

CASE REPORT

A case report on herbicidal intoxication with mecoprop

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Abstract

Mecoprop is a hormone-type phenoxy herbicide that is found in many household weed killers. We describe a case of a 55-year-old female who was admitted to the intensive care unit after an intentional overdose with paroxetine and mecoprop. She developed severe refractory distributive shock, hyperkalaemia, hyperthermia, coma with absent brainstem reflexes, haemorrhagic gastrointestinal ulcerations, anaemia, leukopenia, thrombocytopenia and marked coagulopathy. She was treated with intensive supportive management, mass transfusion, dantrolene, sodium bicarbonate and intravenous lipid emulsion. She eventually made a full recovery. This report highlights the dangers, clinical presentation and treatment of phenoxy herbicide intoxications.

Introduction

Mecoprop, or 2-methyl-4-chlorophenoxypropionic acid (MCPP), is a hormone-type phenoxy herbicide that is found in household weed killers, mainly used for the control of broad-leaved weeds.^[1,2] Only a few intoxications with mecoprop have been described and published, mostly between 1979 and 1988. Reported clinical findings are loss of consciousness, hypotension, rhabdomyolysis, renal failure and hyperthermia.^[3-9] In many cases intoxication was fatal.^[6-9] The United States Environmental Protection Agency has classified MCPP as toxicity class III (slightly toxic).^[10] We describe a case of MCPP intoxication leading to distributive shock, coma with absent brainstem reflexes and gastrointestinal ulceration. Supportive respiratory and haemodynamic care and treatment with dantrolene, sodium bicarbonate and intravenous lipid emulsion infusion led to complete recovery.

Case presentation

A 55-year-old female patient, known with a short history of

depression, was discovered at home after an intentional drug overdose with 1600 mg of paroxetine, 120 mg of temazepam, 80 mg of oxazepam, 75 mg of oxycodone and an unknown quantity of MCPP (bottle concentration 600 g/l). She developed multiple symptoms of intoxication (*table 1*). On arrival, the emergency medical services found she was pulseless with an ECG that showed a sinus bradycardia of 30/min, consistent with pulseless electrical activity. Advanced life support was given for two minutes before return of spontaneous circulation. In the emergency department she was comatose with a score of E1M1V1 on the Glasgow Coma Scale (GCS) and she was intubated without sedation or muscle relaxing agents. ECG showed a broad complex tachycardia. Lab results revealed severe respiratory acidosis and hyperkalaemia. A nasogastric tube was inserted and activated charcoal administered. The hyperkalaemia was treated with intravenous calcium chloride and an insulin and glucose infusion. The patient was admitted to the intensive care unit (ICU) where sodium bicarbonate infusion was added in order to alkalisate the urine, to increase MCPP elimination. A few hours after admission the patient developed distributive shock for which she was given large volumes of intravenous fluids and high doses of norepinephrine. She developed hyperthermia with temperatures up to 41.6 and an ocular clonus. Because of a differential diagnosis which included serotonin syndrome, active cooling and a dantrolene infusion were initiated. Neurologically the patient remained E1M1Vtube on the GCS, with sedation only administered briefly during the dantrolene infusion. As well as coma, the breathing stimulus, cough reflex and normal oculocephalic reflexes were absent and bilateral Babinski signs were observed. An electroencephalogram resembled a burst-suppression pattern, without evidence of a non-convulsive epileptic state. Since the distributive shock persisted and because MCPP is

