Original Article

Acute Pesticide Poisoning in Children: A Review of 50 Cases

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Received :28.08.2018 *Accepted: 23.10.2018*

ABSTRACT

Background: Pesticide poisoning is very common in Tunisia. Various factors are involved in the analysis of the clinical presentations and the severity of this condition. Major factors are the chemical nature of the pesticides and the quantity entered the body.

Methods: This is a retrospective study, reporting the pediatric cases that presented to us with signs and symptoms of pesticide poisoning. Fifty cases pesticide poisoning were admitted to the hospital between January 2013 and October 2016.

Results: A total of 50 pediatric cases were included in this study with the mean age of 3 years and 4months. The poisoning was accidental in 49 cases and self-inflicted in one, with the mode being oral (N=45), respiratory (N=2) and cutaneous (N=3). The average duration of hospital care for these patients was 2 hours and 30 minutes (range: 30 min-24 hr). The clinical manifestations of poisoning noted were due to muscarinic and nicotinic receptors inhibition. Upon clinical examination, 29 patients had no pesticide in the gastric lavage fluid and urine and demonstrated no abnormal cholinesterase activity. The therapeutic management was mainly symptomatic with antidote medications prescribed (atropine and oxime). All patients had favorable outcomes and no death occurred.

Conclusion: This study demonstrated the frequency of pesticide poisoning in a pediatric setting and the importance of early management. Optimal therapeutic approaches were evaluated, demonstrating that prevention still remains the best solution in such cases.

Keywords: Atropine, Organophosphates, Oxime, Pediatric Cases, Poisoning, Preventive Management**.**

IJT 2018 (6): 27-31

INTRODUCTION

The main targets of pesticides are various living organisms, such as fungi, weeds, insects, mites, nematodes, mollusks, and rodents. Pesticide poisoning remains a public health problem in many nations worldwide [1, 2]. Insecticides including organophosphates (OP) and carbamates are the main causes of acute pesticides poisoning in children [1, 2]. According to the World Health Organization's report, the annual cases of pesticide poisoning are estimated to be one to five million, with several thousand being fatal [3]. The exact number of children involved in these incidents is unclear because the majority of previous studies focused on suicide by OP substances in adults. However, according to some sources, the incidence is likely to be significant [1, 2]. Pesticide poisoning is very common in Tunisia and ranks the 3rd highest according to recent reports from the Emergency Medical Assistance Center (CAMU). The severity of pesticide toxicity depends on the nature of the OP product and the quantity involved [4]. The clinical presentations of acute poisoning result from the inhibition of cholinesterase receptors at the synaptic junctions or the effects on erythrocytes in plasma. The presentation includes three syndromes: *muscarinic*, *nicotinic* and *encephalic* that may coexist in the same patient. The aim of this study was to examine the epidemiological, clinical and therapeutic characteristics of acute pesticide poisoning in children and to propose the optimal preventive measures.

MATERIAL AND METHODS

This was a single-center, retrospective study, conducted in Pediatric Department B at Children's Hospital in Tunis, Tunisia. All patients (N=50) were under 16 years old and were hospitalized for acute organophosphate poisoning between January 2013 and December 2016. The diagnosis was made based on the signs, symptoms, clinical examinations relevant to pesticide poisoning, and history of accidental or deliberate exposure to pesticides reported by the patients or relatives. Patients with unclear on incomplete medical records were excluded from the study.

The clinical and laboratory data were collected from the hospital records. For each patient, the variables under study were: demographics (age, gender & origin), circumstances of poisoning, time elapsed between the poisoning event and the first medical care given, clinical symptoms, medical treatment, biological outcomes at discharge, and prognosis. A complete clinical assessment was made at the time of admission for each patient, consisting of the status or levels of: glycemia, creatinine, blood urea, liver function tests, amylase,

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serum creatine phosphokinase (CPK), lactic dehydrogenase (LDH) and hematological parameters.

