An uncommon but lethal poisoning – Amitraz

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CASE REPORT

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Abstract

Amitraz, a centrally acting alpha-2 adrenergic agonist, is increasingly being used for treatment of ectoparasitic infestation in cattle. Its effects in humans may mimic organophosphate poisoning. We report a case of poisoning after suicidal ingestion of Amitraz. The patient presented in a deeply comatose state with respiratory depression, bradycardia and mydriasis (instead of miosis, the more common presentation in previous reports). He recovered completely within 24 hours with adequate supportive measures. The importance of this case report is highlighted by the increasing use of this compound, the life-threatening presentation, the excellent prognosis with early recognition and supportive management and the limited human toxicological data.

Key Words
Amitraz, Poisoning, α₂ adrenergic agonist

Background

Amitraz, 1,5 di-(2,4-dimethylphenyl)-3-methyl-1,3,5-tri-aza-penta-1,4 diene, is a formamidine pesticide which is increasingly being used as an insecticide and an acaricide.¹ Its varied uses include treatment and control of generalised demodicosis in canines, ticks and mites on cattle and sheep, psylla infection of pears and also for control of red spider mites on fruit crop.¹,² The formulations available for commercial use contain 12.5–50% of Amitraz in an organic solvent like xylene and is diluted with water before use.³,⁴ Amitraz is an uncommon poisoning in humans and may occur via oral, dermal or inhalational routes. Being a centrally acting alpha-2 adrenergic agonist, it can present with life-threatening effects such as varying degrees of central nervous system (CNS) depression, hypotension, bradycardia, hypothermia and respiratory depression. We would like to emphasise that although Amitraz poisoning has a life-threatening presentation, most cases result in complete recovery if appropriate supportive treatment is instituted in a timely fashion. A limited number of case reports of human intoxication have been published, many of which are from Turkey. Most of these cases are those of accidental intake in children. This is thought to be the second case report from India to date. Thus, it significantly contributes to the limited pool of data available about this poison, thereby allowing timely recognition and treatment.

Case details

An 18-year-old male patient, was brought to our emergency department (ED) with a history of consumption of 50ml of Amitraz poison six hours before being brought to our ED. He had consumed the poison after a quarrel with his father. Subsequently, he vomited and informed his parents, thus he was taken to a hospital in their locality. He was given a gastric lavage and intravenous crystalloids were started. Over the next couple of hours, his sensorium deteriorated. There was no history suggestive of seizures. The patient did not have any known premorbid medical condition and had no history of prescription drug usage. He was referred to our hospital for further management.

On arrival at our ED, he was deeply comatose with a Glasgow Coma Scale (GCS) of 4/15. His heart rate was 52 beats per minute and blood pressure was 96/68mm Hg. He had a shallow respiration with a respiratory rate of 16/min. Oxygen saturation at presentation was 75% on room air, which improved to 99% with oxygen delivered via a 60% venturi face mask at a flow of 15L/min. On examination of the CNS, his pupils were bilaterally dilated (5mm) and not
reacting to light, all four limbs had hypotonia and there was bilateral flexor plantar response. Bowel sounds were sluggish. Other systemic examinations were normal. There were no excessive oral secretions or any fasciculations. Baseline line blood investigations (complete blood count, renal function test, serum electrolytes, liver function test), plasma butyrylcholinesterase level, electrocardiogram, chest X-ray, routine urine testing were normal. A urine test for drugs of abuse was negative. Blood alcohol level was normal. The patient was given supportive treatment in our intensive care unit in the form of intravenous fluids, proton pump inhibitors and oxygen by venturi mask. Vital signs were constantly monitored. Urine output was adequate. Over the next 24 hours, he gradually regained complete consciousness. His heart rate was 78 beats per minute, blood pressure was 124/84 mm Hg and he maintained normal oxygen saturation under room air. Neurological examination was normal. Bowel sounds returned to normal. He was transferred to the general ward and was subsequently discharged after consulting the psychiatrist and a clinical psychologist.