lipophilic, intravenous lipid emulsion (intralipid 20%) was administered to enhance redistribution and elimination of toxic compounds. Amoxicillin-clavulanic acid was given for possible aspiration pneumonia. After initial signs of stabilisation, the patient's condition drastically worsened on the second day after admission. Severe shock and hypoxaemia ensued, rendering the patient in an extremely critical condition. She developed upper gastrointestinal bleeding and anaemia with a haemoglobin decline from 7.5 to 4.8 mmol/l. Gastroscopy showed superficial ulcerative lesions in the distal oesophagus and stomach, without signs of active bleeding (*figure 1*). Further lab results revealed thrombocytopenia, leukopenia, and coagulopathy without signs of liver failure. The patient was treated with an esomeprazole infusion and a massive blood transfusion protocol was enacted. Because of the possibility of septic shock due to bacterial translocation from mucositis, hydrocortisone and tobramycin were administered. From the fourth day of admission the patient's respiratory and haemodynamic status improved and from the ninth day of admission there was a return of the brainstem reflexes and consciousness. Subsequently her ICU admission was complicated by a critical illness polyneuropathy with respiratory exhaustion (for which a percutaneous dilatational tracheostomy was inserted), ventilator-associated pneumonia and hyperactive delirium. After 43 days of ICU treatment, the patient had shown almost full neurological recovery, with only mildly impaired memory encoding remaining. She was transferred to the general medicine department and discharged to a rehabilitation centre shortly after.

Discussion

MCCP is a hormone-type phenoxy weed killer, widely used for the control of broad-leaved weeds and mainly used in lawns and

grass crops.^[1,2] Most hormonal phenoxy weed killers contain a combination of MCCP and one or more chemically related compounds such as 2,4-dichlorophenoxyacetic acid (2,4 D), 3,6-dichloro-2-methoxybenzoic acid (Dicamba) and 2-methyl-4-chlorophenoxyacetic acid (MCPA).^[11,12] Although their use is widespread, self-poisoning with herbicides remains rare. A few cases have been published on chlorphenoxy herbicide poisoning, most of these over 25 years ago.^[3-7,9] Clinical findings in these reports are summarised in *table 2*. The most significant clinical findings in our patient were prolonged coma with absent brainstem reflexes, gastric bleeding with anaemia, thrombocytopenia, leukopenia and coagulopathy. We consider all of these to be caused directly by MCCP. Although the initial period of our patient's coma could be attributed to benzodiazepine, opioid, SSRI and MCCP intoxication, the prolonged duration of absent brainstem reflexes suggests that MCCP intoxication is responsible. The elimination half-life of the other ingested agents does not account for the ongoing coma and absent brainstem reflexes, which lasted for nine days.^[13] Prolonged coma has been described in many patients suffering from MCCP intoxication, but the duration of the absent brainstem reflexes is unique to our case report.^[3,4,8] The corrosive damage resulting in gastrointestinal haemorrhage has been reported once and is probably caused by a surfactant which is a component of chlorphenoxy herbicides.^[8] Our patient became anaemic due to gastric bleeding. Leukopenia and thrombocytopenia may have been the result of haematopoietic cytotoxicity caused by chlorphenoxy herbicides, which has been described previously and is supported by toxicology studies in rats.^[3,8,14] Other findings in our case include a hypoxic cardiac arrest, distributive shock and hyperthermia. These have all been described in previous case reports on phenoxy-type intoxications.^[3,4,8,12,15,16] In our case

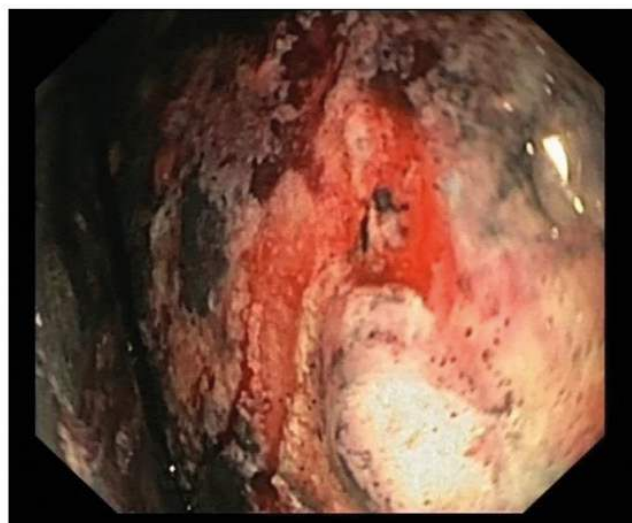
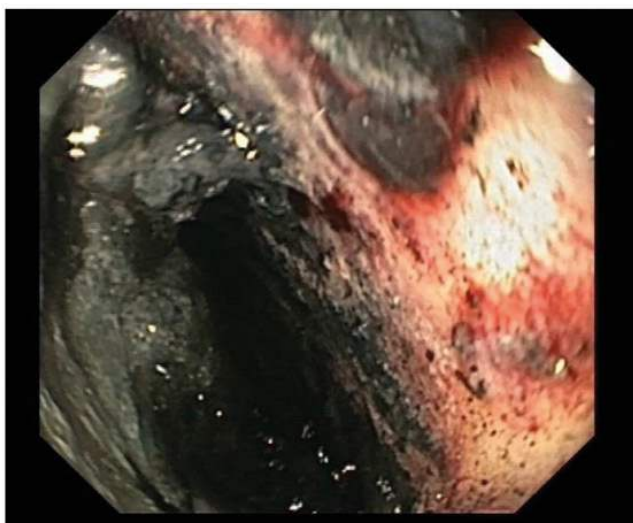


