discovery of ventricular fibrillation macroscopically at thoracotomy, confounded this diagnosis. The identification of ventricular fibrillation in this case was serendipitous and not the result of a hunt. Our equipment—a Lifepak Physiocontrol 9—subsequently passed electronic medical engineering assessment. The decision to proceed to thoracotomy was based on patient age, the probability of underlying toxic but reversible insult, and failure to re-establish a cardiac output following standard ALS protocols. Our intention was to improve cardiac output by internal massage[9 10] pending reversal of a toxic insult. We could find no report in the literature that described thoracotomy to identify ventricular fibrillation. This case reinforces the advice contained in resuscitation literature,[11–13] which suggests that we defibrillate asystole if in any doubt about the cardiac rhythm.

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Accidental colchicine overdose. A case report and literature review

M J Maxwell, P Muthu, P E Pritty

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Colchicine overdose is uncommon but potentially life threatening. It is a safe drug when used according to established therapeutic guidelines but causes serious systemic effects if ingested in doses that exceed the recommendations. Overdose must therefore be recognised early and treated appropriately to optimise the outcome. A fatal case of colchicine overdose caused by inappropriate self medication is reported and to the best of the authors' knowledge, there has been no report of fatal accidental overdose in the United Kingdom. The pharmacology of colchicine, the clinical features associated with overdose, and the options for treatment are discussed.

A 41 year old white man was brought to the accident and emergency (A&E) department after ingesting 53×500 µg colchicine tablets over the previous 24–48 hours in an attempt to alleviate the pain of acute gout. The number of tablets was calculated from those remaining in a recently prescribed bottle.

On arrival he reported abdominal pain, diarrhoea, and vomiting for the preceding 24 hours. He was alert and orientated but was peripherally vasoconstricted and tachycardic with a blood pressure of 108/70. Breathing was laboured and shallow with a respiratory rate of 40 breaths/minute but lungs were clear. There was mild abdominal distension but bowel sounds were normal. Electrocardiogram was unremarkable.

While in A&E the patient had a witnessed electromechanical dissociation (EMD) cardiac arrest without warning. He was intubated, cardiopulmonary resuscitation started, and 1 mg adrenaline (epinephrine) given intravenously. Full recovery occurred after two minutes and he was extubated. After arrest ECG showed multifocal ventricular ectopics. He then had two further witnessed EMD cardiac arrests of identical pattern, although he was not intubated, and again completely recovered after each. The patient was then transferred to the intensive care unit for further observation and treatment.

Laboratory investigations showed a white cell count 31.3×10^9/l, platelets 341×10^9/l, urea 10.4 mmol/l, creatinine 391 mmol/l, ALP 1320 U/l, ALT 82 U/l, bilirubin 43 µmol/l, INR 3.2, magnesium 0.58 mmol/l, and corrected calcium 2.03 mmol/l. Arterial blood gas results showed a profound metabolic acidosis (pH 7.00, pCO_2 6.30, pO_2 7.72, HCO_3^- 11.5).

His clinical condition and acidosis worsened (pH 6.90, HCO_3^- 9.7) and he was intubated and given a bicarbonate infusion with some improvement (pH 7.05, HCO_3^- 15.5). Chest radiography showed bilateral patchy shadowing throughout both lung fields. He remained cardiovascularly unstable and required dopamine, adrenaline and noradrenaline infusions to maintain blood pressure.

Oliguria and then anuria ensued and were not responsive to supportive measures. He continued to deteriorate and death occurred approximately 11 hours after admission.

DISCUSSION

Colchicine is a naturally occurring alkaloid with weak anti-inflammatory activity derived from the autumn crocus *Colchicum automnale* and the glory lily *Gloriosa superba*. It has been used extensively in the treatment of gout for many centuries and also been recommended in preventing attacks of familial Mediterranean fever[1] and in the treatment of primary biliary cirrhosis,[2] amyloidosis,[3] and condyloma acuminata[4]

Colchicine has potent anti-mitotic activity, which is caused by its binding, both reversibly and selectively, to tubulin, the microtubular protein that disrupts the function of the mitotic spindles in those cells capable of dividing and migrating. Although colchicine is taken up equally by all cells it is thought that those which have the highest cell turnover (that is, the greatest mitotic activity) are most affected.[2 5–7]

