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Abamectin poisoning: a case report and review of literature

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Abstract

Abamectin, a widely used insecticide in Sri Lankan agricultural practices is recognised to occasionally cause serious neurological and cardio-respiratory consequences, and very rarely fatalities following human intoxication. We report a young male presenting with agitation, generalised seizures, coma, respiratory failure, and metabolic acidosis following attempted suicide with abamectin ingestion. He improved after 48 hours of intubation, mechanical ventilation and supportive intensive care. This reported case and review of literature is aimed at creating awareness on toxicology and clinical manifestations of abamectin poisoning.

Key words: abamectin, abamectin poisoning, seizures following poisoning

Introduction

Abamectin ($C_{95}H_{142}O_{28}$), ivermectin and six other 16-membered macrocyclic lactone derivatives belong to the broad chemical group of Avermectins.(1,2) Since their discovery in 1978, Avermectins are semi-synthetically manufactured or extracted directly from a toxin of *Streptomyces avermitilis*, a saprophytic actinomycete.(1) Abamectin is an insecticide, whereas ivermectin is an anti-helminthic and miticide used therapeutically in medical and veterinary practice. Both have different mechanisms of action. Abamectin is commercially manufactured as a mixture of Avermectin B1a (80%) and B1b (20%),(2) and is sold as 18 g/L EC (emulsifiable concentrates)[figure 1] and 20 g/L SC (suspended concentrates) in Sri Lanka. The department of Agriculture, Sri Lanka recommends abamectin to be used in diluted form, against mites (*Tatranychus spp., Hemitararsonemus latus*), leaf miners (*Liriomyza huidobrensis*), fruit borers (*Tuta absoluta*), root nodule nematodes (*Meloidogyne spp.*), cinnamon upper leaf galls (*Trioza cinnamon*) and aphids (*Aphis gossypii* and *Myzus persicae*).(3) Cases of abamectin poisoning were mostly reported from Asian countries with an agricultural background. (4-12) The exact prevalence of the abamectin poisoning in Sri Lanka is not known, and only three reported cases of attempted suicide with poisoning leading to severe acute neurological and pulmonary complications have been reported in the past decade. (13-15) The distribution and selling of abamectin is largely unregulated, making it a potential cause of insecticide poisoning. We report a case of a healthy young adult with life-threatening neurological and respiratory complications following abamectin poisoning, who completely recovered with supportive intensive care. The case is followed by a brief discussion and review of literature on relevant toxicology. This case also emphasises the importance of awareness of the serious consequences of this pesticide which is being used as a mode of suicide and intoxication in Sri Lanka.

Case presentation

A 25-year-old previously healthy man, from an agricultural background was brought to the nearest hospital within 2 hours of self-ingestion of abamectin pesticide (100 mL, 18 g/L EC). Vitals were stable on

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Figure 2 - A bottle of Abamectin, 18g/L emulsifiable concentrate, available in Sri Lanka

admission. He was initially treated with gastric lavage via nasogastric tube and activated charcoal (50g). Four hours post ingestion, he became agitated, developed generalised tonic clonic movements with oral frothing and subsequently had a drop in both GCS (13/15 to 8/15 E2V1M5) and on-air saturation (98 to 80 mmHg). He was intubated and transferred immediately to the Intensive Care Unit (ICU) for ventilator support. On admission to the ICU, he was drowsy but arousable and afebrile. He had a pulse rate of 105 beats per minute, blood pressure of 126/80 mmHg, mid-sized (3mm) pupils responsive to light, normal fundoscopy, generalised hypotonia, normal reflexes and down-going plantars. There were no signs of ptosis, meningism, or any abnormal eye or limb movements. He was maintaining spontaneous breaths at 26 per minute with a saturation of 95% on ventilator support (FiO2 of 35% and later weaned to 25%). Urine output was adequate. Monitoring of vitals and urine output, sedation with midazolam infusion (2 mg/h), gastro-protection with ranitidine (i.v. 50mg b.d.), thromboprophylaxis with enoxaparin, intravenous hydration and nutritional support were included as part of supportive intensive care.