Discussion

Amitraz is increasingly being used worldwide in veterinary medicine and agriculture. It can cause poisoning in animals and humans via oral, dermal or inhalation routes. The toxicity from this poisoning can be attributed to both Amitraz and the solvent, xylene. Although the ingested dose of Amitraz cannot be determined because it is diluted at 1 part in 500 before usage, the acute oral median lethal dose (LD50) for rats is 800mg/kg body weight. Amitraz is a α adrenergic agonist and the effects resemble that of Clonidine. It stimulates α2 receptors in the CNS and α2 and α1 receptors in the periphery. The clinical manifestations due to this pharmacodynamic property include CNS depression (drowsiness, coma, convulsion), respiratory depression, hypotension, Bradycardia, hypothermia, miosis (presynaptic effect at low doses) or rarely mydriasis (postsynaptic effect at higher doses), polyuria (inhibition of antidiuretic hormone and renin) and intestinal distension. Our patient had deterioration of sensorium progressing to deep coma within approximately 150 minutes after consumption of the poison. CNS depression developing within 30 to 180 minutes was seen as one of the most common manifestation in other studies. Seizures have been reported by Yilmaz et al and Ertekin et al and responded to treatment with injectable diazepam or lorazepam. The solvent, xylene, may additionally cause acute toxic signs like CNS depression, ataxia, nystagmus, stupor, coma and episodes of neuroirritability. Although our patient had mild respiratory depression and bradycardia, he improved with oxygen supplementation and did not require atropine for the bradycardia. Significant respiratory depression and bradycardia requiring mechanical ventilation and atropine respectively have been reported in previous studies. Unlike most of the earlier studies where miosis was predominant, our patient presented with mydriasis which has rarely been seen after consumption of Amitraz in some studies. Our patient did not have polyuria as seen occasionally in some study groups. Amitraz can also inhibit prostaglandin E2 synthesis and thus contribute to the hypothermia caused by central α2 adrenergic agonist action.

The laboratory investigations of our patient were normal except decreased oxygen saturation on arterial blood gas analysis which was also noted by Yilmaz et al. Amitraz is a potent hepatotoxic drug which acts by decreasing hepatic glutathione activity but the liver enzymes have been shown to return to baseline within 48 hours. It is a potent inhibitor of liver monoamine oxidase enzyme in rats. Hyperglycemia and glycosuria has been seen in some studies. α2 adrenergic stimulation reduces insulin secretion and increases glucagon secretion as demonstrated in perfused rat pancreas by Abu-Basha et al. Kalyoncu et al reported hyponatremia in three cases. Our patient did not have any of the above metabolic abnormalities.

If the patient presents with bradycardia and miosis, organophosphate poisoning should be considered as a possible differential diagnosis. Other symptoms and signs of organophosphate poisoning should be looked for and a plasma butyrylcholinesterase level should be estimated in such cases. Amitraz level in the blood was not done because it was unavailable at our institute and our referral laboratories.

There is no antidote available for Amitraz poisoning. Management involves supportive measures like gastric lavage (though Yilmaz et al advises against it, unless the patient is first intubated because of chances of aspiration pneumonia due to petroleum distillates in Amitraz formulations), activated charcoal administration, and securing the airway. Additional measures depending on the patient’s condition can be instituted like oxygen supplementation or mechanical ventilation for respiratory depression, atropine for severe bradycardia, intravenous fluids and vasopressors for hypotension, diazepam or lorazepam for seizures. In most studies, the CNS depression recovered within 4–28 hours like in our patient. Most cases completely recover with aggressive supportive treatment.
Only two cases of death due to this drug have been reported in the literature.  

Through this report, we wish to contribute to the limited human toxicological data on Amitraz. With the increasing usage of Amitraz in veterinary medicine and agriculture, the emerging problem of this unusual poisoning is bound to increase. We would like to emphasise that though Amitraz poisoning may have a life-threatening presentation, early initiation of aggressive supportive management is the key to a favourable outcome.

References

PEER REVIEW
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CONFLICTS OF INTEREST
The authors declare that they have no competing interests.

CONSENT
The authors declare that:
1. They have obtained informed consent for the publication of the details relating to the patient in this report.
2. All possible steps have been taken to safeguard the identity of the patient.
3. This submission is compliant with the requirements of local research ethics committees.