To confirm the diagnosis, the red blood cells' acetylcholinesterase activity (AChE) was performed at admission, using heparinized blood samples by Ellman (Sigma-Aldrich, France) colorimetric method, compared with the normal values of 5.14 to 8.94 IU/ml GR UI/l). The activity of plasma butyryl-cholinesterase (BChE) was assessed by Cobas Integra (Roche, Switzerland), based on the normal values for children being: 5,320-12,920 IU/l). Cholinesterase activity measurement and all other toxicological analyses were performed at CAMU.

Analysis of Pesticides in Body Fluids

The measurement of pesticides was made from the gastric aspirate and/or urine samples by thin layer chromatography (TLC). Gas liquid chromatography (GLC) and Fourier transform infrared spectroscopy were used to identify the OP chemical components.

Statistical Analyses

Descriptive statistical analyses, including continuous and categorical data, were performed and summarized. Data distributions were reported as simple and relative frequencies in percentage for the qualitative variables. Means, standard deviations, medians, and the minimum and maximum values were tabulated for the quantitative variables. All statistical analyses were performed, using SPSS Software version 20.

RESULTS

Fifty pediatric patients due to pesticide poisoning were admitted. The mean age of the children was 3 years and 4 months [range: 11months -14 years], with equal number of boys and girls. The mean age for girls was 3 years and 6 months [range: 12 months-14 years] while that for the boys was 3 years and 2 months [range: 11months - 12 years]. The age group under 4 years old accounted for 84% of the study population versus 16% for the age group over 4 years.

Among the patients, there were 30 cases (60%) that occurred in rural areas while 20 cases (40%) occurred in cities, all of which in the parental homes. 19 cases were reported in the summer, 15 in autumn, 10 in the spring and 6 in the winter. The poisoning occurred accidentally in 49 cases (98%), while it was self-inflicted in one case (2%). The organophosphate product was ingested in 45 cases (90%), inhaled in 2 cases (4%) and entered the body transcutaneously in 3 cases (6%). The mean time of hospital admission elapsed after poisoning was 2.5 hours (range: 30 min-24 hr).

The reported clinical symptoms in the patients are presented in Table 1. The standard biological assessments performed for all patients were normal, with no cholestasis or cytolysis, no renal damage or homeostasis disorder detected. Also, rhabdomyolysis and pancreatic abnormalities were not detected in these children. The results of serum cholinesterase assays were normal for 39 patients, with the mean value being 6700 IU/l [range: 5400-8700 IU/l]. In 29 patients, there was no pesticide found in urine, blood and gastric fluid samples. The presence of pesticides in the stomach was established via gastric lavage in 20 patients (40%) and by performing activated charcoal test in 7 patients (14%). Also, we administered oxygen to three children (6%) due to their respiratory complaints. Further, muscarinic antagonist treatment with atropine was indicated in 10 patients (20%), and we used oxime, an acetyl cholinesterase activator, to treat 7 patients (14%). The prognosis was favorable for all of the patients with complete remission of their symptoms. The mean hospital stay for the patients was 27 hours [range: 24-48 hours]. Lastly, all of the identifiable patient data were kept strictly confidential throughout the study.

Table 1. Patients' Clinical Characteristics.

Clinical Symptom	Patients (n)	Percentage
Miosis	10	20
Mydriasis	1	2
Coma	4	8
Salivation	6	12
Rhinorrhea	1	2
Bronchorrhea	5	5
Diarrhea	14	28
Muscle Weakness	6	12
Cramps	1	2
Fasciculation and Seizure	1	2
Bradycardia	1	10
Tachycardia	10	20
Hypotension	3	6

DISCUSSION

Organophosphate pesticides are classified for their toxicity in animals from the most to the least fatal, i.e., Class I to Class IV. In general, OP's (with P=O function) are direct, rapid and potent inhibitors of enzymes, due to the function of phosphate and oxygen molecules [5, 6]. The OP having P=S function, are indirect enzyme inhibitors, and are metabolized to their active compound P=O, such as parathion, which is converted to paraxon, the active metabolite. These products are characterized by high lipid solubility and tissue affinity, particularly in the central nervous system (CNS). These characteristics are the reason for the prolonged inactivation of the enzymes and consequently the serious toxicity leading to severe neurological complications secondary to cerebral anoxia, especially by parathion and dichlorvos [7]. After bodily absorption, many OP must be activated in the liver before becoming toxic to humans [8]. These mechanisms justify the delay between OP ingestion and occurrence of symptoms in our study.

