

**Case Report****AMITRAZ Poisoning: Uncommon and Overlooked Human Toxicity of a Common Pesticide**

Authors

**Dr Dipankar Das<sup>1</sup>, Dr Prabal Rajvanshi<sup>2</sup>, Dr Gangadhar Buduga<sup>3</sup>, Dr Rahul Arya<sup>4</sup>,  
Dr Mohd Javed<sup>5</sup>**<sup>1,4,5</sup>Postgraduate resident, Department of General Medicine, V.M.M.C and Safdarjung Hospital<sup>2</sup>Professor and Consultant, Department of General Medicine, V.M.M.C and Safdarjung Hospital  
SAARC expert on poisonings<sup>3</sup>Senior resident, Department of General Medicine, V.M.M.C and Safdarjung Hospital**Abstract**

*Amitraz is a widely used pesticide worldwide. Chemically it is a triazapentadiene, having predominant effect as centrally acting  $\alpha_2$  adrenergic agonist. Human toxicity of amitraz is an unusual occurrence mostly due to accidental ingestion or suicidal attempt and limited number of such cases have been published in the literature. Its toxicity clinically mimics commonly occurring Organophosphorus poisoning. Clinically it poses as threat to human life due to lack of awareness among clinician and lack of specific treatment protocol. Hereby reporting of our case prove beneficial to clinical practitioners.*

*This case is about a 17 yr old male ingesting amitraz 25ml of 12.5% w/v (3.12gm) in suicidal attempt on 29<sup>th</sup>, April, 2018 at 8.30pm. within 1 hour he developed nausea, dizziness and drowsiness for which he was taken to a primary clinic where Gastric lavage was done 1.5 hour after poisoning. Afterwards he was admitted in Safdarjung hospital, new Delhi, which is a tertiary care hospital. He developed miosis, bradycardia and respiratory depression. The patient improved gradually on atropine fluids and Inotropes. The patient regained consciousness in 26 hours after poisoning.*

**Conclusion:** *amitraz poisoning is accompanied with numerous symptoms varying from central nervous system depression (drowsiness, coma, and convulsion), to miosis, or, rarely, mydriasis, respiratory depression, bradycardia, hypotension, hypertension, hypothermia or fever, hyperglycemia, polyuria, vomiting, decreased gastrointestinal motility, and intestinal distension. Most symptoms are explained by its agonistic action of on  $\alpha_1$  and  $\alpha_2$  receptors. For Management a valid and proven antidote is not yet available for use on humans. So supportive care with atropine for bradycardia and IV fluids & if needed Inotropes greatly makes impact on the early recovery of the patient. Close monitoring for complications particularly central nervous system, respiratory system and cardiovascular system is of utmost importance.*

**Keywords:** *Amitraz, central nervous system, bradycardia, miosis supportive management,*

**Introduction**

Amitraz is a pesticide used worldwide on both animals and crops. It is used to control pests including generalized demodicosis in canines,

ticks and mites in cattle and sheep, psylla infection in pears and also red spider mites in fruit crops<sup>1,2</sup> It contains triazapentadiene [1,5 di- (2,4-dimethylphenyl)-3-methyl-1, 3,5-tri azapenta 1,4 diene], an insecticide from the formamidine

family. Commercial formulations of amitraz generally contain 12.5-20% of the drug in organic solvents, especially Xylene, which is also used as a solvent in paints, cleaners, and glues<sup>3</sup>.

Amitraz stimulates  $\alpha_2$  adrenergic receptor sites in the central nervous system (CNS) and  $\alpha_1$  adrenergic and  $\alpha_2$  adrenergic receptor sites in the periphery<sup>4</sup>. It also inhibits monoamine oxidase (MAO) enzyme activity and prostaglandin E<sub>2</sub> synthesis.

Amitraz poisoning may occur through the oral or dermal routes and potentially through inhaling<sup>5</sup>. Poisoning is accompanied with numerous symptoms varying from central nervous system depression (drowsiness, coma, and convulsion), to miosis, or, rarely, mydriasis, respiratory depression, bradycardia, hypotension, hypertension, hypothermia or fever, hyperglycemia, polyuria, vomiting, decreased gastrointestinal motility, and intestinal distension<sup>6</sup>.

