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Amitraz (Acaricide) Poisoning: A Study of this Unusual Emerging Poison

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Abstract

Background: Amitraz is a pharmaceutical, veterinary, and agricultural product which is used worldwide under numerous generic names as an acaricide and insecticide. Because of its widespread use, Amitraz has emerged as one of the common poisoning in rural areas. *Aims and Methods:* To report the clinical features, laboratory findings and the management instituted for the patients with acute Amitraz Poisoning and review the previously reported cases. *Results:* Total sixteen (Ten male and six female) patients aged between17 to 48years were admitted to our department. The ingested amount was ranging from 15 ml to 30 ml.The initial signs and symptoms were impaired consciousness, drowsiness, vomiting, disorientation, miosis, mydriasis, hypotension, hypertension, tachycardia, bradycardia, tachypnea, bradypnoea, and hypothermia. Six patients required mechanical ventilation. CNS depression resolved spontaneously within 8–48 hours in all. The length of hospital stay was three to sevendays; all the patientsrecovered. *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 ofcomplete recovery. Public awareness isrequired to prevent poisoning by such compound, especially among the illiterate farmers.

Keyword: Amitraz; Disorientation; Miosis; Mydriasis; Tachycardia; Bradycardia;Tachypnea; Bradypnoea, Hypothermia.

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Introduction

Amitraz is a synthetic compound with insecticide and acaricide properties used worldwide on both animals and crops to control pests. Its wide spectrum makes it appropriate for numerous conditions varying from red spider mites on fruit crops to ticks, lice, or keds on livestock [1-5]. 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 [4,6,7]. It is diluted with water before applying to plants and animals [16].

When humans are exposed to amitraz, the symptoms and signs result from both xylene and amitraz [1]. Poisoning presents with numerous symptoms varying from central nervous system (CNS) 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 [1-3, 8-15]. Xylene may cause acute toxic signs, such as: CNS depression, ataxia, impaired motor coordination, nystagmus, stupor, coma, and episodes of neuroirritability [4]. Amitraz is an alpha 2 adrenergic agonist and the observed clinical effects of amitraz poisoning resemble similar effects caused by other central acting alpha2 adrenergic agonists such as clonidine [1,2,4,8]. It stimulates alpha 2 adrenergic receptor sites in the CNS and alpha1 adrenergic and alpha 2 adrenergic receptor sites in the periphery [16]. It also inhibits monoamine oxidase (MAO) enzyme activity and prostaglandin E2 synthesis [2,9,17,18]. Amitraz poisoning may occur through the oral or dermal routes and, potentially, by inhalation [10].

We report our experience with 16 cases and review the clinical features, management and preventive strategies.

Aim of the Study

To report the clinical features, laboratory findings and the management instituted for thepatients with acute Amitraz Poisoning.

Subjects and Methods

16 adults poisoned with amitraz poisoning were admitted to Bapuji Hospital attached to J.J.M. Medical College, Departmentof Emergency Medicine between 2015 and 2016.The proprietary name like TICTAC of the ingested veterinary formulation, which contains 12.5% amitraz and xylene. Diagnosis was made according to a compatible exposure history and clinical findings. Cases were analyzed as per age, sex, route of poisoning, initial symptoms, clinical features, laboratory findings, level of consciousness in ICU using Glasgow Coma Scale, pupillary signs, heart rate, blood pressure, respiratory failure, requirement of ventilatory support, body temperature, blood sugar level and urine output. We reviewed their medical charts and detailed demographic data, intoxication route, ingested dose, onset and duration of effects, clinical and laboratory presentations, management, and outcome.

Result

Total sixteen (ten male and six female) patient aged between 17 to 48 years were admitted to our department. Table 1 shows the demographic, clinical, and laboratory data. All poisonings were suicide attempt and intoxication occurred orally in all. The estimated ingested dose ranged from 15ml to 30ml. Estimated time between ingestion and presentation was 30mins–9hrs.The predominant initial symptom was impaired consciousness. Nine patients were presented with drowsiness, nine with vomiting, and three of themhad disorientation.