Figure 1. Gastroscopy on the fourth day of admission showing retention of activated charcoal and superficial ulcerative lesions in the distal oesophagus and stomach, without signs of active bleeding

benzodiazepine and opioid intoxication may have contributed to the respiratory depression. Aspiration pneumonia and bacterial translocation following mucositis may have added to the severity of the distributive shock. Hyperthermia is thought to be caused by the acidic nature of chlorphenoxy herbicides, which enables them to act as uncouplers of oxidative phosphorylation and therefore increase body heat.^[4,6,17,18] It is often accompanied by rhabdomyolysis and renal failure; however, in our patient creatine kinase and creatinine levels remained normal.^[3,4,8,16] In our patient hyperthermia may have been exacerbated by a serotonin syndrome from paroxetine intoxication. Chlorphenoxy compounds are well absorbed from the gastrointestinal tract and excreted almost completely unchanged in the urine. Levels can be estimated in both urine and plasma using gas-liquid chromatography. Chlorphenoxy concentration levels over 1000 mg/l have been reported.^[18] Unfortunately we could not find a laboratory able to perform these specific tests. The average half-life of MCPP is approximately 17 hours and varies widely, depending on the urinary pH.^[12,18] Increasing chlorphenoxy herbicide elimination by inducing urine alkalinisation with an infusion of sodium bicarbonate has previously been described as a successful treatment.^[4,13,19] Schmoltdt et al. and Flanagan et al. demonstrated a significant fall in MCPA half-life after alkalinisation.^[15,19] In 2004, the American Academy of Clinical Toxicology and the European Association of Poisons Centres and Clinical Toxicologists affirmed these findings and recommended treating acute 2,4 D and mecoprop poisoning by alkalinising urine.^[20] After urine alkalinisation our patient's condition remained critical. Since MCPP is a lipophilic substance, treatment with intralipid was started. This relatively novel therapy has never been described in case reports as a treatment for phenoxy acids intoxication. Its mode of action is not completely understood, but various potential mechanisms have been proposed. The most often cited is the 'lipid sink' theory, which suggests that administration of lipids expands the intravascular lipid phase resulting in extraction of the offending lipid-soluble drug from its target tissue.^[21] After administration of intralipid an improvement was observed in our patient's haemodynamic status, with a decrease in norepinephrine administration as can be seen in *figure 2*. Although unproven, and with uncertainty around the timing of administration, we think intralipid could be considered to be an adjunctive therapy in patients with severe chlorphenoxy acid herbicide intoxication.

Conclusion

Acute phenoxy-type herbicide intoxications are rare but dangerous and should be taken extremely seriously. Physicians treating these intoxications may consider administration of sodium bicarbonate and intravenous lipid emulsion. Our case shows that despite severe clinical signs, such as absent brainstem reflexes for nine days, patients suffering from MCPP intoxication can make a full recovery. We therefore strongly

Table 1.

