospitalisation. During Days 1 and 2, urine dipstick analysis, packed cell volume (PCV), total protein (TP), and VBGA were performed twice daily, and USG monitored q4h.

2.3 | Case progression

By 4 h of hospitalisation, cardiac rhythm was regular with improving tachycardia (72 to 48 bpm) determined by auscultation, and repeat ECG on Day 2 confirmed normal sinus rhythm with no premature complexes detected. Twenty-four hours after admission, the gelding's mentation was dull and moderate colic signs developed despite passage of several piles of formed manure. Improvement in other clinical parameters (normal CRT, jugular fill and blood lactate) suggested adequate tissue perfusion. Improved glomerular filtration rate (GFR) was reflected by the return of urea to normal reference range and regular hyposthenuric–isosthenuric urinations. Proteinuria resolved by Day 2 but glucosuria persisted on urine dipstick testing with coinciding normoglycaemia until Day 4, suggestive of possible proximal renal tubular damage due to formaldehyde toxicity; urinary enzymuria and/or fractional excretion of electrolytes were not tested and might have helped to support this interpretation. Persistence of mucous membrane hyperaemia and tachycardia, and an increasing trend in both temperature (38.3°C) and severity of leukopenia (Table 1) suggested progression of SIRS. Repeat abdominal ultrasound revealed

normal stomach size but an increase in stomach wall measurement with a diffusely corrugated appearance had developed (8 mm gastric wall thickness; reference up to 7.5 mm).[22] On-going thickening of the small intestine (up to 6 mm wall thickness), left large intestinal thickening (5–6 mm wall thickness; reference 2–4 mm),[19,22,23] normal right dorsal colon and caecal wall thickness, and fluidy caecal luminal content were also demonstrated. Presumptive gastroenterocolitis due to formaldehyde toxicity was considered explanation for the signs of colic and worsening SIRS, as mucosal necrosis and subsequent inflammation and ulceration are described in human cases of ingestion. Non-steroidal anti-inflammatory drug therapy was commenced (flunixin meglumine 1.1 mg/kg IV q12h). On Day 3, hypoglobulinaemia developed accompanying existing hypoalbuminaemia, this panyhypoproteinaemia suggested progressive, on-going PLE.

The horse progressively improved from Day 3 onwards with normalisation of clinical parameters, normal mentation, and continued passage of formed faeces. Additionally, he remained sound at the walk. Improving pain score and no colic signs were observed from Day 4 onwards. Water per os was introduced during Day 2, and the volumes permitted were increased incrementally to ad libitum by Days 3 and 4; this approach was due to concerns the horse might be at risk of ileus and gastric reflux. Leukopaenia and clinical signs of SIRS resolved by Day 5, allowing the discontinuation of the lidocaine CRI and digital cryotherapy. Flunixin was reduced to 0.5 mg/kg IV q8h on Days 4 and 5, and discontinued on Day 6. IV fluid therapy was also discontinued on Day 6, and appropriate hypersthenuria was demonstrated following discontinuation of IV fluids. Re-feeding was not commenced until after Day 5 once colic signs had resolved and analgesia had been tapered, as well as to ensure adequate enteral rest for enterocyte replacement considering the diffuse extent of gastrointestinal injury anticipated from the intoxication. Trends in daily serum total protein measured by refractometer (values not included in tables) stabilised from Day 4 onwards, serving as an approximate indicator of gastrointestinal mucosal integrity (increasing trend suggestive of resolving PLE). A 'low bulk diet' was gradually introduced by incremental increases in grazing time (grass intake), and a commercial pelleted feed (NRM Low GI Sport®) to provide additional calories, protein and a balanced vitamin and mineral ration. The gelding's bodyweight dropped to 536 kg by Day 7 but increased to 550 kg at hospital discharge. Ultrasonographic gastrointestinal wall thickness measurements were within normal limits on Day 11. Re-feeding was well tolerated with no signs of colic, a good appetite was demonstrated and formed faecal consistency.

