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Amitraz Poisoning: The Not So (Un) Dangerous Poisoning

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Abstract

Amitraz is a member of the formamidine family of pesticides. Its structure is 1,5 di-(2,4-dimethylphenyl)-3-methyl-1,3,5-triazapenta1,4-diene. It is used as an agricultural insecticide for fruit crops and as an acaricide for dogs and livestock. The clinical manifestations of amitraz (impaired consciousness, drowsiness, vomiting, disorientation, miosis, mydriasis, hypotension, bradycardia, respiratory depression, hypothermia, generalized seizures, hyperglycemia and glycosuria) can be explained by the agonist action of amitraz on α1 and α2 receptors. Drowsiness is the predominant manifestation whereas seizures and deep coma is also reported. Bradycardia and hypotension are the cardiovascular manifestations and respiratory

depression too is common. Liver biochemistry, renal biochemistry, serum electrolyte and blood gases are rarely effected. Management of amitraz poisoning is still considered to be supportive and symptomatic with monitoring of nervous system, cardiovascular and respiratory systems. The place for gastric lavage and activated charcoal is controversial but may still be considered for treatment. Atropine is effective for symptomatic bradycardia and inotropic support might be needed for hypotension despite adequate fluid resuscitation. Diazepam or Lorazepamis generally effective for convulsions although some patients needed intubation and ICU care. Around 33% of patients developed respiratory failure and 20% of them needed mechanical ventilation. Although the reported fatality rate is 2%, the actual rate may be more.Case reports on amitraz poisoning in Asian adults are rarer and we could only find a few cases reported in Southeast Asia. So the general awareness regarding the management of this toxin among clinicians is lacking in Asian countries. Here we review the case report of 3 patients with amitraz poisoning with life threatening clinical picture.

Keywords

Amitraz poisoning, Symptoms, Management, Literature review

Introduction

Amitraz is an antiparasitic active ingredient used in veterinary medicine in livestock and pets against some **external parasites** (lice, mites, ticks). It is also used against agricultural pests.[1,2]It contains triazapentadiene[1,5 di- (2,4-dimethylphenyl)-3-methyl-1,3,5-tri-azapenta- 1,4 diene][3]; an insecticide from the formamadine family. Commercially available formulations generally contain 12.5–20% of the compound in organic solvents. The US Environmental Protection Agency classifies amitraz as slightly toxic by the oral and inhalation routes (Toxicity Category III) and moderately toxic by the dermal route (Toxicity Category II) [4]. There have been very few case-reports from our country till date mostly due to underreporting of cases. This is further compounded by the fact that the toxidrome mimics organophosphate (OP) poisoning. Majority of amitraz poisoning occurs due to accidental ingestion by children. Here we present case series of young females with amitraz poisoning who developed CNS depression, bradycardia and hypotension requiring inotrope support.

Case Presentation

Case 1

A twenty four year-old female presented following self-ingestion of around5ml of amitraz (12.5 W/V) following a family dispute leading to the compulsive act. Five hours following ingestion, on admission to the hospital, her Glasgow comascale (GCS) was 10/15. Pupils were equal and 3 mm in size. Deep tendon reflexes were normal. She had bradycardia with a heart rate of 40beats per minute, hypotension with a blood pressure of 70/50 mmHg and a respiratory rate of 18 cycles per minute. Gastric lavage was performed along with intravenous fluid boluses. She was given supportive care; but because of the central nervous system (CNS) depression and respiratory failure, she was placed on ventilatory support. she developed sudden onset bradycardia and hypotension. Cardiopulmonary resuscitation (CPR) as per advanced cardiac life support (ACLS) protocol was initiated. Intravenous vasopressors like noradrenaline and dopamine was given to maintain blood pressure. Patient was started on atropine sulphate and we titrated the dose of atropine sulphate till the signs of atropinisation, following that patient were started on maintenance dose

of atropine. Her bradycardia persisted for 36 hours and she was drowsy for 12 hours.ECG revealed sinus bradycardia with a normal QT duration and the blood sugar was normal throughout. Full blood count, liver function tests, Urine full report, serum creatinine and electrolytes were normal. Arterial blood gases revealed mild respiratory alkalosis with a pH of 7.47, pCO2 of 28 mmHg and a HCO3− of 17.4 mmol/L. She was shifted to ward on day 3. She recovered fully within 72 h and was discharged on day 5.

