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Near-Fatal Amitraz Intoxication: The Overlooked Pesticide

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Abstract: Amitraz is commonly used in agricultural industries throughout the world as a farm-animal insecticide. Despite its widespread use, amitraz intoxication is extremely rare and mainly occurs through accidental ingestion by young children. Severe, life-threatening amitraz intoxication in adults is very rarely recognized and reported. Described herein is a previously healthy 54-year-old patient who accidentally ingested a mouthful of liquid amitraz concentrate, and rapidly developed life-threatening clonidine-like overdose syndrome, manifested as nausea, vomiting, hypotension, bradycardia, bradypnoea, and deep coma. Supportive treatment, including mechanical ventilation, and atropine administration resulted in full recovery within 48 hr. Very few cases of near-fatal amitraz poisoning in adults have been described in the medical literature, leading to low awareness of physicians in general practice to the potential toxicity of amitraz. As a consequence, cases of amitraz poisoning are not recognised and therefore erroneously treated as the much more commonly recognized organophosphate and carbamate intoxication. In our discussion, we review the clinical and laboratory manifestations of amitraz poisoning, including clinical hints that aid in the recognition of this often-overlooked diagnosis. Differentiation of amitraz intoxication from the much more commonly seen pesticide-related organophosphate and carbamate intoxication is of utmost importance, in order to avoid erroneous, unnecessary, and often dangerous treatment.

Amitraz is a commonly used pesticide, employed by farmers throughout the world for the treatment of insect infestation in farm animals. It is usually provided in highly concentrated liquid solutions (usually containing xylene as a solvent), while its preparation in agricultural use requires dilution in 1:500 to 1:1000 ratios. Ingestion of small quantities of amitraz is associated with self-limiting nausea and vomiting, while ingestion of larger quantities may result in clonidine-like overdose syndrome. Herein, we report a patient who, upon consumption of a small quantity of amitraz concentrate, developed a severe clonidine-like overdose syndrome associated with life-threatening coma.

Materials and Methods

A 54-year-old male farmer was referred from a rural hospital to our Emergency Services, for evaluation and treatment of presumed organophosphate poisoning. The patient had ingested a mouthful (estimated 20–30 cc) of liquid pesticide, which he erroneously thought was juice. After 30 min. he developed nausea and vomiting. While being transferred to our medical center, he became progressively bradycardic, bradypnoeic, and had a declining mental status. No convulsions were noted. His medical history was unremarkable, with no medical conditions and no history of alcohol and drug abuse. The patient strongly denied consumption of any medication, including over-the-counter, natural and alternative drugs. No atherosclerotic, hypercoagulable, or bleeding tendencies were noted.

On admission the patient appeared deeply unconscious, with no response noted to painful stimuli. Vital signs included a blood pressure of 90/60 without features of tissue hypoperfusion, bradycardia of 60 beats per min., and a respiratory rate of 7 breaths per minute. Pupils were equal, widened and unreactive to light. The rest of the physical examination was unremarkable, including any evidence of trauma, focal neurological deficits, or pathological neurological reflexes. Clinical signs of organophosphate intoxication, including miosis, excessive sweating, salivation, and urinary and foecal incontinence were lacking.

Laboratory evaluation was notable for severe hyperglycaemia of 28 mmol/l (in a previously normoglycaemic patient). Other laboratory findings were unremarkable, including complete blood count, biochemistry (including kidney and liver function tests), arterial blood gases (taken after mechanical ventilation), urinalysis, serum ethanol levels, toxic screen (for opiates, benzodiazepines, methadone, cocaine, amphetamines, cannabinoids, barbiturates), and osmolar gap. Sputum examination was unremarkable and blood and urine cultures were sterile. Chest X-ray and total body CT scanning were normal, and lumbar puncture and encephalomyogram were unremarkable. Serum pseudocholine-esterase level was within normal range (4.3 units/ml).

The patient was admitted to the intensive care unit, mechanically ventilated, and aggressive fluid infusion was initiated. Due to the presumed diagnosis of organophosphate intoxication, the patient was administered several doses of intravenous atropine and a single dose of pralidoxime. After the return of normal pseudocholine-esterase levels and the acquisition of the ingested bottle, the diagnosis of amitraz poisoning was made and all other treatment was discontinued. Supportive treatment resulted in a gradual regaining of consciousness and resolution of hyperglycaemia after 48 hr of admission. The patient was then extubated, discharged after 4 days of hospitalization, and has been doing well since.

Results and Discussion

Accidental or suicidal intoxication involving insecticides is a common and emerging problem throughout the world. Rapid neurological deterioration following a brief exposure to a small amount of pesticide is most commonly caused by organophosphate or carbamate poisoning. These cholinesterase-inhibiting agents, predominantly used in the agricultural industry as pesticides, may cause, upon acute exposure, a dramatic, life-threatening syndrome consisting of

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excessive lacrimation, salivation, diarrhoea, emesis, miosis, bradycardia, loss of consciousness and respiratory depression. Aggressive treatment with anticholinergics and oximes may result in complete recovery (Vidair 2004).

