ANIL AGGRAWAL'S
Internet Journal of Forensic Medicine and Toxicology
The world's first online journal devoted entirely to forensic medicine and toxicology · Published 1 January and 1 July

VOL. 16, NO. 1 · JANUARY – JUNE 2015
Downloaded from www.anilaggrawal.com · ISSN 0972-8074 (Online) · https://www.anilaggrawal.com/ij/vol_016_no_001/papers/paper001.html

Amitraz - A New Poison With Unusual Neurotoxic Effects.

Swati C. Aundhakar[1*], Sanket K. Mahajan[2], Makarand B. Mane[3], Shirish M. Agrawal[4]

[1]Professor & Head, Department of Medicine, Krishna Institute of Medical Sciences University, Karad, Maharashtra-415 110, India
[2]Resident Doctor, Department of Medicine, Krishna Institute of Medical Sciences University, Karad, Maharashtra-415 110, India
[3]Lecturer, Department of Medicine, Krishna Institute of Medical Sciences University, Karad, Maharashtra-415 110, India
[4]Resident Doctor, Department of Medicine, Krishna Institute of Medical Sciences University, Karad, Maharashtra-415 110, India

Contact: Dr. Aundhakar · dr.swatiaundhakar@yahoo.co.in

CITE THIS ARTICLE

Aundhakar SC, Mahajan SK, Mane MB, Agrawal SM. Amitraz - A New Poison With Unusual Neurotoxic Effects.. *Anil Aggrawal's Internet Journal of Forensic Medicine and Toxicology* [serial online], 2015; Vol. 16, No. 1 (January – June 2015): [about 6 p]. Available from: https://www.anilaggrawal.com/ij/vol_016_no_001/papers/paper001.html

ABSTRACT

Amitraz is an insecticide/acaricide of formamidine pesticides used worldwide to control ectoparasites in animals. Its effects in humans may mimic organophosphate poisoning. Amitraz poisoning is a rare disorder characterized by central nervous system (CNS) and respiratory depression, bradycardia, hypotension, hypothermia, hyperglycemia, nausea and vomiting. Poisoning may occur either by oral inhalation and dermal route. Here we will discuss one such patient of amitraz poisoning who presented to us in a comatose state with respiratory depression, bradycardia and miosis thus mimicking organophosphate poisoning. He recovered completely within 5 days. 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.

Keywords: Amitraz, Insecticide, α-adrenergic agonists

Introduction

Amitraz, 1,5 di-(2,4-dimethylphenyl)-3- methyl-1,3,5-tri-aza-penta-1,4 diene is a member of the formamidine pesticides.[1] It is an acaricide and insecticide indicated for the treatment of

generalized demodicosis in dogs, for control of ticks and mites on cattle and sheep, and to control psylla infestations of pears.[2] Amitraz is a pharmacologically active compound which has α2-agonist actions. The stimulation effect of α2-receptors are in part responsible for neurotoxic and preconvulsant effects.[1] Adverse reactions and side effects have been reported in animals exposed to the product but only a limited number of human intoxication cases have been published in the literature. Cases of human poisoning with amitraz are extremely rare in the literature. The reported effects include CNS depression, hypothermia, bradycardia, hypotension, hyperglycemia, glycosuria, vomiting and respiratory failure.[3] Mortality in humans due to amitraz poisoning has been reported in some research studies (Bonsall and Turnbull 1983; Abu-Al Ragheb et al. 1986). Sporadic fatal cases due to accidental industrial inhalation or ingestion of this product have also been reported (Abu-Al Ragheb et al. 1986). Here, 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. Also, very few cases of amitraz poisoning have been reported in India so our case report will significantly contribute to the limited pool of data available about this poison in India, thereby allowing timely recognition and treatment.

Case History

A 35 years old male was brought to emergency department of Krishna hospital with history of consumption of about 30 ml of amitraz compound followed by one episode of vomiting half an hour before being brought to emergency department. He consumed the poison due to some financial problem at his home. Subsequently, he started becoming drowsy and breathless. He was immediately shifted to ICU. In ICU, he underwent endotracheal intubation with mechanical ventilator support (Intermittent Positive Pressure Ventilation Mode) and was given a gastric lavage, activated charcoal and intravenous crystalloids. Atropine was started owing to history of compound consumption and bradycardia. Over the next couple of hours, his sensorium deteriorated and he went into deep coma. 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.

On admission, His pulse rate was 42 beats per minute and blood pressure was 130/80mm Hg. He had a shallow respiration with a respiratory rate of 10/min. Oxygen saturation at presentation was 68% on room air, which improved to 97% with mechanical ventilator support. On examination of the CNS, he was deeply comatose with a Glasgow Coma Scale (GCS) of 4/15, his pupils were bilaterally constricted (2mm) and not reacting to light, all four limbs had hypotonia with absent reflexes and bilateral plantar response was not elicitable. 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), cholinesterase level, electrocardiogram, chest X-ray, routine urine testing were normal.