Colchicine is rapidly absorbed from the gastrointestinal tract after ingestion. It undergoes significant first pass hepatic metabolism, which primarily involves deacetylation. Subsequent to this, the metabolites undergo widespread enterohepatic recirculation before being excreted in bile and faeces. It is thought that the extended time period during which the gastrointestinal mucosal cells are exposed to colchicine may explain the prominence of the gastrointestinal symptoms of toxicity. Renal clearance also accounts for 10%–20% of colchicine removal and if normal renal function exists larger fractions can be excreted via this route if a toxic amount has been ingested. Increased urinary excretion also occurs in the presence of hepatic disease, as there is a reduction in the capacity for deacetylation. However, if renal and hepatic diseases coexist the possibility of toxicity greatly increases.[5–8]

Overdose with colchicine is uncommon and we are not aware of similar report of fatal accidental overdose in the United Kingdom. It exhibits a low therapeutic index although there is great variation in the dose required for significant morbidity. Patients have survived ingestion of more than 60 mg[9] but conversely others have died after ingesting only 7 mg over a prolonged period.[10] There does not seem to be any clear cut separation between non-toxic, toxic or lethal doses of colchicine. Indeed, symptoms of gastrointestinal toxicity such as nausea, vomiting, diarrhoea and abdominal pain are seen in 80% of patients on full therapeutic doses and are used as the clinical endpoint in dose titration.[5]

Overdose with colchicine constitutes a toxicological emergency and rapid intervention is required. The symptoms of toxicity are well described in the literature and can be separated into three characteristic phases (table 1).

This patient had three EMD cardiac arrests, from which full recovery was made each time, and an episode of self limiting ventricular tachycardia. Cardiotoxicity is much reported upon in the literature. Commonly, this manifests as arrythmias, namely sinus bradycardia, sinus tachycardia, ventricular fibrillation, and complete atrioventricular block. ECG changes of ST elevation in leads I, II and V3-V6 have also been reported.[11 12] However, the pattern of repeated cardiac arrests and a self limiting arrhythmia that we describe in this case have not previously been reported.

There are various suggestions to explain the effect that colchicine has on the heart. It is thought that there may be a direct toxic effect on the myocardial cells with impairment of impulse generation and cardiac conduction.[13 14] This has not been proved, although a similar mechanism of direct toxicity is seen on the cells of skeletal muscle.[15] It is also possible that the profound acid-base disturbances and electrolyte derangements associated with overdose will play a significant part.[8]

Gastrointestinal decontamination with gastric lavage and activated charcoal is often performed, and may help despite colchicine being rapidly absorbed because there is extensive enterohepatic recirculation.[8] Consequently, it is important that efforts are made to remove any remaining colchicine because the retrieval of even small amounts can greatly benefit prognosis.[11]

Table 1 Phases of colchicine toxicity

Phase	Symptoms
I 0–24 hours	Nausea, vomiting, diarrhoea, abdominal pain, and anorexia Electrolyte imbalance and hypovolaemia Peripheral leucocytosis
II 2–7 days	Bone marrow hypoplasia, profound leucopenia, and thrombocytopenia Cardiac arrythmias and cardiovascular collapse Respiratory distress, hypoxia, pulmonary oedema, and ARDS Oliguric renal failure Rhabdomyolysis Electrolyte derangements Metabolic acidosis Mental state changes Seizures Peripheral neuropathy and ascending paralysis
III 7th day onwards	Rebound leucocytosis Transient alopecia

The large volume of distribution of colchicine and the fact that 50% of its plasma concentration is linked to proteins means that methods of extracorporeal removal are ineffective. Therefore, haemodialysis, although of benefit in the treatment of any associated renal failure, is not used to increase elimination.[2 5]

Currently in the United Kingdom there is no specific treatment commercially available for the treatment of colchicine toxicity. However, the successful outcome after the use of colchicine specific Fab fragments has been reported.[5 16] Colchicine specific Fab fragments consist of the light chain and variable region of the heavy chain and are derived from goats.[2] Their mechanism of action is similar to that of digoxin specific Fab fragments, namely binding to the target drug allows redistribution into the intravascular compartment and thus the removal of substantial amounts from peripheral sites.[12] There is a high affinity between the Fab fragment and colchicine and this acts to prevent the drug returning to these peripheral binding sites.[9]

CONCLUSION

Overdose with colchicine is associated with a high mortality rate with death occurring secondary to rapidly progressive multiorgan failure. It is important therefore that the potential dangers of this drug are recognised by clinicians on its prescription, and that patients are given an understandable explanation of its effects including the point at which to cease ingestion. A careful watch must also be made of the number of tablets prescribed to avoid unintentional overdose of this potentially lethal drug.

