Amitraz Poisoning: Clinical and Laboratory Findings

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Manuscript received: November 25, 2002, Initial review completed: January 11, 2003; Revision accepted: September 8, 2003.

Amitraz is an insecticide/acaricide of formamidine pesticides used worldwide to control ectoparasites in animals. 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. In this study, we present seven pediatric patients with amitraz poisoning. The initial symptoms were unconsciousness, dizziness and vomiting; and emerged within 30-150 minutes. The length of stay in the intensive care unit (ICU) was between 18-62 hours.

Key words: *Amitraz, Children, Intensive care unit, Poisoning.*

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 a_2-agonist actions. The stimulation effect of a_2-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. The reported effects include CNS depression, hypothermia, bradycardia, hypotension, hyperglycemia, glycosuria, vomiting and respiratory failure(3-5).

In Turkey amitraz is available under the proprietry name Kenaz , 12.5% emulsifable concentrate amitraz. This paper presents the clinical and laboratory findings and therapeutic management of the patients with amitraz poisoning admitted to our intensive care unit.

Subjects and Methods

Seven cases of amitraz poisoning were admitted to Dr. BehÖcet Uz Children's Hospital, Emergency Department between 1999-2001 and were evaluated retrospectively. Cases were analyzed according to age, sex, the routes and modes of poisoning, first symptoms, the time to the appearance of first symptoms, clinical and laboratory findings (state of consciousness in the ICU, pupillary signs, heart rate, blood pressure, respiratory failure, requirement for mechanical ventilation, body temperature, blood glucose level, urinary output), therapeutic management, length of stay and survival.

Results

Age of the patients ranged between 2-6 years. These included five boys and two girls. *Table I* shows the demographic data and clinical and laboratory findings in cases retrospectively. Six cases were poisoned by oral and one case by dermal route. Oral

poisoning occured by accidental swallowing, and the ingested amount was 25 mL (3.13 g) in one case and 30 mL (3.75 g) in another, in the rest it was unknown. Dermal poisoning occured by applying treatment of lice by a parent in one case.

Unconsciousness was the predominant initial symptom, the others being vomiting and dizziness. First symptoms appeared within 1 h in four cases. Four of the children presented with coma and two with a somnolent state on admission to the ICU. Initially, miosis was apparent in three cases. Except for one hypotensive case, blood pressure levels were unaltered. Respiratory failure was present in four cases, two of them required mechanical ventilatory support for less then 10 h. Body temperature was decreased (<36ºC, axillary) in two cases. A mild increase in blood glucose level was observed in two cases. Transaminases, blood urea nitrogen, creatinine, serum electrolyte levels, ECG and urinary output were within normal ranges in all cases.

Gastric lavage and activated charcoal were administrated in five cases. Hypotension improved after the administration of intravenous fluids. Bradycardia and miosis responded to 1-4 doses of atropine administration. CNS depression resolved spontaneously within 6-20 h. The length of stay in the ICU was between 18-62 h. All cases recovered fully within 3 days.

Discussion

Formamidines have toxic effects on both animals and humans and previous studies have reported the reversible nature of these effects(3). The present information about amitraz and formamidine pesticides is frequently built on animal studies because of the limited human intoxication cases.

The acute oral median lethal dose (LD50) for the rats is 800 mg/kg(2). Amitraz is a potent inhibitor of rat liver monoamine oxidase(6).

Animals given amitraz show signs of CNS depression or CNS stimulation according to the dose level and to some extent, depending on the species. High doses have a CNS depressive effect with reduced spontaneous activity, bradycardia, respiratory depression and hypothermia. Death resulted from respiratory depression. At low doses CNS stimulation may occur, as manifest by hyperreactivity to external stimuli such as handling, considerably increased food consumptions(7). Topical application amitraz in the dog has been shown to increase plasma glucose and supress insulin release(8).

Animals that survive after poisoning by potentially lethal dose of amitraz show complete recovery from all signs and symptoms in about 7-10 days(9).

The clinical signs reported in previous papers on human poisonings are CNS depression, drowsiness, vomiting, myosis, bradycardia, hypotension and hyperglycemia(10-12). CNS depression, which is probably attributable to the a_2-adrenoceptor action, was the predominant sign in our cases. In previous studies the duration of CNS depression has ranged from a few hours to 24 h(3,4). CNS symptoms began within 30-150 minutes and resolved within 6-20 h in our cases.

Co-existence of bradycardia and miosis may suggest organophosphate poisoning(4). In our series bradycardia was present in two cases and miosis accompanied one of them. Cholinesterase levels of this case were documented to be within normal range; moreover there were no other findings of organophosphate poisoning.