2.4 | Case outcome

The horse was discharged from hospital on Day 14. Re-examination by the referring veterinarian 10 days following discharge included normal findings on physical examination, normal gastric mucosa on gastroscopy and normal haematologic and biochemistry values. Based on these results omeprazole and sucralfate were discontinued, and the horse was gradually re-introduced to higher bulk feeding (grass hay) over a 3- to 4-week period. The owner continues to use the referring veterinarian for the horse's veterinary needs, who reported no concerns at approximately 12-months post-hospital discharge, the horse appeared in good condition and had returned to ridden work.

3 | DISCUSSION

In this case of accidental 10% formalin intoxication by nasogastric intubation in a horse, case management was conducted based on the expected sequelae extrapolated from the human literature as the equine lethal dose of systemic formaldehyde is unknown. IV formalin has been described as a treatment in select equine cases experiencing haemorrhage.[24] In this case series, the most utilised dose described was 50 mL of 10% formalin diluted in 1 L of isotonic fluid (equating to 2 g formaldehyde or 0.004 g/kg for a 500 kg horse), this parenteral dose showed no short-term complications.[24] Based on a bodyweight of 596 kg the horse in the present report received 0.12 g/kg formaldehyde enterally with clinical findings of intoxication, with intensive supportive care this horse survived the lower limit of the estimated lethal dose in humans (0.12–0.16 g/kg).

In human medicine, formalin ingestion is rare with majority of reports in the literature being accidental, suicidal or homicidal.[5,13,14,16,17,25–27] Gastrointestinal signs are accompanied by metabolic acidosis and MODS. Gastrointestinal signs in humans are characterised by nausea, abdominal pain, vomiting, diarrhoea, haematemesis, and melena due to local corrosion of the gastrointestinal mucosa and secondary necrosis, inflammation, ulceration and potential perforation. Severity of toxicity is proportional to the dose, concentration and duration of formaldehyde exposure.[5] In this case, gastroenterocolitis was suspected based on the clinical and diagnostic findings presented, while the route of nasogastric intubation spared the oesophagus. Initial small intestinal thickening and hypomotility followed by large colon thickening on Day 2 might reflect transit time of formaldehyde and systemic absorption prior to reaching the colon. The stomach and small intestine were likely exposed to the largest dose, and the small intestine for the longest exposure (due to its surface area), which might explain why these structures had relatively thicker wall measurements compared to the large intestine overall.[5] Panhypoproteinaemia by Day 3 reflected the degree of gastrointestinal mucosal injury and possible ulceration, supported by the worsening neutropaenia and left shift likely due to marginalisation and sequestration in inflamed bowel. There was concern that gastric reflux due to small intestinal ileus might occur but this did not transpire. Stricture formation (oesophageal, gastric or small intestinal) is the most common gastrointestinal sequelae with a typical onset of 2–4 weeks following ingestion in humans.[5,28] The absence of colic with re-feeding, normal gastroscopy at Day 24 and health status 12 months post-intoxication collectively indicate stricture formation did not occur.

Accumulation of formic acid systemically results in unmeasured anion metabolic acidosis.[5,6] At presentation, venous blood gas and biochemistry analysis revealed high unmeasured anions but there was

