Case Report

Amitraz poisoning – A case report of a common but highly misconstrued cause of poisoning in Zambia

Frighton Brighton Mutete[1], Nicola Bweupe[1], Kaseya OR Chiyenu[1,2], Katongo Hope Mutengo.[1*]

[1]*Department of Internal Medicine, Livingstone Central Hospital, Ministry of Health, Livingstone, Zambia*
[2]*Intensive Care Unit, Livingstone Central Hospital, Ministry of Health, Livingstone, Zambia*

ABSTRACT

Amitraz is a widely available insecticide but whose human poisoning is highly under-recognized and mistaken for organophosphate poisoning. As a result, it is often mismanaged possibly resulting in suboptimal clinical outcomes. We present a case of a 55-year-old man who ingested Amitraz pesticide 3 hours prior to admission following a suicide attempt. His clinical condition rapidly deteriorated necessitating admission to the Intensive Care Unit. As there is no known effective antidote for human Amitraz poisoning in current medical practice, he was managed supportively but with excellent clinical outcome. Despite the lack of an effective antidote for human Amitraz poisoning, appropriate supportive management yields excellent clinical outcomes. However, misdiagnosis and incorrect treatment may result in severe effects on the body systems causing coma and respiratory failure which often yields fatal outcome especially in resource-limited settings like Zambia.

INTRODUCTION

Amitraz is a formamidine derivative insecticide that dissolves in organic solvents acetone, toluene and xylene. It works as an α2 agonist in the central nervous system (CNS) and an α_2 and α_1 agonist peripherally[1]. It also causes inhibition of both Monoamine Oxidase (MAO) and prostaglandin E_2 synthesis. The clinical presentation of Amitraz poisoning often has CNS, cardiovascular, respiratory, urinary, gastrointestinal and metabolic features.

Amitraz is normally sold as a 12.5 to 50% formulation dissolved in an organic solvent mostly Xylene[1,5]. It is used as an ectoparasite to control Demodicosis in canines, ticks and mites in cattle and sheep, Psylla in pears and also Red Spider infection in fruit crops[1-6]. Human exposure can be intentional or accidental via inhalation, skin contact or ingestion[1,4].

Few cases have been reported in Sub-Saharan Africa. For example, a systematic review by Dhooria *et al* showed that only 69 cases have been reported in South Africa as of the year 2011 and 1 case in Kenya as of the year 2012[7]. Despite being a common pesticide used among most small-scale farmers in Zambia, there is little awareness of Amitraz poisoning and subsequent management. The poisonous effect may be misconstrued either as organophosphate or carbamate poisoning in view of similarities in clinical presentation. We present a case of a 55-year-old Zambian man with Amitraz poisoning.

Case presentation

A 55-year-old Zambian man presented to the Emergency Department of Livingstone Central Hospital (LCH), a tertiary institution in the Southern Province of Zambia, with a history of having ingested an unknown quantity of Amitraz (brand name Triatix) 3 hours before presentation. He had ingested the poison in a suicidal attempt following a domestic dispute. The patient was initially rushed to

Corresponding author:
Department of Internal Medicine, Livingstone Central Hospital, Ministry of Health, Livingstone, Zambia
Katongo Hope Mutengo;
katmutengo@yahoo.com

Keywords: *Amitraz, Poisoning, Organophosphate, Treatment, Antidote*

a local primary health facility after he reported having ingested all contents of a full bottle of Amitraz. He was said to have been given activated charcoal and later referred to this hospital. There was no history of vomiting, diarrhea or copious secretions from the mouth or nose.

On presentation to the Emergency Department (ED), the patient was semi-conscious with a Glasgow Coma Scale (GCS) of 10/15 (Motor-6, Verbal-2, Eyes-2) with pinpoint pupils bilaterally. He had no secretions, and the lungs were clear on auscultation. However, the peripheral oxygen saturation (SPO_2) was 86-88% on ambient air. The respiratory rate was 20 breaths per minute. The blood pressure was not recordable with a feeble pulse of 70 beats per minute. The heart sounds were regular. The patient was hypothermic with a temperature of 35.2°C. The abdomen was distended with sluggish bowel sounds. Tendon reflexes were normal. Based on these findings, the patient was presumed to have organophosphate poisoning (OPP).

