

1 CASE REPORT

2 Amitraz Poisoning; A case study

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5 Received April 11, 2012; Accepted May 28, 2012

6 This paper is available online at <http://ijpt.iums.ac.ir>

7 ABSTRACT

8 Amitraz, an insecticide/acaricide of the formamidine pesticides group, is a α_2 adrenergic agonist and of
 9 the amidine chemical family generally used to control animal ectoparasites. Poisoning due to amitraz is
 10 rare and characterized by central nervous system and respiratory depression, bradycardia, hypotension,
 11 hypothermia, hyperglycemia, nausea and vomiting. Few cases of intoxications in human beings due to
 12 this pesticide have been published in the literature. However, a clear and specific treatment protocol
 13 does not exist and this makes the successful managements of this poisoning (presented in the case
 14 reports) a probable useful guide for clinical practitioners in other poison centers. Management of amitraz
 15 poisoning is still considered to be supportive and symptomatic. We present a case of amitraz poisoning
 16 who successfully managed by supportive treatments in a 20 years old female.

17 **Keywords:** Amitraz; Bradycardia; Miosis; Central nervous system

18 Amitraz, a triazapentadiene compound and a 43 amitraz poisoning who was conservatively managed in
 19 member of the amidine chemical family is a 44 intensive care unit (ICU) for 36 hours and experienced a
 20 formamidine pesticides used worldwide. It is used as an 45 complete recovery.

21 insecticide/acaricide to control animal ectoparasites [1-
 22 223]. Commercial formulations of amitraz generally
 23 contain 12.5-20% of the drug in organic solvents, 46
 24 especially xylene, which is itself used in paints,
 25 cleaners, and glues [4]. Amitraz is a α_2 -adrenergic
 26 agonist stimulating α_2 adrenergic receptors in the central
 27 nervous system (CNS) and both α_1 and α_2 adrenergic
 28 receptors in the periphery. It also inhibits monoamine
 29 oxidase (MAO) enzyme activity and prostaglandin E₂
 30 synthesis [5].

31 Poisoning occurs through oral, inhalational (the most
 32 potential), and dermal routes and is accompanied by
 33 numerous signs and symptoms varying from CNS
 34 depression (drowsiness, coma, and convulsion), to
 35 miosis, or rarely, mydriasis, respiratory depression,
 36 bradycardia, hypotension, hypertension, hypothermia or
 37 fever, hyperglycemia, polyuria, vomiting, decreased
 38 gastrointestinal motility, and intestinal distension [4].
 39 Adverse reactions and side effects have been reported in
 40 animals exposed to the product; however, only few
 41 human intoxication cases have been reported in the
 42 literature. We present a young female patient with

46 CASE STUDY

47 A 20-year-old female referred to L.G. Hospital in
 48 Ahmedabad, Gujarat, India after the ingestion of 2 to 3
 49 full table spoons of amitraz chemical (10% solution) in
 50 a suicidal attempt. Her first symptoms had begun about
 51 one hour post ingestion and included nausea and
 52 dizziness, after which vomiting had ensued. Her family
 53 had immediately brought her to our center where
 54 gastric lavage with normal saline and administration of
 55 activated charcoal (1 g/kg) were performed. She was
 56 then admitted to ICU for further management.
 57 At presentation, she was drowsy but followed the
 58 verbal commands. Her blood pressure, pulse rate,
 59 respiratory rate, and temperature were 126/80 mmHg,
 60 90 bpm, 24/min, and 36.8°C, respectively. Analysis
 61 of blood gases showed PaO₂ of 106.4, O₂ saturation
 62 of 96%, pH of 7.40, PCO₂ of 34.0, and HCO₃⁻ of 21.6.
 63 Other lab tests were as follow: blood urea nitrogen: 13
 64 mg/dL; creatinine: 0.80 mg/dL; sodium: 138.9 mEq/L;

potassium: 4.48 mEq/L; alanine transaminase: 15.7 IU/L; blood glucose: 95 mg/dL (normal range, 70 to 110 mg/dL); PT: 14.7; INR: 1.03; calcium: 9.33 mg/dL; and magnesium: 2.2 mg/dL. In complete blood count, hemoglobin, white blood cells, and red blood cell count were reported to be 6.72 g/dL, 8260/mm³, and 4.58×10⁶/mm³, respectively. Chest X-Ray was normal. One unit of packed cell was injected due to the low hemoglobin level. No special treatment was performed except for gastric decontamination and cardiac and respiratory monitoring. Atropine (once; 4mg stat) was also administered for the treatment of the patient's transient bradycardia. During the ICU stay, the patient developed premature ventricular contractions (PVCs) which were treated by administration of one dose of lidocaine (1.5 mg/kg) and resolved in 24 hours. By the following day, she was completely conscious and able to answer to the questions. She completely recovered and was discharged from the hospital the afternoon of the second day of admission.

