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## Research Article

# THE CLINICAL PROFILE AND COMPLICATIONS OF AMITRAZ POISON, A NEAR-FATAL POISONING

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### ABSTRACT

**Introduction:** Amitraz is a member of the formamidine pesticide indicated for the treatment of generalized demodicosis in dogs, for control of ticks and mites on cattle and sheep. Amitraz has  $\alpha_2$ -agonist stimulatory actions responsible for neurotoxic and preconvulsant effects. **AIM:** to study the clinical features, laboratory abnormalities, complications, and outcome of the patients with acute amitraz intoxication. **Material and Methods:** Our study is a prospective observational study done on 12 cases presented in emergency deptt. and got admitted in medicine deptt. of GMC Haldwani. **Results:** Analysis of the clinical features revealed mainly CNS involvement, miosis/mydriasis, hyperglycemia, polyuria, hypotension, bradycardia and nonspecific complaints like pain abdomen, vomiting etc. Treatment with  $\alpha_2$ -receptor antagonist Yohimbine was given to every case of amitraz poisoning and has shown improved survival even in critical cases in our study. **Conclusion:** In patients who presented with combination of exposure to an insecticide with features of hyperglycemia, drowsiness and features similar to organophosphorous poison physician should always think of amitraz poisoning that will help to initiate rapid treatment for this rare, potentially life threatening intoxication.

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## INTRODUCTION

Amitraz is a triazapentadiene compound and it is a member of formamidine pesticides and is used worldwide (1). Amitraz is used as an insecticide/acaricide for controlling the ectoparasites in animals (2). 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. Amitraz is an  $\alpha_2$  adrenergic agonist (1-3). It 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 (4). It also inhibits monoamine oxidase (MAO) enzyme activity and prostaglandin  $E_2$  synthesis (1). Amitraz poisoning may occur through the oral or dermal routes and potentially through inhaling (5). 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, hyperglycaemia, polyuria, vomiting, decreased gastrointestinal motility, and intestinal distension (1).

## MATERIAL AND METHODS

This study is done at the Department of Medicine, GMC Haldwani and associated STM hospital. This was prospective observational study done on 12 confirmed cases of amitraz poisoning of age more than 15 years admitted in our hospital from July 2017 to Nov 2018. All patients were informed about the study and informed consent was taken. Patients were enrolled in study with the following inclusion and exclusion criteria.

### Inclusion Criteria

1. Patients of age of 15 years and above were included.
2. Evidence of confirmed amitraz poisoning (those who brought container/label of amitraz on admission / during period of hospitalisation).

### Exclusion Criteria

1. Poisoning with other compounds along with amitraz

### Diagnostic methods

Complete blood count (hematology autoanalyzer), Peripheral blood film for cell morphology, random blood sugar, liver

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function test, renal function test, urine examination, blood and urine culture and sensitivity, chest X-ray PA view, ultrasonography of abdomen. Other appropriate blood tests and CSF examination were done wherever needed.

A detailed history and complete general and systemic examination was done for cases recruited in the study as per case sheet proforma and the data was analysed using SPSS (Statistical Package for Social Sciences) Version 15.0 statistical Analysis Software (SPSS, Inc., Chicago, IL).

## OBSERVATIONS AND RESULTS

A total of 12 patients were hospitalized, out of which 2(16.7%) were males and 10 (83.3%) were females. Male: female ratio of 1:5.(Table 1)

**Table 1** Sex distribution of amitraz poisoning cases.

Sex	Number of cases	Percentage (%)
Male	2	16.7%
Female	10	83.3%
Total	12	100%

Majority of the patients were between the age group of 21-40 years with the highest incidence between the age group of 21-30 years. (Table 2)

**Table 2** Age distribution of malaria cases in study population

Age Groups (years)	Number of cases	Percentage (%)
21-30	6	50%
31-40	4	33.3%
41-50	1	8.3%
51-60	1	8.3%
>60	0	0%
Mean±SD	24.7±11.67	

Out of 12 patients, 7 were farmers by occupation, 3 were in occupation indirectly related to farming (eg.-goat rearing, farm labourers, cow and buffalo rearing), 2 patients had pets (dog).Analysis of marital status showed that 11 patients (91.7%) out of 12 were married, and remaining one was unmarried. The most common intention of poisoning was suicidal in 11 patients; in remaining 1 it was accidental. The route of poisoning was oral in all the cases. Most of patients had low Socioeconomic status. No seasonal variation found. The amount of amitraz consumed was from 5-25 ml (100 to 150 mg/kg) in eight subjects and was unknown for the other four cases Onset of symptoms started from 30 minutes to 90 minutes after ingestion. Time between ingestion and presentation was 30 minutes to 12 hours.

In the initial clinical evaluation six cases presented with miosis, two with mydriasis, and four with normal size pupils. Hypotension was present in four cases. There was bradycardia in four cases and tachypnoea in four. Three had a decreased body temperature (below 36°C). Short generalised seizures were observed in three cases; they responded to diazepam treatment.

CNS depression resolved spontaneously within 4-28 hours (median 12 hours) in all patients. The length of hospital stay was two to three days. All the patients had good outcomes with no long term morbidity.