Table 1 shows the trend in arterial blood gas and biochemical parameters. The initially evident mild metabolic acidosis, elevated lactate (3 mmol/L), CRP, and neutrophil leucocytosis following the seizure and intubation normalised after 48 hours. ECG showed small q waves in inferior leads with no acute progressive changes. Serum electrolytes (including sodium, potassium, calcium, magnesium), serum creatinine , blood urea , liver profile , coagulation studies (PT/INR: 1.08; APTT: 31 seconds), cardiac biomarkers, blood picture, chest radiography, electroencephalography and non-contrast computed tomography of brain were normal. Urine and blood cultures didn't reveal any growth.

He was extubated after 48 hours. Subsequent vital parameters were normal and no focal neurology were evident. He exhibited features of moderate depression with impulsive behavioural traits due to acute financial stressors, and thus was commenced on sertraline and a small dose of risperidone. Out-patient psychiatry follow up was arranged. The patient was discharged on the 4th day with complete recovery and no residual neurological deficits. Review at one-week post discharge was unremarkable.

Discussion

Abamectin functions by increasing gamma amino butyric acid (GABA) neurotransmitter release and GABAA receptor activation with subsequent improvement of membrane permeability for chloride ions. The outcome is central nervous system inhibition and immediate**,** irreversible neuromuscular paralysis in susceptible insects.(16) Typical concentration of abamectin residues in or on crops is very minimal (0.025 ppm) as they are degraded rapidly by sunlight and by action of soil microbes. They also have low water solubility and tight binding to soil, thereby having less tendency of leaching into groundwater.(17) Abamectins also cross blood brain barrier sluggishly and have a low affinity to mammalian GABAA receptors, thus having a wide margin of safety, and low risk to humans.(18) However, toxicities are believed to occur above a lethal dose of 10 mg/kg.(19,20) Our patient had consumed 100 cc (1800 mg), which is three times the lethal dose (36.0 mg/kg). The GABAergic effects of abamectin contribute to neurological manifestations and an increase in nitric oxide levels is attributed for hypotension in non-human mammals.(21,22) Chronic exposure to abamectin was associated with impaired sperm maturity in a Turkish study.(23)

Literature on human abamectin poisoning is limited to case reports and case-series.(4-5,19) As in our case, most reported cases of abamectin present in an attempt to commit suicide with oral ingestion.(4-12) Parenteral and transcutaneous routes of absorption are also reported.(4) Mild exposure results in nausea, vomiting, diarrhoea, anxiety, irritability and

Table 1 - Trend of blood gas and blood investigation parameters

Parameter	Day 1	Day 2	Day 3
White blood cell count (x10^3/uL)	24.3	20.4	12.8
Neutrophil count (x10^3/uL)	22.3	17.8	10.1
Haemoglobin (g/dL)	14.2	13.1	12.4
Platelet count (x10^3/uL)	330	280	235
Haematocrit (%)	44.0	38.9	37.2
C-reactive protein(g/dL)	14.4		8.4
pH	7.34	7.46	7.75
PaCO2 (mmHg)	38.0	29.2	32.5
PaO2 (mmHg)	151.9	167.3	143.9
Bicarbonate (mmol/L)	21.9	21.2	22.8
Anion gap (mmol/L)	12.8	12.2	7.7
Lactate (mmol/L)	4.1	0.6	0.6
PiO2/ FiO2 (mmHg)	434.1	535.3	513.9

weakness.(4-6) Flushing, redness and dryness has also been reported with mild exposures.(7) Moderate toxicity causes dilated pupils, ptosis, confusion, coma, and seizure.(4-6) Complications of coma, hypotension, respiratory failure, aspiration pneumonia, metabolic acidosis as in our case are commonly reported with severe intoxications.(4, 6-7) Seizures, cerebellar ataxia, nystagmus, dilated pupils, rhabdomyolysis are rarely reported.(4,8,13) Therefore our patient had clinical features of severe intoxication. Electroencephalographic evidence of serious cerebral dysfunction can be seen even with ingestion of 20g of abamectin.(9) Myoclonus and polyneuropathy have been reported following very high doses (414.2 mg/kg).(10) Fatalities, however, are rare.(4-5) Abamectin is not known to cause residual neurological defects and often results in complete resolution. Hence, the prognosis of patients with abamectin poisoning is likely to be favourable unless they are complicated by severe hypotension or aspiration. A Taiwanese case series of eighteen patient-exposures to abamectin (20 g/L) and one exposure with ivermectin (10 g/L) demonstrated a dose-response relationship of clinical features(4) Four patients in this series were asymptomatic, eight had minor symptoms with mean ingestion of 23 mg/kg (4.2 to 67 mg/kg), seven manifested with severe symptoms such as coma, four with aspiration from respiratory failure and three with hypotension, after a mean ingestion of 100.7 mg/kg. Only one fatality resulted from multi organ failure on the 18th day of poisoning after a dose of 88 mg/dL. In a Thai series of 49 patient-exposures, the majority(33) were asymptomatic or had mild symptoms and the rest had severe complications such as coma and hypotension of whom five succumbed to death.(5) Six of the 18 cases reported by Wu Liqiang, developed acute pulmonary oedema, while four developed cardiorespiratory arrest.(11) In a recently conducted Chinese study, 7 of 64 patients with self-harm with Abamectin required ICU care, of whom 17 required intubation, 4 required inotropic support and 4 fatalities were reported.(4,12) Coma, hypotension and aspiration pneumonia may serve as poor prognostic indicators.(7)