He was started on atropine infusion of 16mg/hour, titrated according to the heart rate to maintain the heart rate of 110/min for first 24 hours. He was adequately hydrated and the urine output was strictly monitored. After 48 hours, his BP started falling and dropped down to 70/50 mmHg. He was started on dopamine infusion which was continued for 24 hours and then tapered off slowly and completely after patient's BP was stabilized. Gradually, over a period of 4 days, he was weaned off the ventilator and the atropine infusion was tapered and omitted over next 4 days. He was late on

discharged after 6 days of stay in hospital in a haemodynamically stable condition, after a counselling session by a psychiatrist.

Discussion

Formamidines show toxic effects on both humans and animals and studies presented until now have reported the reversible nature of these effects. The EPA classifies Amitraz as Class III – slightly toxic.[4] Although the ingested dose of Amitraz can not be determined because it is diluted at 1 part in 500 before usage, the acute oral medical lethal dose (LD50) for the rats is 800mg/kg body weight.[5] Amitraz is a potent hepatotoxic drug acting by decreasing hepatic glutathione activity. [5]

Amitraz stimulates alpha 2 receptors in the CNS and alpha 2 and alpha 1 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)[9] and intestinal distension. CNS depression developing within 30 to 180 minutes was seen as one of the most common manifestation in other studies.[9]

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. Co-existence of bradycardia and miosis may suggest organophosphorus Poisoning.[6] In our case, bradycardia was present along with miosis. At the same time, there was no other finding of Organophosphorus Poisoning.

Garnier et al reported plasma amitraz concentration of 100 ng / ml , 2 hours after ingestion in an asymptomatic patient and of 500 ng / ml after 2 hours in a patient with drowsiness. Plasma levels are generally unlikely to be of clinical use because of their limited availability. [7]

No antidote is available for this poisoning. Only two cases of death due to this drug have been reported in the literature.[9] The main approach while treating the patients of Amitraz intoxication includes hemodynamic stabilization by proper hydration, maintaining airway, oxygen administration, reduce absorption of poisonous material and measure to improve elimination of the toxin from the body..[8] In most studies, the CNS depression recovered within 4-28 hours unlike in our patient. Most cases completely recover with aggressive supportive treatment, just like our patient.

Conclusion

Amitraz is a deadly poison – with mainly central nervous system and respiratory system depression, without any antidote. Early and aggressive management helps in excellent patient outcome in the form of complete recovery. Also, a lot of public awareness is required to prevent poisoning by such a deadly compound, especially among the illiterate farmers who use such compounds, day-in and day-out, even without knowing its hazards.

References

1. Jorens PG, Zandijk E, Belmans L, Schepens PJ, Bossaert LL. An unusual poisoning with the unusual pesticide amitraz. Hum Exp Toxicol 1997; 16: 600-601.

2. Jones RD. Xylene / Amitraz: Pharmacological review and profile. Vet Hum Toxicol1990; 32: 446-448.
3. Ulukaya S, Demirag K, Moral AR. Acute amitraz intoxication in human. Intensive Care Med 2001; 27: 930-933.
4. Amitraz - From Wikipedia, the free encyclopedia “http://en.wikipedia.org/wiki /Amitraz”
5. V Ertekin1, H Alp2, MA Selimoglu3, M Karacan4, Amitraz Poisoning in Children: Retrospective Analysis of 21 Cases. *JIMR* 2002; 30(2): 203-205.
6. Hasan AAgin, OSebnem OCalkavur, Hakan Uzun, Mustafa Bak, Amitraz Poisoning: Clinical and Laboratory Findings. *Indian Pediatrics* 2004;41: 482-486.
7. Garnier R, Chatigner D, Djebbar D, Letter to the Editor Hum Exp. Toxicol. 1998, 17 : 294 as quoted in Haddad and Winchesteter’s Clinical Management of Poisoning ;and Drug Overdose , 4th Ed. – 2007, Edited by M.Shannon, Stephen Borron and M.Burns : in Pyrethrins, Repellants, and other Pesticides. P1188.
8. Z Doganay, D Aygun, L Altintop, H Guven, F Bildik, Basic toxicological approach has been effective in two poisoned patients with Amitraz ingestion: case reports. *Human and Experimental Toxicology*, 2002; 21: 55-57.
9. Yilmaz HL, Yildizdas DR. Amitraz poisoning, an emerging problem: epidemiology, clinical features, management and preventive strategies. Arch Dis Child. 2003;88:130-4.