In the initial clinical evaluation two cases presented with miosis, six with mydriasis, and eight with normal size pupils. Hypotension was present in seven cases and hypertension in two cases. There was bradycardia in elevencases,tachycardia in seven cases,bradypnoea in four cases and tachypnoea in four cases. Seven had a decreased body temperature (below 36°C). Blood glucose was higher than 126 mg/dl in eleven cases. ABG was showing respiratory acidosis in six cases and respiratory alkalosis in two cases. Urinary output was normal in all cases. Blood urea nitrogen, creatinine, serum sodium and potassium concentrations, and ECG were normal in all cases. Six patientsrequired mechanical ventilation support for about 24 to 48 hrs.

Gastric lavage and activated charcoal performed for all patients. Seven patients with hypotension received intravenous fluid repletion, with five improving and two requiring noradrenaline infusion for 24 hours. CNS depression resolved spontaneously within 8–48 hours in all patients. The length of hospital stay was three to seven days. All the patients had good outcomes with no long term morbidity.

Discussion

Formamidines show toxic effects on both humans and animals and studies presented until now have reported the reversible nature of these effects [19]. The EPA classifies Amitraz as Class III slightly toxic [20]. The present knowledge about Amitraz and Formamidines pesticides is frequently built on animal studies because of the limited human intoxication. Amitraz is a potent hepatotoxic drug acting by decreasing hepatic glutathione activity [21].

Animals given Amitrazshow signs of CNS depression or CNS stimulationaccordingto the drug level and to some extent depending on the species. High doses have a CNS depressive effect with decreased spontaneous activity, bradycardia, respiratory depression and hypotension. Death resulted from respiratory depression.

Animals that survive after poisoning by potentially lethal dose of Amitraz show complete recovery from all signs and symptoms in about 7-10 days [19].

The clinical features reported in previous studies on human poisoning are CNS depression, CNS stimulation,vomiting, miosis, bradycardia, hypotension, hyperglycemia and respiratory failure [19-21], in our study also same clinical features were present. In previous papers the duration of CNS depression has ranged from few hours to 24 hours [19-21], however in our study CNS symptoms resolved over a period of 8-48 hours.

Co-existence of bradycardia and miosis may suggest organophosphorus Poisoning [19]. In our study bradycardia was present in eleven casesand mydriasis accompanied in six and miosis in two.

Table 1: Demographic data, and clinical and laboratory findings of cases

Sl. no	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
Age (years)	26	18	30	17	35	18	29	30	21	41	25	48	28	32	20	22
Gender	Male	Female	Male	Female	Female	Male	Male	Female	Male	Male	Male	Female	Male	Male	Male	Female
Place of Poisoning	Rural	Rural	Urban	Rural	Urban	Urban	Rural	Rural	Rural	Rural	Rural	Urban	Urban	Rural	Urban	Rural
Type of exposure	Suicidal	Suicidal	Suicidal	Suicidal	Suicidal	Suicidal	Suicidal	Suicidal	Suicidal	Suicidal	Suicidal	Suicidal	Suicidal	Suicidal	Suicidal	Suicidal
Route of poisoning	Oral	Oral	Oral	Oral	Oral	Oral	Oral	Oral	Oral	Oral	Oral	Oral	Oral	Oral	Oral	Oral
Amount Ingested(ml)	15	20	25	15	30	15	20	25	30	20	25	30	15	15	20	25
Time lag	4hrs	4hrs	2hrs	5hrs	30mins	3hrs	5hrs	9hrs	8hrs	5hrs	9hrs	3hrs	2hrs	4hrs	1hr	6hrs
Vomiting	-	+	+	+	+	-	-	+	-	+	-	+	+	-	+	+
Disorientation	-	-	-	-	-	-	+	+	-	-	-	+	-	-	-	-
Drowsiness	+	+	-	+	-	-	-	-	+	+	+	-	+	-	+	+
Body temperature (°C)	37.5	35	36	36.5	37.2	35.8	37	36.8	35.5	35	35.6	36.8	35.4	37.3	35.6	37
Heart rate/min	108	110	78	130	98	102	66	102	104	110	84	90	76	88	66	96
Respiratory rate/min	16	12	18	24	20	18	16	20	10	36	12	16	10	1	14	20
Blood pressure (mm Hg)	114/70	120/80	110/70	100/60	170/110	110/70	122/84	160/70	100/70	134/70	130/76	110/60	110/60	100/70	90/60	130/70
Bradycardia during hospital stay	+	+	+	-	-	+	-	-	-	+	+	+	+	+	+	+
Hypotension during hospital stay	-	+	+	-	-	+	-	-	-	+	-	+	-	+	+	-
Blood glucose (mg/dl)	130	154	138	126	137	110	155	177	90	353	135	122	202	126	136	131
ABG	Normal	Resp Acidosis	Normal	Resp alkalosis	Normal	Normal	Normal	Normal	Resp Acidosis	Resp alkalosis	Resp Acidosis	Normal	Resp Acidosis	Normal	Resp Acidosis	Resp Acidosis
Urine output	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Mechanical ventilation time	-	36hrs	-	-	-	-	-	-	24hrs	48hrs	24hrs	-	32hrs	-	48hrs	-
Recovery of CNS Depression	36hrs	48hrs	-	20hrs	-	-	8hrs	10hrs	16hrs	40hrs	20hrs	-	24hrs	-	36hrs	10hrs
Inotropes	-	+	-	-	-	-	-	-	-	-	-	-	-	-	+	-
Duration of stay	3days	6days	3days	3days	3days	4days	3days	3days	4days	5days	4days	3days	4days	3days	7days	3days
Out come	Cured	Cured	Cured	Cured	Cured	Cured	Cured	Cured	Cured	Cured	Cured	Cured	Cured	Cured	Cured	Cured