Abamectin poisoning is scarcely reported in Sri Lanka. The three local case reports to date were associated to suicide in young individuals from agrarian regions of Sri Lanka. Karunathilake et. al described a 30-year-old male from Polonnaruwa presenting with acute confusion (GCS – 9/15), blurred

vision, partial ptosis, mydriasis (3mm), nystagmus, ataxia, agitation but with normal haemodynamic and biochemical parameters, within 3 hours of ingesting 720 mg of abamectin (18 g/L EC).(13) The patient completely recovered without intubation within 24 hours. Pirasath et al. reported a 29-year-old female from Kilinochchi presenting with low GCS (10/15), mydriasis, ptosis, ataxia, mild mixed acidosis, lactate of 1.9 mmol/L with normal cardio respiratory and other biochemical parameters within an hour of ingesting 1800 mg of abamectin (18g/L EC).(14). She was agitated for 12 hours, but improved after a non-intubated, observational period of 24 hours in the intensive care unit. Sirisena et al recently reported a 55-year old male from Kandy presenting with low GCS (13/15), transient bilateral ptosis and mydriasis managed with activated charcoal and supportive observational care alone.(15) Contrary to these cases, our patient did not have ptosis, nystagmus or ataxia, but had generalised seizures complicated with lower GCS (8/15), mild metabolic acidosis with hyperlactaemia and impending respiratory failure requiring intubation, supplementary ventilatory care for 48 hours.

The early onset of symptoms of intoxication indicates quick gastrointestinal absorption, thus implying the necessity of gastric decontamination by means of lavage in the initial hours after poisoning. Activated charcoal is also used for decontamination as abamectin is extensively excreted with faeces. Skin decontamination with soap and water and eye decontamination with clean water or saline should be performed if needed.(24) Supportive care and close monitoring at least in the high dependency setting is the mainstay of treatment.(25) Intubation and ventilatory support is essential in the setting of airway compromise as in coma, respiratory depression and help in preventing aspiration pneumonia.(4) Hypotension often is fluid responsive, and rarely warrants inotropic support.(22) The use of GABAergic medications such as benzodiazepines and barbiturates should be avoided. Also, GABAergic stimulation from recent or concomitant alcohol ingestion may delay recovery. Although a dedicated antidote is currently unavailable, the potential utility of flumazenil, a GABAA receptor antagonist as a detoxifying agent has been studied with ambiguous results. Chung et al demonstrated no benefit of giving flumazenil(4), whereas Sun et al noted an enhanced recovery and minimised hospital costs with use of flumazenil.(26) Picrotoxin, another GABAA antagonist that is used as an effective antidote for ivermectin in veterinary practice, is a potential antidote for abamectin poisoning in humans.(22)

Conclusion

Abamectin intoxication causes GABAergic activation, leading to life threatening complications at large doses. The prognosis of patients with abamectin poisoning is likely to be favourable unless they are complicated by coma, severe hypotension or aspiration. The lack of epidemiological data limits the understanding of the burden of abamectin intoxication in Sri Lanka. Nevertheless, adequate awareness on abamectin related toxicological effects is essential for medical professionals taking care of agrarian communities. The emerging trend of self harm using abamectin is a matter of concern. This urges the need to implement suitable measures to regularise production and marketing of the insecticide.

Declarations

Author contributions
The principal author (AR) and the co-authors (WKSK and SB) have major contributions in preparation of the manuscript.

Conflicts of interest
No conflicts of interest to be addressed regarding this case report.

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