**Table 3** Clinical features of amitraz poisoning

Symptoms	Number of patients	Total Percentage (n=12)100%
Vomiting	11	
Dizziness	4	
Disorientation	3	
Abdominal pain	5	
Drowsiness	5	
Respiratory difficulty	2	
<b>Signs</b>		
Hypotension	2	
Bradycardia	4	
Miosis and mydriasis	8	
Bradypnoea	3	
Altered mental status	2	
Altered Tendon stretch reflexes	3	
Hypothermia	2	
Convulsion	2	
Polyuria	8	
Gastrointestinal hypomotility	6	
Hyperglycaemia	8	

On laboratory investigations, Blood glucose was higher than 6.66 mmol/l (120 mg/dl) in 8 cases who also had glycosuria. They were not known diabetic initially. Their blood sugar level returned to normal values on subsequent follow up without any treatment. Serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels increased minimally in 5 cases but all recovered to normal within two days. Urinary output was increased (>3 ml/kg/h) in 8 cases. Blood urea nitrogen, creatinine, serum sodium and potassium concentrations were deranged in 4 cases) and ECG were normal in all cases.

**Table 4** Biochemical Parameters in amitraz poisoning

Biochemical Parameters	No. of patients	%(n=12)
Hyperglycemia	8	
Metabolic alkalosis	4	
Deranged Liver function (SGPT)	5	
Deranged Renal function (S.Creat., B.Urea, Urine R/M)	4	

Management- A nasogastric tube was inserted and gastric lavage done and lavage sample preserved, then all the patients were admitted to the intensive care unit facility of our hospital. Symptomatic treatment was given as there is no specific antidote for the poisoning. Treatment with  $\alpha_2$ -receptor antagonists Yohimibine was given to each case that improved survival, even in critical case. Patients with bradycardia responded to 1 - 3 doses of atropine i.v (0.6 mg). Hypotension responded to fluid therapy, and two requiring dopamine (5  $\mu$ g/kg/min) infusion for four hours were required. The average duration of ICU stay of 12 patients was 24-48 hours. However, two patients required mechanical ventilation for respiratory depression (mean duration of mechanical ventilatory support: 50 +/- 16 hours)

No problem was noted in the patient or the fetus in a pregnant, 27-year-old patient, who was intoxicated with 15mL amitraz. In this study, there was 100% survival with the case fatality rate being 0%. All patients were discharged without neurological sequel.

## DISCUSSION

Amitraz is a veterinary agriculture product sold worldwide under various trade names (MITAC, TRIATOX, TRITIX, TAKTIC, ECTODEX etc). The reported effects include CNS depression, hypothermia, bradycardia, hypotension, hyperglycaemia, glycosuria, vomiting, convulsions and respiratory failure. Central nervous system depression was the predominant sign in our case, constant with the effect of amitraz on  $\alpha_2$ -adrenergic receptors. The observation of respiratory depression concomitant with central nervous system depression may suggest a direct inhibitory effect of the agent on the respiratory center (6). The sedative effects of  $\alpha_2$ -agonists are dose dependent (7).

CNS depression, which is probably attributable to alpha-2-adrenoceptor action, was the predominant sign in our cases. CNS symptoms, in our cases, began within 30-60 minutes of consumption, and were resolved within 8-10 hours. In previous reported studies, the duration of CNS depression has ranged from a few hours to 24 hours<sup>3, 4</sup>. Sometimes, amitraz poisoning could be confused with organophosphorus compound poisoning, if bradycardia and miosis are present in the same patient. However, hypothermia was not observed in any of our cases. Amitraz poisoning has been increased in recent years, more so in rural areas. The minimal toxic dose reported was 3.57 mg/kg<sup>9</sup>. There was no mortality in our 12 patients admitted with acute amitraz poisoning. The basic approach to the patient with acute amitraz poisoning includes initial stabilization, treatment to reduce absorption and measures to improve elimination of toxin. The medical management is initially symptomatic and supportive with particular attention towards monitoring and evaluation of respiratory, cardio-vascular and central nervous system. There is no specific antidote to amitraz. Treatment with  $\alpha_2$ -receptor antagonists such as Yohimibine has shown improved survival, even in critical case. Increased intake may lead to coma and respiratory failure. All cases may eventually recover completely.

## CONCLUSION

A retrospective analysis of cases of acute amitraz poisoning showed that it is not an uncommon entity in rural population, although its reported incidence is low in urban areas. The most common clinical feature is CNS depression and patients should be watched for signs of impending respiratory failure. There is no specific antidote for amitraz poisoning and management should be symptomatic and supportive.

The patient can be saved if timely managed. The incidence of amitraz poisoning is consistently increasing probably because of easy availability without any prescription. The incidence can be minimized by proper public education, involvement of regulatory authorities and national poison control centers. There is no legal control on sale and lack of strict licensing norms. Farmers are negligent about use of protective equipments and awareness about toxic effects as well as safety. Accidental amitraz poisoning could be prevented by designing child proof packages and with warning labels on its containers.

The coexistence of bradycardia, miosis, and respiratory depression may lead to confusion with organophosphorus or opioid poisoning; however both should be excluded.

Possible amitraz poisoning should be considered in patients with a combination of pesticide exposure, hyperglycemia, bradycardia. Increased awareness among clinicians is required for timely diagnosis and appropriate management of this potentially life-threatening intoxication.

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