Other insecticides, widely used in the private sector, include pyrethrins, pyrethroids, diethylmethylbenzamide (DEET) and organochlorines. These chemicals are generally considered to be safe, and very rarely induce convulsions and gradual neurological deterioration if consumed in excessive doses (Yang *et al*. 2002). In patients who develop acute loss of consciousness following insecticide ingestion, whose clinical features are incompatible with those of organophosphate and carbamate poisoning, one other unique, yet often overlooked possibility exists, namely amitraz poisoning (Proudfoot 2003).

The formamidine pesticide amitraz, 1.5-di-(2,4-dimethylphenyl)-3-methyl-1.3.5-triaza-penta-1.4-diene, is widely available and used throughout the world for the control of ectoparasites in farm animals and crops. Amitraz is marketed under many trade names, including Taktic, Ectodex, Mostraz, Triatix, Metaban, Mitac, Acadrex, Kenaz, and Atarac, and usually supplied as a highly concentrated 12–20% aqueous solution, which is amply diluted in water before use (Jorens *et al*. 1997).

Amitraz poisoning may be caused by ingestion of as little as 10 cc of the highly concentrated solution. Intoxication is rarely caused by dermal or inhalational exposure. In contrast to amitraz' widespread use, very few rare cases of intoxication mostly in children, have been reported (Yaramis *et al*. 2000; Aydin *et al*. 2002). A few cases have been reported in adults, and only a handful of these intoxications were life-threatening (Kennel *et al*. 1996; Garnier *et al*. 1998; Leung *et al*. 1999; Ulukaya *et al*. 2001; Yilmas & Yildizdas 2003). The discrepancy between the widespread availability of amitraz and the low rate of reported intoxication is thought to be attributed to both under-reporting of amitraz poisoning in remote rural areas, and under-diagnosing of this insecticide-related intoxication, which is often mistakably regarded as organophosphate or carbamate poisoning.

Amitraz intoxication is uniquely mediated through α_2-adrenergic receptor agonist effects, similar to those of the α_2-agonist clonidine (Altobelli *et al*. 2001). Symptoms usually appear within 5 min.–3 hr of exposure, and include nausea and vomiting, severe central nervous system depression, hypotension, bradycardia, respiratory depression, mydriasis, and infrequently miosis. In some cases miosis appears first, followed by midriasis. Papillary light reflex is often absent. Polyurea is caused by a reduction of ADH secretion and inhibition of its renal effect. In contrast to organophosphates, amitraz causes decreased gastrointestinal motility and decreased salivation (Harvey *et al*. 1998).

One laboratory finding that is a hallmark of amitraz poisoning and may greatly support the diagnosis is the presence of hyperglycaemia and glycosuria, caused by amitraz' inhibition of insulin release and stimulation of glucagon secretion. Other laboratory findings are mainly non-specific and may include a mild and transient elevation in liver enzymes and non-specific electrocardiographic STT changes (Kennel *et al*. 1996).

Treatment is mainly supportive, consisting of haemodynamic and respiratory monitoring and stabilization. The use of activated charcoal may be beneficial, but clinical benefit has not yet been proven. Whenever gastrointestinal decontamination is considered, it is important to make sure the patient has protected airways. This is particularly important in amitraz poisoning, as aspiration of hydrocarbons, that are commonly used as solvents in amitraz concentrates, may cause additional extensive mucosal damage. Severe bradycardia may respond to recurrent atropine administration, respiratory depression may require mechanical ventilation, while neurological improvement is usually spontaneously evident within 48 hr of exposure (Ulukaya *et al*. 2001). Treatment with α_2-adrenoreceptor antagonists, such as yohimbine and atipamezole, has been shown in animal models to improve survival and may be attempted in very severe cases of human exposure (Andrade & Sakate 2003). Pralidoxime has no role in the treatment of amitraz intoxication. When treated, most patients with amitraz poisoning recover fully, while a delay in diagnosis and treatment may result in death.

Conclusion

The diagnosis of amitraz intoxication is extremely challenging. The co-existence of neurological deterioration, bradycardia, and infrequently miosis in individuals that were exposed to insecticides most often leads to confusion with organophosphate overdose. Coma, respiratory depression and miosis are also hallmarks of the much more commonly encountered opiate overdose. Overdose with medications such as tricyclic antidepressants, barbiturates, and phenothiazides may produce similar findings.

In patients who present a combination of exposure to an insecticide, hyperglycaemia, and lack of the classical features of organophosphate poisoning, awareness of the physician is required for the diagnosis of amitraz poisoning. Correct diagnosis will help initiate rapid treatment for this rare, potentially life-threatening intoxication.

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