INVESTIGATIONS	VALUE	NORMAL RANGE
WBC	7390/mm^3	3500- 10000/mm^3
Platelets	201000/mm^3	150000-400000/mm^3
Serum creatinine	0.84 mg/dl	0.6-1.3 mg/dl
Serum potassium	4.3meq/L	3.5-5.5 meq/L
AST/ALT	17/19 U/L	15-37/14-63 U/L
Alkaline Phosphates	43 U/L	46-116 U/L

Case 2

A twenty two year-old female presented following self-ingestion of around 10 ml of amitraz (12.5 W/V) following a family dispute leading to the compulsive act followed by 2-3 episodes of vomiting. Four hours following ingestion, on admission to the hospital, her Glasgow coma scale (GCS) was 9/15. Pupils were equal and 3 mm in size. She had bradycardia with a heart rate of 48 beats per minute, hypotension with a blood pressure of 78/54 mmHg and a respiratory rate of 16 cycles per minute. Gastric lavage was performed along with intravenous fluid boluses. She was managed at our center with IV fluids, Ryles tube feed, IV antibiotics, and supportive measures. She was given supportive care; but because of the central nervous system (CNS) depression and respiratory failure, she was placed on ventilatory support. She developed seizures and was treated with diazepam and antiepileptics.

ECG revealed sinus bradycardia with sinus arrhythmias in between with changes of myocarditis. Troponin T was raised. Blood sugar was normal throughout. A peripheral blood smear showed neutrophilic leukocytosis. Arterial blood gases revealed mild respiratory alkalosis with a pH of 7.54, pCO2 of 27.5 mmHg and a HCO3− of 20.3 mmol/L.On fifth day of admission, she developed sudden onset bradycardia and hypotension. Cardiopulmonary resuscitation (CPR) as per advanced cardiac life support (ACLS) protocol was initiated; however, despite all measures, she succumbed to her illness

INVESTIGATIONS	VALUE	NORMAL RANGE
WBC	26700/mm^3	3500- 10000/mm^3
Platelets	326000/mm^3	150000-400000/mm^3
Serum creatinine	0.76 mg/dl	0.6-1.3 mg/dl
Serum potassium	3.4meq/L	3.5-5.5 meq/L
AST/ALT	132/86 U/L	15-37/14-63 U/L
Alkaline Phosphates	84 U/L	46-116 U/L
Troponin T	0.290 ng/ml	0 – 0.014 ng/ml
CK-MB	59 U/L	0-25 U/L

Case 3

The case is about a 24 years old female ingested around 15 ml of amitraz poison (12.5%) as a suicidal attempt on 10 am which was about 1.5 h before her hospital admission. She complained of pain abdomen ,nausea, vomiting, and dizziness. Immediately, her family took her to our hospital . No history of generalized tonic-clonic movements, loose stools, hematemesis, melena, hematuria was present. She had heart rate of 80 beats per minute, hypotension with a blood pressure of 80/60 mmHg and a respiratory rate of 16 cycles per minute. Gastric lavage was performed along with intravenous fluid boluses. Urea (24), Creatinine (0.72), Na^+ (135; norm = 135-145), K^+ (4.1), SGOT (29), SGPT (24), ALK. Phosphates (54), Blood glucose (85 mg/dL; norm = 70-110 mg/dL), PT (13.3), Troponin T (0.01; normal 0-0.014) and CBC (WBC: 7960, HCT: 37.3, platelets: 187000/mm^3). Chest X-Ray was normal.ECG revealed sinus bradycardia. She was given supportive care; but because of the central nervous system (CNS) depression and respiratory failure, on day second she was placed on ventilatory support. On day 4 of admission, she developed sudden onset bradycardia and hypotension. Cardiopulmonary resuscitation (CPR) as per advanced cardiac life support (ACLS) protocol was initiated; however, despite all measures, she could not be revived and declared dead.