Symptoms	Differential diagnosis/cause	Investigations	Management
Cardiac arrest	Hypoxia	No cardiac output. ECG: sinus bradycardia 30/min. Consistent with PEA	Advanced life support (2 min)
Hyperkalaemia (7.2 mmol/l)	1. Mecoprop toxicity 2. Respiratory acidosis	N/A	Calcium chloride, insulin/glucose
Distributive shock	1. Mecoprop toxicity 2. Sepsis from aspiration pneumonia/bacterial translocation from mucositis	PICCO: CI 2.6, GEDI 506, EVLWI 7.6, SVRI 1595, SVV 12. Bedside cardiac echo: hyper-dynamic LV, kissing ventricles. Blood cultures: E. coli. Sputum cultures: E. coli and S. aureus	IV fluids, noradrenaline, antibiotics Management mecoprop toxicity: • Activated charcoal: decrease mecoprop absorption • Sodium Bicarbonate: alkalinization of urine to increase mecoprop elimination • Intralipid 20%: enhance redistribution and elimination of mecoprop
Hyperthermia (T 41.6), ocular clonus, bilateral Babinski signs	1. Serotonin syndrome (paroxetine intoxication) 2. Mecoprop toxicity	N/A	Active cooling and dantrolene infusion Mecoprop toxicity management as above
Prolonged coma (E1M1Vt) with absent brainstem reflexes for nine days	Mecoprop toxicity	EEG: burst suppression pattern	Mecoprop toxicity management as above
Upper GI bleeding	Corrosive damage caused by mecoprop	Gastroscopy: superficial ulcerative lesions in oesophagus and stomach	Esomeprazole infusion
Anaemia (Hb 4.8 mmol/l), thrombocytopenia ($30 \times 10^9/l$), leukopenia, ($1.73 \times 10^9/l$), coagulopathy (APTT 75.6s, PT 32.9s)	1. Upper GI bleeding 2. Haematopoietic cytotoxicity caused by mecoprop	N/A	Massive transfusion protocol Mecoprop toxicity management as above

N/A = not applicable;

advocate continuing treatment and supportive care in the ICU department until MCPP is considered fully eliminated.

Disclosures

All authors declare no conflict of interest. No funding or financial support was received.

Table 2. Clinical findings in mecoprop intoxication

Author	Type of intoxication	Clinical findings						Death or recovery
		Respiratory	Haemodynamic	Neurologic	Gastro-intestinal	Metabolic	Other	
Dickey, 1988	MCPP, ioxynil	Tachypnoea	Tachycardia, asystole	Myosis, agitation, muscle rigidity		Hyperkalaemia, elevated serum CK, metabolic acidosis, hyperthermia	Liver and renal necrosis, pulmonary and cerebral oedema on autopsy	Death
Fraser, 1984	MCPP, 2,4-D, dicamba		Hypotension	Coma	Abdominal distension, vomiting	Metabolic acidosis, leukocytosis	Blood in pleural cavity on autopsy	Death
Meulenbelt, 1988 (first case)	MCPP	Tachypnoea, hypoxaemia	Hypotension, supraventricular tachycardia	Coma, muscle cramps		Metabolic acidosis, petechiae, rhabdomyolysis, kidney failure, hyperkalaemia, anaemia, thrombocytopenia, elevated liver enzymes, LDH and myoglobin		Recovery
Meulenbelt, 1988 (second case)	MCPP, ethanol	Hypoxaemia, apnoea	Hypotension, tachycardia	Coma, muscle cramps, low tendon reflexes	Vomiting	Metabolic acidosis, rhabdomyolysis, renal failure, hyperkalaemia, anaemia, thrombocytopenia, leukopenia, elevated LDH and myoglobin		Recovery
Nisse,	MCPP, ethanol	Hypoxaemia, apnoea	Hypotension, tachycardia	Coma, muscle cramps, low tendon reflexes	Vomiting	Metabolic acidosis, rhabdomyolysis, renal failure, hyperkalaemia, anaemia, thrombocytopenia, leukopenia, elevated LDH and myoglobin		Recovery
Prescott, 1979	MCPP, 2, 4-D	Tachypnoea, hypoxaemia	Tachycardia, T-wave flattening and inversion	Confusion, agitation, coma, miosis, absent tendon reflexes, myotonia	Vomiting	Metabolic acidosis, elevated serum CK, urea, aminotransferase and LDH, hyperthermia		Recovery
Wells, 1981 (first case)	MCPP,	Tachypnoea, hypoxaemia	Tachycardia, T-wave flattening and inversion	Confusion, agitation, coma, miosis, absent tendon reflexes, myotonia	Vomiting	Metabolic acidosis, elevated serum CK, urea, aminotransferase and LDH, hyperthermia		Recovery
Wells, 1981 (second case)	MCPP,			Coma				Recovery
Osterloh, 1983	MCPP, 2,4-D, chlorpyrifos		Supraventricular tachycardia, hypertension, hypotension, QT interval prolongation, widened QRS, peaked T waves, bradycardia, asystole	Confusion, coma, myoclonus, miosis	Diarrhoea	Metabolic acidosis, hyperkalaemia, hypocalcaemia, hypophosphataemia, renal failure, thrombocytopenia	Pulmonary oedema, duodenal haemorrhage and liver necrosis on autopsy	Death