Adverse reaction 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.

We hope this case report will help increasing awareness about this substance poisoning among the clinicians.

### Case

A young male aged 17 year presented in emergency medicine of Safdarjung hospital, new Delhi at around 8.45 am on 30<sup>th</sup> march, 2018 with complaints of altered sensorium. On history taking attendant revealed that the patient had ingested 25ml RIDD, 12.5% w/v (3.125gm) an Indian brand for amitraz at around 8.30 pm, on 29<sup>th</sup> march, 2018 in suicidal attempt. He was 65 kg in weight, resulting in 48 mg/ kg of amitraz poisoning. Within 1 hr he developed nausea, dizziness & became drowsy. He was taken to a nearby hospital approximately 1.5 hr after poisoning where he received IV fluids and gastric lavage was done. Afterwards patient was referred to this hospital's emergency block. There was no history of convulsions. On examination patient

was drowsy (Glasgow coma scale E2V2M3), Patients vitals were BP -90/50, PR-58/min, RBS-96mg/dl, temp-96.7<sup>0</sup>F, respiratory rate =16/min. Deep tendon reflexes were diminished, planter reflexes were mute. Miosis was present and pupils were bilaterally sluggishly reactive to light. There was no hypersalivation and chest was clear bilaterally. Arterial blood gases, analysis was: (pH-7.37), (pCO<sub>2</sub>- 30.1), (PO<sub>2</sub>-109), (SPO<sub>2</sub>-97.2), (HCO<sub>3</sub>-17.1). 1.2mg of IV atropine and IV fluids were given @100ml/hr. Patient was kept on propped up position and oxygen inhalation supplied @ 6lt/min. Patients vitals were closely monitored. After 8 hr patient vitals deteriorated; blood pressure fell to 80/54mmhg, Pulse rate 56/min, respiratory rate 12/min. Immediately 2 units of normal saline along with 1 unit of DNS infused at fast rate. Injection atropine 1.2 mg administered every hourly. After 2 hr when it failed to increase the blood pressure noradrenaline tartrate 8mg in 500ml normal saline infusion @50ml/hr and dopamine in dose of 5 $\mu$ g/kg/min started. Gradual improvement in both vitals and sensorium seen in next 6 hrs. Blood pressure increased to 120/70, PR:84/min, respiratory rate 18/min. Inotropes were stopped after tapering over 1hr. arterial blood gas analysis showed: (PH=7.314), (PCO<sub>2</sub>=40.2), (HCO<sub>3</sub>=19.8), (P0<sub>2</sub>=91.2), (SP0<sub>2</sub>=95.4). patient regained consciousness, followed verbal commands and spontaneous eye opening seen.

His blood reports were found to be: Hb-14.5gm/dl, TLC-10900/mm<sup>3</sup>, Platelets-292000/mm<sup>3</sup>, Na<sup>+</sup> - 139, K<sup>-</sup> 4.3, Blood Urea-18, serum creatinine-0.6, serum bilirubin-0.7, SGOT/PT-20/14, ALP-151, urine routine and microscopic examination were normal. Chest x ray PA view and ECG found to be showing sinus bradycardia.

Psychiatry consultancy was taken and opined that it was an impulsive behavior that led the patient to suicidal attempt.

The patient was discharged in good health on the evening of 1<sup>st</sup>April, 2018 and advised to attend psychiatry OPD for further evaluation.

## Results and Discussion

Amitraz is a pharmaceutical, veterinary, and an agricultural product which is used worldwide. It can cause poisoning in animals and humans when ingested, inhaled, or after skin exposure.

Predominantly CNS depression was present in our case due to the alpha-2 agonistic effects of the poison. In concordance with the previous studies its effects are dose dependent and higher dose have more CNS depressive effects.<sup>7</sup> The patient had ingested 25 ml of 20% amitraz solution and was enough to cause altered sensorium (drowsiness), diminished deep tendon reflexes and bilateral mute planter reflexes. The patient regained consciousness in about 26 hours. The resolution time for CNS depression was reported to be 2-48 h in the previous reports<sup>3-6,6,10</sup>

It also has inhibitory effects on the respiratory center. In our case Respiratory rate initially at presentation was 16/min, but after 8 hrs of hospital stay respiratory inhibitory effect became more predominant and rate decreased to 12/min.