Discussion

Amitraz is an α2 adrenergic agonist and mimics clonidine in its manifestations. It acts as an agonist on both pre- and postsynaptic α2-adrenergic receptors[4, 5.Presynaptic] receptor stimulation inhibits norepinephrine discharge, while stimulation of postsynaptic receptors leads to effects similar to α1-stimulation[4].This is what produces the most of the clinical manifestations, altered sensorium (83%), miosis (50%), bradycardia (47%), vomiting (36%), respiratory failure (34%) and hypotension (31%) [6]. Hypothermia (24%) due to inhibition of Prostaglandin E2 synthesis and hyperglycemia (48%) are distinctive features of this poisoning[6].Miosis may be seen due to the presynaptic effect at low doses, or rarely mydriasis may also be seen due to postsynaptic effect at higher doses.

As in our patients, drowsiness was the predominant manifestation observed in cases of amitraz poisoning[1]and is probably due to the alpha 2 agonist action. In a case series by Yilmaz, H. L., impaired consciousness was predominant with drowsiness,

disorientation and a median pediatric Glasgow coma scale of 9[1].

In this study patients had short generalized seizures and Ertekin, V. et al., also reported generalized seizures following Amitrazpoisoning[7] . In all the cases seizures responded to diazepam. Deep coma and vomiting[7]were also described. Ataxia, stupor, and coma were attributable to the xyleneand propylene oxide components in amitraz[8].Shitole, D. G. et al., had reported cerebral edema in the CT brain of a patient who was found unconscious following Amitrazpoisoning[9].

Miosis with absence of light reflex is also commonly seen[1].Mydriasis has also been described but less commonly[1].This is because at low doses, α2 adrenergic agonists induce miosis by its effect on presynaptic receptors and in higher doses causemydriasis by its action on postsynaptic receptors In our patient, the pupil size was normal.

The α1 and α2 agonistic action of amitraz causes bradycardia and hypotension[3] which were seen in several case reports[1, 2.]Some needed intravenous fluid for resuscitation [9]and some patients were treated with atropine for bradycardia and hypotension[1].In a few cases dopamine was also given as a second line inotrope.

Kalyoncu and colleagues had reported respiratory alkalosis in two cases, respiratory acidosis in three cases, and metabolic acidosis in five cases . Mild respiratory alkalosis was seen in the arterial blood gas analysis of our patient.

Minimal increases in the level of serum ALT and AST were also reported rarely.

There is no specific antidote for amitraz poisoning and the management is supportive with monitoring and evaluation of the respiratory, cardiac, and central nervous systems. The role of activated charcoal has not been studied, and there are no data comparing the effectiveness gastric lavage and activated charcoal in relation to amitraz. However it may still be considered for treatment.

Atropine has been used with success in patients who developed bradycardia[1]. For hypotension, intravenous fluid resuscitation and inotropic agents (dopamine or noradrenaline) can be added as needed[1].Seizures respond to diazepam and lorazepam .[1]Oxygen should be given if the oxygen saturation drops and some patients with severe respiratory depression need intubation and intensive care unit (ICU) stay[1].

Conclusion

The diagnosis of amitraz intoxication is extremely challenging. The co-existence of neurological deterioration, bradycardia, and infrequently miosis in individuals that were exposed to insecticides most often leads to confusion with organophosphate overdose. It presents with rapidly progressing and life-threatening clinical picture. In spite of this there is no antidote for human Amitraz poisoning in current medical practice, the prognosis is good if the patient is given supportive management in a high dependency setting as illustrated by our patient who was discharged 5 days after admission without complications. But it could also be fatal in very small amount, So more reporting is needed since awareness about amitraz, its toxicity, and its management. The Amitraz poisoning and its management knowledge is poor among medical practice, our article will increase the knowledge and awareness about early and better treatment of patient with amitraz poisoning.

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