Carbamates have the same mechanism of OP with potent transcutaneous penetration, except for the lack of absorption through respiratory tract. However, unlike OP's, the cholinesterase inhibition is reversible. The

carbamate-cholinesterase complex hydrolyzes spontaneously in a few hours and the toxin is destroyed. Therefore, there is no nicotinic or CNS syndrome. This is the major differential diagnosis for OP poisoning, which is clinically indistinguishable from carbamate toxicity, and the treatment approach is essentially the same as observed for OP poisoning. Oxime is not indicated due to the spontaneous hydrolysis of the carbamate-cholinesterase binding, but pralidoxime is recommended when atropine treatment is poorly effective or ineffective [9].

In this study, the toxicity diagnosis was made based on anamnestic and clinical arguments, without biological confirmation, so we didn't identify the product responsible of poisoning except when it was presented to us by the family. However, we believe that OP and carbamate were the most common pesticides, causing children poisoning due to their common application in agriculture, hence the easy availability to children and family. In Tunisia, pesticide poisoning accounts for 11% of all acute toxicities seen in the emergency department of the Poisoning Center in Greater Tunis. In this study, the majority of pesticide poisoning occurred in rural areas (60%), due to its popular usage in agriculture.

Children aged one to four years old were well represented in this study, which is consistent with similar data reported by other studies [10-13]. At this age, children are curious about their surrounding materials and are often unaware of the impending danger. It is also the age of the acquisition of walking or hand to mouth activity. Pesticides are involved in accidental exposure when they are left negligently within the reach of children or due to accessible storage. However, poisoning is not always accidental in children. In this study, self-inflicted poisoning was observed in a girl over the age of 10 years, which was a suicide attempt following a family argument. Apart from the obvious accidental or suicidal attempt, the issue of criminal poisoning deserves attention regardless of the age of the victim. The overall male to female ratio in our population was 1:1, unlike those reported by two studies that suggested the male predominance in accidental poisoning was due to boys' impulsivity [14, 15].

In our study population, the route of OP toxicity was mainly oral (90%), and to a lesser extent cutaneous (6%) and respiratory (4%). We also noted 6 cases of concomitant OP administration. In the annual report of the American Association of Poison Control Centers (AAPCC, 2009), the reported routes of exposure in descending order were: digestive (84%), cutaneous (7%), pulmonary (5%) and ocular (4%) [16]. In a Portuguese study [17], two cases of acute OP poisoning were reported in a 4-year-old girl and her 6-year-old brother following the use of an insecticide as anti-lice shampoo. In the current study, pesticide poisoning was more common in the spring and summer (68%) than in the fall and winter (32%). This is due to the high usage of OP's as herbicides, insecticides, and fungicides in agriculture, and to a much lesser extent at homes [18, 19].

Few studies have been conducted on pesticide poisoning in children [20, 21]. The early detection of the pediatric accidents makes it possible to limit the quantity of the toxin absorbed in domestic cases, compared to the industrial incidents in which adults are the major victims. The diagnosis of pesticide poisoning is rather difficult in children. It was suspected on admission only in 57% of cases in a study by Zweiner and Ginsburg [21]. In fact, the classic signs of OP poisoning in adults, such as tearing and loss of urine and stool are difficult to differentiate in children from simple crying or normal voiding and defecation due to tantrum. However, CNS involvement appears to be predominant in pediatric groups. In the study by Lifshitz *et al*. [22], all children presented with neurological disorders, such as hypotonia, stupor and coma on admission, whereas muscarinic signs were not always present. In the study by Zweiner and Ginsburg [21], nearly 25% of children poisoned with OP had seizures, compared to 2.4% in adults [21, 23]. According to Lifshitz *et al*. [22], the predominance of neurological signs in children could be explained either by a greater permeability of the blood-brain barrier, facilitating OP penetration into the CNS tissues or due to a preferential inhibitory effect on CNS functions by acetylcholinesterase [23].