He was immediately given oxygen at 4 liters /minute via nasal prongs with an improvement of the SPO_2 to 99%. The patient was given 6mg of atropine over a period of 10 minutes, however, when the bottle of contents was reviewed, the diagnosis of OPP was disregarded and atropine treatment was immediately stopped. An infusion of 0.9% saline was also given at 40mls/kg over 1 hour with an improvement of blood pressure to 84/50mmHg and a mean arterial pressure (MAP) of 61. Given the inadequate MAP after fluid resuscitation, the patient was initiated on inotropic support with dopamine at 5mcg/kg/min which was titrated up by 2mcg/kg/min every 15 minutes to achieve a target MAP of greater than 70mmHg. 3 hours post-admission, the patient's level of consciousness deteriorated with a GCS rating dropping to 3/15. Pupils were dilated and unresponsive to light. Additionally, the patient had poor respiratory effort. He was therefore admitted to the Intensive Care Unit (ICU) in anticipation of respiratory failure. He later went into respiratory arrest and was intubated and given ventilator support. The circulatory shock resolved with dopamine but the patient remained on inotropic support for 48 hours. Arterial blood gases due to the non-availability of the service at LCH. The other laboratory results were as shown in **Table 1.**

Table 1: Results of the initially ordered laboratory tests

Laboratory Parameter	Result	Reference Range
White cell count	10.40x10^9/L	4.00-10.00
Red cell count	4.13x10^9/L	4.89-6.11
Hemoglobin	12.1g/dL	14.3-18.3
Hematocrit	38.3%	41.0-52.0
Mean corpuscular volume	92.7fL	79.1-98.9
Platelets	188x10^9/L	137-373
Neutrophils	88.9%, 9.25x10^9/L	0.96-6.40
Lymphocytes	7.3%, 0.76x10^9/L	1.01-2.97
Monocytes	3.8%, 0.40x10^9/L	0.08-0.61
ALP	71.6 U/L	42.0-98.0
AST	66.1U/L	0.0-45.0
ALT	65.0U/L	0.0-35.0
Albumin	31.2(g/L)	35.0-52.0
Urea	7.4(mmol/L)	2.80-7.10
Creatinine	138.4(µmol/L)	59.0-104.0

On the second day of ICU admission the patient's level of consciousness had improved with the GCS of 14/15 (Eyes-4, Motor-6, Verbal-4). However, the abdominal distension had increased and bowel sounds become sluggish so a nasogastric tube was inserted and the patient kept *nil per os* for three days. During this time the patient was maintained on 5% dextrose. The blood glucose profile remained within the normal range throughout the time the patient was admitted. There was no history of seizures throughout the treatment period.

The patient had made a full recovery on the fourth day with a steady GCS of 15/15. He had also opened bowels and the abdominal distension had resolved. He was therefore discharged from ICU and started on a light diet. The patient was discharged from medical care on the 5th day with no complications. He was seen by a qualified psychiatrist before discharge for psychological support. He remained

asymptomatic when he was reviewed at 2 weeks and 2 months post-discharge and had continued to make steady progress in his social life.

DISCUSSION

Amitraz poisoning is likely common in Zambia especially among rural farming communities where it is used for agricultural and veterinary purposes. It is available in various brand names and does not require a prescription to purchase[2-3]. Locally, insecticides used for veterinary purposes are collectively referred to as 'Dip' and this brings confusion in distinguishing different types of poison. As OPP is the most common poisoning, 'Dip-poisoning' almost always refers to it. As a result, patients are almost always managed as OPP. In addition, Amitraz poisoning may present like OPP[2]. Because of these clinical similarities, our patient was initially thought to have OPP.

Amitraz is a formamidine that stimulates α_2 receptors in the CNS and α_2 and α_1 receptors peripherally[1-6]. Because of its α_2 agonist effect on the CNS, presentation is similar to clonidine poisoning[2]. It also causes secondary inhibition of MAO and synthesis of prostaglandin E_2[6]. Clinical manifestations of Amitraz poisoning are due to these pharmacological properties as well as those of organic solvents used in various preparations[2].

Currently, there is no antidote for treating Amitraz poisoning. Even though α_2 antagonists like Yohimbine and Atipamizole have been used effectively in animals, there are no human trials to support their use[6]. Naloxone which is used as an adjunct in the management of Clonidine poisoning is also not effective[1-3,6]. Therefore, management is supportive as was the case with our patient.