concurrent lactic acidosis, hypoproteinaemic alkalosis, strong ion difference alkalosis and respiratory alkalosis with a net mild alkalaemia (Tables 2 and 3). Plasma half-life of formic acid in circulation is approximately 90 min[29]; therefore, the peak of unmeasured anion metabolic acidosis might have occurred prior to admission with a time lag for compensatory alkalotic downregulation. Formic acid has also been linked to renal tubular necrosis and acute renal failure in humans, often amplified by severe circulatory collapse.[5,30] Although hypercreatininaemia did not accompany the increased urea, and acknowledging that increased urea could be pre-renal considering initial clinical signs of dehydration and hypovolaemia as well as the history of NSAID administration by the referring veterinarian, the on-going glucosuria (with concurrent blood glucose measurements less than the renal threshold for horses) could have been renal, reflecting proximal tubular epithelial dysfunction.[20] However, basal glucosuria can also occur during critical illness. In humans a 'soft' (lower) renal threshold for glucose in critically ill patients has been suggested, whereby the mechanism for this possibly still relates to renal tubular epithelial dysfunction.[31] Changes in serum creatinine is a key determinant for meeting criteria for acute kidney injury (AKI), in both human and veterinary medicine.[32–35] However, renal injury is a dynamic process and serum creatinine can remain within normal reference range despite renal disease and reduced GFR.[36,37] Some reports suggest that increases in urinary glucose might precede elevations in creatinine in cases of renal tubular toxicity.[38] Urinary enzymuria and fractional excretion of electrolytes would have been required to provide further evidence of early nephrotoxicity in this case.[36] Serum symmetric dimethylarginine could have also been measured as an equine biomarker for AKI; however, one study in horses suggested its utility may be limited in subclinical AKI.[39] Another differential for increased serum urea, considering the context of concurrent gastrointestinal disease in this case, is haemorrhage of the proximal gastrointestinal tract.[40,41] Although the horse did develop hypoalbuminaemia as one might see with clinically significant haemorrhage, a concomitant decrease in RBC count and haematocrit was not observed, making this theory less likely. Whether renal tubular injury occurs in horses similarly to humans with systemic formaldehyde toxicity at the dose of 0.12 g/kg enterally remains speculative.

The marked tachycardia and arrhythmia identified at admission might have been due to primary cardiotoxicity, or secondary to hypovolaemia, pain, acid–base–electrolyte disturbance and/or SIRS. A rodent study involving systemic administration of formaldehyde with concurrent regulation of pH to nullify the acidifying effects of formic acid, indicated that the cardiac toxicity demonstrated was more likely due to direct effects of formaldehyde intoxication.[42] Detailed diagnostic investigation of the arrhythmia (e.g. continuous telemetry, echocardiography, serum cardiac troponin I measurement) would have helped determine the clinical significance of the marked sinus tachycardia and occasional SVPCs. Given the horse's overall condition at admission, the apparent rapid resolution of the arrhythmia, and lack of specific antidote for formaldehyde, not electing to perform these diagnostics during the clinical course seemingly did not change the case outcome. Furthermore, the apparent rapidity of resolution with fluid therapy and analgesia treatment might suggest these cardiac abnormalities were more likely secondary and not due to primary formaldehyde cardiotoxicity. However, upon reflection an exercising ECG would have been prudent prior to return to ridden work in order to assess the long-term safety of this horse for riding. The timely resolution of the horse's dull mentation and apparent improvement with multimodal analgesia indicated this mentation was most likely secondary to pain and systemic disease, rather than primary neuronal injury from formaldehyde intoxication. Due to the limited clinical data concerning the cardiac and neurologic systems, the cardiotoxic and neurotoxic potential of the present dose of formaldehyde in horses remains undetermined.

The therapeutic principles for formalin intoxication in humans are predominantly supportive as there is no specific antidote. Guidelines for human treatment are similar to the treatments used in this case with activated charcoal, gastroprotectants, and IV fluid therapy recommended.[5,43] Not an antidote per se, but folinic acid intravenously (1 mg/kg IV q4h) and folic acid (folate) have been described as a means to accelerate the conversion of formic acid to carbon dioxide and water, the rate limiting step in the physiological elimination of formic acid.[13,43,44] No clinical trials of this treatment exist since this type of intoxication is rare and due to the ethical issues surrounding such a study design. Yet being a B vitamin, administering folinic or folic acid to such cases seems reasonably safe and might be beneficial.[43] IV folinic acid was not available, nor considered at the time of hospital admission.