DISCUSSION

Formamidines have been shown to have reversible toxic effects on both animals and human beings [4]. Since there are few reported human intoxications by this pesticide, the existing information about it is frequently built on animal studies. The median lethal dose in its acute oral toxicity (LD₅₀) for the rats is 800 mg/kg [3,4]. The clinical signs and symptoms of this poisoning reported in previous reports include CNS depression, drowsiness, vomiting, miosis, bradycardia, hypotension, and hyperglycemia. The duration of CNS depression has ranged from a few hours to 24 h [4]. CNS symptoms began within 30-150 minutes and resolved within 6-20 h in our case. Sedative effects of α_2 -agonists are dose-dependent [1]. Coma, absence of light reflex, and respiratory failure are due to the ingestion of greater amounts of amitraz supporting its dose-dependent effects. Our patient was fully conscious after 24 h. This time has been reported to be 2-48 h in previous reports. The effect of amitraz on α_1 - and α_2 -receptors causes bradycardia [5]. In addition, literature reported hyperglycemia, hypotension, and bradycardia in amitraz poisoning and attributed them to the alpha-2 adrenoceptor agonist action of amitraz [6]. In our case, bradycardia was also present accompanying with miosis which developed during the course of hospitalization. Co-existence of bradycardia, miosis, and the respiratory depression leads to confusion with organophosphate or opioid poisonings, both of which should be excluded. Using atropine for treatment of bradycardia is controversial. Most studies, however, have reported atropine to resolve both miosis and bradycardia. Atropine is the first line therapy for the bradycardia resulted from vagal stimulation and atrioventricular blocks. Alpha-2 adrenergic drugs can also cause

Although it has been declared that amitraz and its active metabolite inhibit insulin and stimulate glucagon secretion, we did not detect hyperglycemia in our case. This is in contrast with the previous study by Demirel and colleagues that reported hyperglycemia in nearly 64% of the cases [7]. Avsarogullari et al reported hyperglycemia and fast deterioration of the patients (within 5 minutes after the ingestion of the toxin) that were both absent in our case [8]. Elevations of aspartate transaminase was also detected in almost 20% of their patients which was not detected in our case. Usually, levels of BUN, creatinine, and the serum sodium and potassium do not change in this poisoning [2]. However, Kalyoncu and colleagues have reported hyponatremia in their three cases [9]. This is while our patient did not show any evidence of electrolyte abnormalities. On the other hand, while analysis of blood gases was normal in our case, Kalyoncu and associates have reported respiratory alkalosis in two, respiratory acidosis in three, and metabolic acidosis in five cases [9]. We observed PVCs in our patient's electrocardiogram (ECG) which recovered after 24 hours. In contrast, in a study by Aydin and coworkers, non-specific ST changes were detected in the ECGs of seven children with no history of cardiac disease who completely resolved in 24 h and PVCs were not detected [10]. Our case is interestingly very similar to a 54-year-old patient who had referred to Elinav and associates (with a clonidine-like syndrome) and managed in the same way [11]. Although not related to our patient, It is interesting to know that intravenous administration of amitraz can result in respiratory depression, hypotension, bradycardia, hematuria, and edema and hyperemia at the injection site which again are benign and resolve without complications [12]. In conclusion, basic approach to a patient with amitraz poisoning consists initial stabilization, reducing absorption, and increasing elimination of the toxin. Medical management is essentially symptomatic and supportive. No specific antidote exists [2]. Although activated charcoal and cathartic effects have not been evaluated, they are still considered in the treatment protocol of these patients. Attention must be paid to the evaluation of the respiratory, cardiac, and central nervous systems. Increased intake may lead to severe effects including coma and respiratory failure. With supportive management, prognosis is good and the patients are discharged without any organ dysfunction. This is similar to the results of Demirel et

178 al [7] and Avsarogullari et al [8] who reported a good
179 prognosis in amitraz intoxications.

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