Clinical manifestations include CNS depression, drowsiness, coma, convulsions, ataxia and nystagmus, irritability[1]. Our patient presented with CNS depression. Initially, he had drowsiness then later went into a coma. There was no history of ataxia, nystagmus or convulsions. Ataxia and coma have also been attributed to solvents used for example Xylene[1-6]. Our patient's coma lasted for 36 hours, however, other studies have shown that CNS depression ranged from a few hours to 24 hours[3].

Other additional features such as miosis - a pre-synaptic effect at low doses and mydriasis- a postsynaptic effect in high doses, absence of light reflexes, polyuria- due to inhibition of antidiuretic hormone and renin, hyperglycemia, reduced gastrointestinal motility and abdominal distension have been observed[3,8]. Our patient initially had miosis then later developed mydriasis. Although this can be attributed to the atropine that was initially given, the mydriasis persisted for over 4 hours, the period which is beyond the half-life of atropine which made us conclude that there was a possibility of the primary effect of the high dose of Amitraz. Additional reported features like respiratory depression, respiratory arrest, hypotension, and bradycardia were all present in our patient. Even though atropine has been used to treat bradycardia and myosis, its use in Amitraz poisoning remains questionable, hence atropine was stopped in our patient and replaced with dopamine which has been shown to treat both hypotension and bradycardia[2,4].

Most literature describes the onset of action between 30 to 180 minutes after exposure[1,2,6]. In our patient, clinical features manifested within this time frame. However, Kalyoncu *et al* reported onset within 5 minutes to 6 hours with oral ingestion and 5 minutes up to 24 hours after dermal exposure[9].

One of the clinical features differentiating Amitraz from OPP is the absence of hypersecretions. Our patient had no secretions at presentation and throughout the duration of his admission. The SPO_2 at room air was low despite the patient having clear lung fields on auscultation consistent with respiratory depression associated with Amitraz. He later developed respiratory arrest and required intubation and respiratory support; another feature consistent with Amitraz poisoning.

Our patient had hypothermia at presentation but later developed intermittent fever which had resolved at the time of discharge. Most literature report hypothermia attributed to the inhibition of prostaglandin E2[2,3]. However, Ulukaya *et al* had

reported hyperthermia[10]. Our patient also presented with slow gastrointestinal motility and abdominal distension which resolved 4 days later after decompression and being nil per os. Others have reported a rare occurrence of Ogilvie's syndrome (acute pseudo colonic obstruction) which requires the use of neostigmine in its management[6].

The liver enzymes were elevated in our patient. This is in keeping with the report by Herath *et al*. However available evidence does not show any significant alteration in the Liver function tests. Amitraz is a potent hepatotoxic drug that decreases hepatic glutathione activity but liver function tests return to normal within 48 hours[1,3]. The serum creatinine was elevated in our patient but few studies have reported it and its significance is not yet determined. Hematological tests were all normal. Additionally, ECG changes reported by other studies which include bradycardia, ST-segment changes, ventricular arrhythmias and *torsade de pointes*[4] were, however, not seen in our patient.

Dose intake in our patient was unknown but it can be deduced from the clinical presentation that the patient had ingested a substantial amount of Amitraz. The minimal toxic dose that has been reported is 3.57mg/kg[6]. Despite the severity of the clinical features, our patient made a full recovery on supportive treatment.

CONCLUSION

In spite of there being no antidote for human Amitraz poisoning in current medical practice, there is prognosis if the patient is given supportive management in a high dependency setting as illustrated by our patient who was discharged, with no complications, 5 days after admission. However, clinicians need to be aware of the clinical manifestations of Amitraz and correctly identify the poison so as to institute correct treatment to avoid deleterious effects especially if there is a history suggestive of pesticide ingestion.

Acknowledgments

The authors wish to the patient for his cooperation and provision of the information used in the manuscript. Without his support, this manuscript would not have been possible.

Consent

Consent was obtained from the patient before the publication of this case report.

Conflict of interest

The authors declare no conflict of interest.

Abbreviations

ADH: antidiuretic hormone; CNS: central nervous system; ECG: electrocardiogram; ED: emergency department; GCS; Glasgow Coma Scale, ICU: intensive care unit; IV: intravenous; MAO: monoamine oxidase, OPP; Organophosphate poisoning.

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