Due to the shared pathophysiological propensity for intestinal necrosis and ulceration by both phenylbutazone and formaldehyde intoxication, principles of therapy for the former were applied including sucralfate, enteric rest with trophic feeding and a 'low bulk' diet.[45,46] Sucralfate was administered at a higher dose and more frequently than what is typically indicated for equine glandular gastric disease (12 mg/kg PO BID).[47] Sucralfate has been suggested for the treatment of right dorsal colitis to promote colonic healing[46,48] but there is currently no evidence demonstrating the extent of sucralfate's efficacy for treating colonic disease in adult horses. Thus, the selected dose was based on the drug's high safety, lack of contraindications and knowing that the drug acts topically, not systemically. Intestinal enterocyte replacement rate guided the 5-day period of enteric trophic feeding, to allow for the return of normal gastrointestinal function and mucosal barrier integrity. L-glutamine stimulates enterocyte growth and proliferation, downregulates pro-inflammatory pathways, maintains tight-junction proteins, plays a role in the regulation of intestinal gene expression and attenuates cell apoptosis.[21,49,50] There is no research on these specific effects of L-glutamine in equine models but it has been shown to improve clinical outcomes in rat and porcine models that have suffered from acute gastrointestinal insults such as trauma or infection.[21] The dose of L-glutamine was extrapolated from the human literature.[21] Molasses was administered as an affordable carbohydrate source to prevent the development of hypertriglyceridemia.[51] In the authors' hospital, molasses is routinely used for this purpose at 1 mL/kgbwt/day (providing approximately 4.2 kCal/kgbwt/day).

Retrospectively, partial parenteral nutrition might have further benefited the horse and lessened the weight loss experienced during this period. This weight loss was 11% of the horse's bodyweight by Day 7, which recovered to 8% of admission weight by the time of discharge. Both reduced gastrointestinal fill from restricted intake then a 'low bulk' diet and loss of body condition likely contributed to the horse's weight loss, considering the contents of the large intestine contribute approximately 13% to the bodyweight of a horse.[52,53] Monitoring blood triglyceride concentrations would have provided evidence for or against the adequacy of the chosen feeding protocol. Surviving cases of formalin ingestion in humans is scarce, in one recent report a nasal duodenal tube for post-pyloric feeding was not placed until Day 4 once the patient showed stabilisation, parenteral nutrition was not reported prior to tube placement. Furthermore, this patient's diet was not expanded until after the removal of the duodenal tube on Day 13.[13] In the present case, a 'low bulk' diet was achieved by short frequent feedings when food was re-introduced after Day 5, with an aim to reduce the functional load on the gastrointestinal tract.[45,46] For this purpose fresh grass was introduced and a commercial pelleted feed (NRM Low GI Sport®) was used with a feed analysis of 35% fibre, 14% crude protein and a digestible energy of 11 MJ/kg. When fed at 5.0 kg/day this was equivalent to 24 k cal/kgbwt/day which met the resting energy requirement for 'stall maintenance' (22–23 kcal/kgbwt/d).[54]

Anuria was not observed in this case as described in some human reports[13,16] and diuresis appeared to be sufficient protection against further potential renal tubular epithelial injury. IV fluid therapy was continued until Day 6 as tubular epithelial regeneration was expected to take numerous days should injury have occurred. Furthermore, diuresis might have aided urinary clearance of formic acid, being a water-soluble chemical.[5,43] Due to initial concerns of potential nephrotoxicity, NSAIDs were considered contraindicated while the horse showed concurrent signs of hypovolaemia. However, once hypovolaemia was corrected and adequate renal perfusion was maintained with continuous IV fluid therapy, flunixin was added when evidence of SIRS and pain progressed, as a tubular disease mechanism was suspected in this case and NSAID-associated nephrotoxicity is not typically tubular in aetiology. Risk for clinical laminitis was addressed with continuous digital cryotherapy, and beyond Day 1 of hospitalisation evidence of laminitis resolved. Although the horse was sound at discharge, long-term consequences are unknown as neither baseline nor follow-up foot radiographs were performed.