In contrast, in Zweiner and Ginsburg's study [21], seizures appeared to be secondary to hypoxia, rather than a direct toxic effect on the CNS [22]. In all cases, the neurological signs are classical in children and the absence of muscarinic signs should not rule out the diagnosis. In our study, the muscarinic syndrome was predominant and presented as digestive and visual disorders in 14 children, and as miosis in 10 children. Nicotinic syndrome was less common; we found tachycardia in 10 cases and asthenia in 6 cases. Meanwhile, the CNS syndrome was found only in 5 children, with coma in four cases and seizures in one.

Symptomatic treatment is essential in OP poisoning and must be started as soon as possible to preserve the vital functions (pulse, blood pressure & breathing). In this study, only 3 children required oxygen supply at a rate of two L/min, because of bronchial hyper-secretion and hypoxia. After OP ingestion, gastrointestinal decontamination is most effective by gastric lavage within the first hour. However, this method is still effective up to 4 hour post-ingestion. After four hours, OP's are no longer found in the gastrointestinal tract [7]. Late gastric lavage beyond 12 hours, if not repeated, would also be useful according to some authors [24] but its benefit remains controversial [25, 26]. In this study, 20 patients underwent gastric lavage after a mean delay of 3 hours.

Treatments

In practice, two specific therapies have been introduced since 1950 without any well-designed clinical trial:

1. Muscarinic antagonist, Atropine: At present, there are 30 protocols for atropine administration in acute OP poisoning [27], without any systematic clinical trial to compare varying atropine regimens [7, 28]. The conventional atropine dosage may be adjusted for optimal efficacy in some cases. In this study, only 10 children benefited from conventional dose administration of atropine without reporting adverse effects.

2. Acetylcholinesterase inactivator, Oxime: This drug inactivates acetylcholinesterase by phosphorylation. It must be used in addition to atropine since it temporarily binds to cholinesterase molecules [7, 29-31]. In this study, only seven children received this drug (Pralidoxime).

According to the literature, the reported fatality varies from 4 to 30% of cases. In the United States, OP poisoning has been responsible for 50% mortality in children and 10% in adults [32]. In Morocco, a retrospective study of all cases of acute pesticide toxicity in children under 14 years of age reported a mortality rate of 50.8% [33]. Fortunately, in our study, there was no death case observed, most likely due to the low OP dosage taken accidentally compared to the suicidal OP dosages reported in previous studies. Further, there might have been some unreported out-of-hospital deaths among children with pesticide poisoning whom we did not see at all.

Limitations of Study: The principal limitations of this study were:

- The small number of patients included
- The normal cholinesterase activity in our cases
- The negative toxicological analyses
- The diagnosis of toxicity was suspected based on anamnestic arguments and clinical impressions, without biological confirmation or severity classification of OP toxicity.

CONCLUSIONS

Our results revealed that most of the pesticide toxicity cases occurred in preschool children, indicating a need for child-resistant packaging and closures of OP products used as pesticide. It is essential to establish preventive measures to control the use and storage of pesticides, especially in rural areas. We found our protocol for treating the 50 pediatric cases of pesticide poisoning with atropine and oxime in less than three hours from ingestion to be effective with no fatality reported.

We recommend establishing a campaign to increase the public awareness about the harmful effects of pesticides, especially in children. The OP suppliers should post information on emergency situations on the packages and provide their customers with a brochure, containing precautions in handling the compounds as well as the addresses and phone numbers for poisoning centers that are open for service 24 hours a day, seven days a week. We also recommend that a prospective study be conducted to assess the impact of instituting preventive measures on the reduction of the number of pediatric poisoning and deaths due to pesticides.

ACKNOWLEDGEMENT

The authors thank all of the team of the Pediatrics B Department, Children's Hospital, Faculty of Medicine, University of Tunis El Manar. Tunis, Tunisia.

CONFLICT OF INTEREST

The authors declare no conflict of interest influencing the conduction of this study.

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