Cholinesterase levels were normal in all the cases. At the same time there was no other finding of Organophosphurus Poisoning.

Some other poisoning types can present with similar symptoms and signs which might lead to diagnostic confusion.These are caused by opioids, organophosphates, and centrallyacting alpha 2 adrenergic agonist drugs, particularly clonidine. Sedative hypnotics such as barbiturates, benzodiazepines, phenothiazines, and tricyclic antidepressants may sometimes display similar signs and symptoms. Therefore, physicians should inform their diagnosis by combining the information obtained from the patients / attendentsabout the exposure history, observing the specific symptoms of poisoning and using the toxicological screening and more specific measurements.

Kalyoncu andcolleagues [24], reported respiratory alkalosis in two cases, respiratory acidosis in three cases, and metabolic acidosis in five cases. In our study six patients found to have respiratory acidosis and two were having respiratory alkalosis were seen. In the study by Aydin and colleagues[25], non-specific ST changes were reported in the ECGs of seven children withno history of cardiac disease who recovered completely in 24 hours. However we did not observe any changes in ECG in the present cases.

Out of 137 cases reported so far 17 (12.4%) suffered severe respiratory depression requiring mechanical ventilation for less than 24 hours [1,3,8,10,13]. However in our study, 6 of 16 (37.5%) required mechanical ventilation support which is significantly higher as compare to previous study, all our patients, were discharged uneventfully in less than a week.

Amitraz has been shown to have anti-inflammatory and antipyretic activity in vivo and also has been shown to inhibitProstaglandin E2 synthesis [19]. Hence decreased body temperature was seen in seven cases. Garnier et al reported plasma amitrazconcentration of 100 ng / ml, 2 hours after ingestion in an asymptomatic patient and of 500 ng / ml after 2 hours in a patientswith drowsiness. Plasma levels are generally unlikely to be of clinical use because of their limited availability [22]. No antidote is available for this poisoning. 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 [23]. As there is no specific antidote for Amitraz poisoning, the medical managementis essentially symptomatic and supportive. In spite of the severe life threatening clinical features, all of our cases recovered completely.

With the present study, we would like to emphasize that the incidence of Amitraz intoxication is increasing due to its worldwide use in veterinary medicine. In order to decrease the incidence of Amitraz poisoning, public health education should be given as primary prevention of poisoning.

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 compound, especially among the illiterate farmers who use such compounds, day-in and day-out, even without knowing its hazards.We believe that action by producers, regulatory authorities, and national poisons control centres can minimizeamitraz poisoning. For example: containers could be redesigned with striking and clear warning labels; public education should be expanded on primary prevention of poisoning using media sources; and there should be new legislation for safety caps on poison containers.

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