An important component of this intoxication was that it occurred as the result of a medical error. Medical errors are an unavoidable part of both human and veterinary medicine. Almost 1 in 10 visits to human hospitals result in some level of adverse event.[55] The magnitude of such adverse events can be extreme, with medical errors reported to be the third leading cause of death in the United States in 2016.[56] In veterinary medicine less has been published on animal safety and medical error, although it is gaining more attention of late.[57–60] A study using an incident reporting system in three veterinary hospitals (university large animal, university small animal, private emergency small animal) investigated the type and severity of errors and found drug errors were most frequent (55%–69% of all errors).[59] Furthermore, errors in medications make up approximately 20% of veterinary treatment-related insurance claims, second only to surgical-related errors.[61] In human medicine interruptions, staffing levels, shift length, fatigue and burnout are factors cited to contribute to medical errors.[62,63] A 'double-check' system has been described for high-risk medication orders as a 'system-based' solution,[57] but has questionable transferability to equine ambulatory practice, which has unique challenges including seasonal long work hours, treating horses in the presence of an owner, after hours on-call, working alone, remote locations, and variable stock supply of vehicles.[64] Furthermore, the referring veterinarian in the present case reported the medication error related to worn hand written labels, container appearance and stock supply of the work vehicle, not a dose error.

Since the accidental administration of 10% formalin to a horse, the clinic has instated measures to prevent future occurrences. Formalin is no longer purchased in bulk and decanted into smaller containers, the clinic purchases 10% formalin in 2 L volumes commercially which also has added health and safety benefits for clinic staff (minimising handling of a toxic substance). The commercial printed labels on single use containers might be more permanent and legible compared with the prior hand-written labelling. When generic containers for holding large volume liquids are used, clear permanent labelling is prioritised. Carrying 2 L of 10% formalin is justified in this practice as the veterinarians regularly perform field necropsy (sheep and cattle), requiring large volumes for fixation of numerous samples. However, 10% formalin is no longer routinely carried on vehicles for this purpose, it is only placed in the vehicle when there are appointments requiring necropsy service. The actions that this clinic adapted might benefit other mixed ambulatory practices. Despite the medical error, the client-veterinarian relationship was preserved and litigation was not pursued. Factors regarding the client–veterinarian relationship that likely contributed to this include: the early identification and transparency of the error, the veterinarian proactively seeking guidance from veterinary peers, and the practice taking financial responsibility and arranging referral. This approach is supported in the literature, where honesty and empathy are key qualities when successfully managing medical errors with clients.[57] Furthermore, the positive effects on the health and well-being of both the animal patients and veterinary health care professionals when 'safety culture' is valued and integrated at a clinical level has been shown to reduce error frequency and improve case outcome when errors do occur.[57,65,66]

4 | CONCLUSION

This report describes the successful management of accidental enteral administration of a high dose of 10% formalin (0.12 g/kg bwt formaldehyde) to a horse. Following human guidelines, treatment was focused primarily on intensive supportive care of the affected body systems including primary insults to the gastrointestinal system and managing the potential risk of nephrotoxicity, cardiotoxicity and laminitis. The horse responded well to treatment, was discharged 14 days

after admission, and was alive and clinically normal 12 months following hospital discharge.

AUTHOR CONTRIBUTIONS

This is a retrospective clinical case report. This report did not involve study design, execution nor data analysis. All authors were involved in the preparation of the manuscript and gave their final approval of the manuscript.

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PEER REVIEW

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DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request: Open sharing exemption granted by the editor for this descriptive retrospective case report.

ETHICAL ANIMAL RESEARCH

Research ethics committee oversight not required by this journal: retrospective study of clinical records.

INFORMED CONSENT

Informed consent was obtained from the owner of the horse described in this report.

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