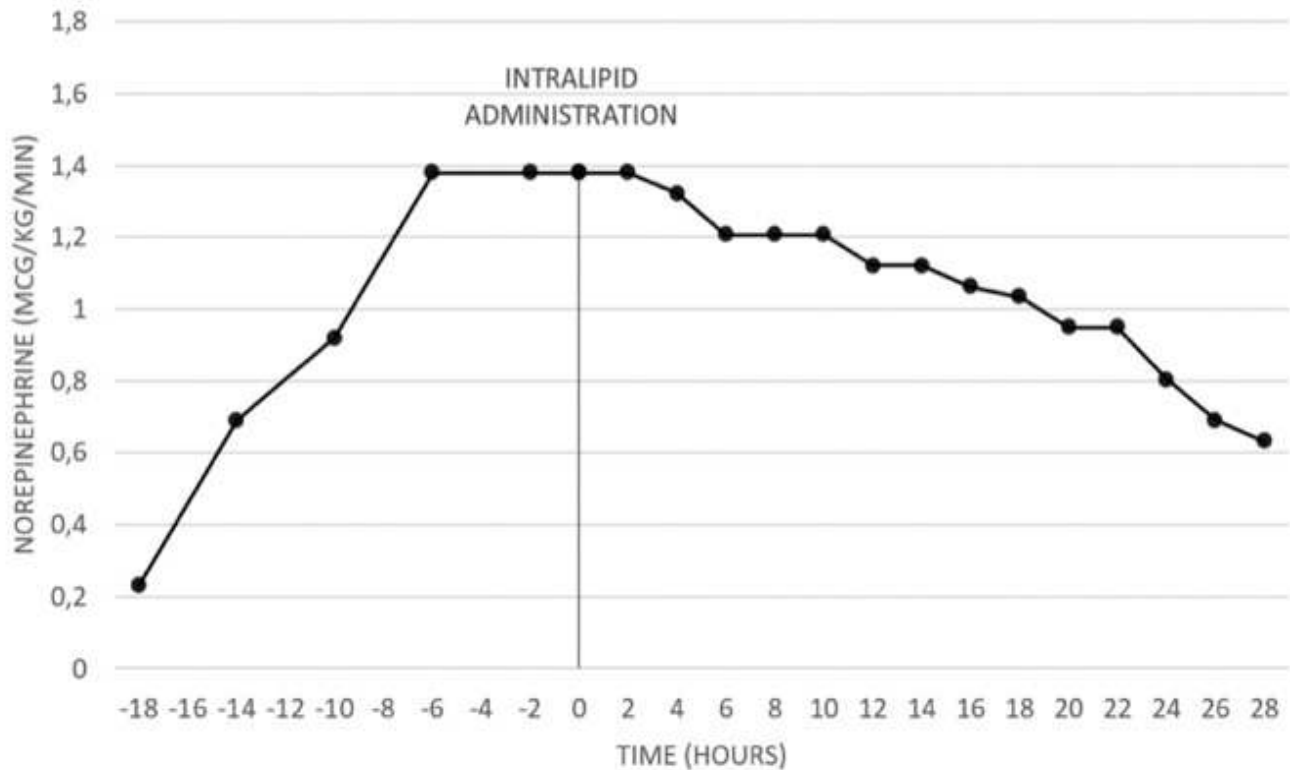


Figure 2. Effect of intralipid on norepinephrine dose

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