TABLE I–*Demographic Data, Clinical and Laboratory Findings of Cases*

Cases	I	II	III	IV	V	VI	VII
Age (years)	3	3	2	3	4	3	6
Sex	F	M	M	F	M	M	M
Mode of intoxication	accidental, ignorance	accidental	accidental	accidental	accidental	accidental	accidental
Route of poisoning	dermal	oral	oral	oral	oral	oral	oral
Initial symptoms	unconsciousness	unconsciousness	unconsciousness	vomiting, drowsiness	drowsiness	unconsciousness	vomiting unconsciousness
Onset of symptoms (min)	90	150	60-90	30-60	90	30-60	60
State of consciousness in the ICU	$E_4M_5V_5$	$E_2M_3V_2$	$E_2M_2V_2$	$E_4M_5V_5$	$E_4M_5V_4$	$E_1M_2V_1$	$E_2M_2V_2$
Coma	–	+	+	–	–	+	+
Tendon stretch reflexes	N	N	N	N	N	N	hypoactive
Miosis	–	+	–	–	–	+	+
Bradycardia (<60 heart rate/min)	–	–	+	–	–	–	+
Blood pressure	N	N	N	N	N	hypotensive	N
Vomiting	–	+	–	+	+	+	–
Body temperature	N	N	decreased	N	decreased	N	N
Blood glucose (mg/dL)	111	127	40	91	94	123	67
Respiratory depression	–	+	+	–	–	+	+
MV time (h)	–	–	4h	–	–	8h	–
Urinary output	N	N	N	N	N	N	N
Length of stay in the ICU(h)	40	26	54	19	18	62	31
Atropine (0.01 mg/kg/dose)	–	1	2	–	1	4	–
Activated charcoal administration	–	+	+	–	+	+	–

F = female, M = male, EMV = eye, motor and verbal response to stimulus (Glasgow Coma Scale), N = normal, MV = mechanical ventilation.

Key Message

- Amitraz poisonong is characterized by central nervous system and respiratory depression.

Amitraz has antipyretic and anti-inflammatory activity *in vivo*, and also has been shown to inhibit prostaglandin E2 synthesis(13). Decreased body temperature was observed in two of our cases. The basic approach to the patient with amitraz poisoning includes initial stabilization, treatment to reduce absorption and measures to improve elimination of the toxin(14). The medical management is essentially symptomatic and supportive. There is no specific antidote. Despite life-threatening symptomatology, all cases may recover completely. In this study we would like to emphasize that the incidence of poisoning with amitraz is increasing due to its widespread use in veterinary medicine. In order to minimize amitraz poisoning, public education should be given on primary prevention of poisoning and besides, producers should redesign containers as childproof packagers with warning labels.

Contributors: SC, HU, MB worked up the cases, HA diagnosed, reviewed the manuscript and with act as guarantor.

Funding: None .

Competing interests: Nil.

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Blood Zinc Levels in Children Hospitalized with Severe Pneumonia: A Case Control Study

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Manuscript received: May 21, 2003, Initial review completed: August 11, 2003; Revision accepted:October 27, 2003.

A case control study was conducted in a referral and teaching hospital in North India on children aged 2 months to 5 years, to compare blood zinc levels in 50 cases of severe pneumonia and 50 age, sex and nutritional status matched controls. Mean blood Zinc levels in cases and controls was 376.1 µg/dL ± 225.73 and 538.52 µg/dL ± 228.0 respectively (P value 0.0003). In logistic regression model severe pneumonia was associated with lower blood zinc level, use of biomass fuel and isolation of H. Influenzae from nasopharyngeal swab. Cotrimoxazole resistant S. pneumoniae were isolated from 95% of cases and 41.2% of controls (P = 0.0004). Therefore, the role of zinc in treatment of severe pneumonia should be investigated.

Key words: *Blood zinc, Children, Pneumonia.*

Acute lower respiratory infections (ALRI) predominantly pneumonia cause approximately 4 million deaths every year, accounting for one-third of all childhood deaths in developing countries(1). Various factors have been associated with acute respiratory infectious (ARI) in general and pneumonia in particular. These include, among others, nutritional status(2,3), family characteristics(2,3) and environmental exposures(2,4). Most of environmental risk factors require multisectoral coordination for modification. In contrast, some of the childhood risk factors can be modified by simple interventions like vitamin A or zinc supplementation(5).

Recent works have provided conflicting(6) evidence on the role of zinc against ALRI. The study hypothesis was that there is no difference in blood zinc levels in cases of severe pneumonia as compared to controls.

The primary objective of this study was to compare blood zinc levels in cases of severe pneumonia with age, sex and nutritional status