The patient also had bradycardia and miosis. These effects are due to  $\alpha$  1 and  $\alpha$  2 agonistic actions of the poison. Bradycardia, miosis, respiratory depression might make clinician confuse it with organophosphate or carbamate toxicity, since all three share several similar clinical features. However, in this case absence of hypersecretory state and presence of hypothermia suggested alternate diagnosis. Opioids, barbiturates, benzodiazepines, phenothiazines and tricyclic antidepressants can also display similar symptoms and signs in overdose.

Two human deaths have been reported following ingestion of amitraz and one had ingested 6 g<sup>1,8</sup> of the compound. The minimum toxic dose reported by Jorens P. G. et al. is 3.57 mg/kg<sup>3</sup>. Our patient had ingested 3150 mg orally (48 mg/kg)

We used atropine 1.2 mg hourly, as the patient had bradycardia and it helped the patient stabilize heart rate. Many studies have found its use helpful in patients to counter both miosis and bradycardia<sup>5,9,10</sup> Hsu and colleagues claimed

that atropine increased heart rate and prevented amitraz induced bradycardia in animals<sup>11</sup>

The patient did not develop hyperglycemia in this case as found in some animal model due to its insulin inhibitory and glucagon stimulatory action.

The patient developed hypothermia (temp-96.6F<sup>0</sup>). The electrolytes, serum urea, creatinine, serum bilirubin, SGOT/SGPT were found to be normal. However, Kalyoncu and colleagues also reported hyponatremia in their three cases<sup>12</sup>.

The arterial blood gas analysis showed initially showed compensated respiratory alkalosis and later analysis revealed acute metabolic acidosis. After 30 hours ABG analysis became normal.

In ECG sinus bradycardia was seen, no other significant changes were noticed. In a study by Aydin and colleagues, non-specific ST changes were reported in the ECGs of seven children with no history of cardiac disease who recovered completely in 24 h<sup>5</sup>.

The American Association of Poison Centers (AAPC) and the European Association of Poison Centers and Clinical Toxicologists (EAPCCT) recommend that gastric lavage should not be employed routinely and to perform only if the patients present early (within one hour of ingestion) and if potentially lethal ingestion is present. In our case, the patient already had gastric lavage done within 1 and half hour at nearby primary clinic.

Several  $\alpha$ 2 antagonist atipamezole or yohimbine have been tried on animals as antidote to reverse the effects of amitraz. But no reports available of its use in human cases.

In our case the patient responded well to the atropine, IV fluids and subsequent inotropic support with noradrenaline and dopamine. At doses of 5-10  $\mu$ g/kg/min, dopamine stimulates  $\beta$ 1 adrenergic receptors and increases cardiac output, by increasing cardiac contractility with variable effects on heart rate. We used dopamine in dose of 5  $\mu$ g/min/kg. Higher dose should be avoided as Amitraz also has MAO inhibitory action. Only few cases are reported about the use of inotropes in amitraz poisoning. Patients might go into Coma

and respiratory failure if exposed to an increased dose as the effects are dose dependent. In severe respiratory depression and need to protect airway in unconscious state patient may require intubation and elective ventilation till the patient regains consciousness. Therefore, to monitor Patients vitals and with focus on respiratory, Central nervous system, and cardiovascular system is of paramount importance.

### Conclusion

Though amitraz poisoning is an unusual occurrence, but clinician should be aware of the manifestations it may have and its treatment strategies. Here we present a case of 17 yr. male ingesting pesticide amitraz 48 mg/kg in suicidal attempt, who started to have drowsiness as first symptom after 1 hour and gradually developed bradycardia and respiratory depression. He improved on atropine, IV fluids, inotropic support and oxygen inhalation @6lt/min and regained consciousness after 26 hours. In amitraz poisoning, patients need to be removed from the contaminated area, early gastric lavage if possible within 1hr can be done. No specific antidote is available yet for use in human cases. Appropriate and timely supportive therapy leads to a favorable response in the patient and mortality rate can be minimized. Due to lack of clear and specific protocol for treatment of amitraz toxicity, a case report on successfully managed patient can conceivably be very valuable as a guide to other clinical practitioners.

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