Contributors

MJM initiated the idea, reviewed the literature and wrote the paper. PM initiated the idea, helped with the literature search and writing the paper. PP reviewed the manuscript and helped with writing the paper. PP acts as the guarantor of the paper.

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Toxicity of brake oil

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Brake oil is an automobile transmission fluid composed of a mixture of toxic glycols and glycol ethers. Three cases of poisoning with toxic glycol based brake fluid are reported who presented with mild metabolic acidosis and acute renal failure. As all the cases had presented late, treatment with ethanol was not started. All of them were treated successfully with haemodialysis.

CASE 1

A 30 year old man presented to the emergency room 72 hours after having consumed 100 ml of brake fluid after intake of 60 ml of whisky (40% proof). He had three vomits immediately after the consumption and a progressive decrease in his urine output the next day. At admission, the pulse was 92 per minute and blood pressure 164/100 mm Hg. The systemic examination was normal. Laboratory investigations revealed normal complete blood counts. The serum biochemistry values are given in table 1. The urine examination did not reveal any crystals of calcium oxalate; however, numerous red blood cells could be seen.

The presence of renal failure necessitated immediate haemodialysis. Hypertension worsened requiring antihypertensive therapy with nifedipine and atenolol. The presence of prolonged oliguria raised suspicion of renal cortical necrosis but the renal biopsy showed only acute tubular necrosis. After receiving 15 haemodialyses over a period of five weeks he went into the diuretic phase of acute renal failure and was discharged soon thereafter in a satisfactory condition.

CASES 2 AND 3

These were two brothers aged 40 years and 35 years. They presented to the emergency services 24 hours after having consumed approximately 40–60 ml of brake oil with 80 ml of rum. Both had many vomits over the next few hours followed by declining urinary outputs. At admission, the pulses and blood pressures of both were normal and systemic examination of both patients did not reveal any abnormality. Laboratory indices obtained showed normal complete blood counts. Serum biochemical values of both are presented in table 1. The urine examination of both patients showed a 2+ proteinuria, plenty of red blood cells but no crystals of calcium oxalate.

Both patients were taken up for immediate haemodialysis. The urine outputs of both remained in the oliguric range. After receiving six haemodialyses in one and eight in the other, both patients went into the diuretic phase of acute renal failure and were discharged a week later in a satisfactory condition.

DISCUSSION

Both ethylene glycol and diethylene glycol are colourless, odourless, sweet tasting compounds with widespread commercial use. Whereas ethylene glycol is used as antifreeze, coolant, and preservative, diethylene glycol has been used as a replacement for glycerine. The earliest reported toxicity of diethylene glycol dates back to 1937 when it was used as a vehicle for preparing sulfanilamide elixir.[1] According to a document by Dow Chemical Company, a leading producer of automobile liquids, brake fluid is a transmission fluid composed of a mixture of several glycols like ethylene glycol, diethylene glycol, polyethylene glycol, polypropylene glycol

Table 1 Laboratory parameters of patients presenting with brake oil intoxication

	Sodium/ potassium (mmol/l)	Urea in mmol/l and creatinine in μmol/l	Calcium/ phosphorous (mmol/l)	Arterial pH	Arterial Po_2 kPa	Arterial Pco_2 kPa	Serum bicarb (mmol/l)
Case 1	136/4.6	64.3/972.4	1.5/2.4	7.25	12.6	3.3	15
Case 2	137/4.9	53.6/371.2	1.8/1.7	7.30	13.0	4.6	20
Case 3	134/5.2	71.4/848.6	2.4/2.0	7.27	12.5	3.9	10