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A Report on the Incidence of Organophosphate Poisoning among Patients Admitted to King Abdul-Aziz Medical City, Riyadh, Saudi Arabia over a Period of 12 Years

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Authors' contributions

This work was carried out in collaboration between all authors. Author MKAM was the principal investigator of the research project, responsible for designing of the entire work and overall write-up. Author FAA was responsible for data collection and associated with writing, interpretation of results along with attending to comments of referees. Author A. Alanazi assisted in supervising the entire work. Author NA assisted in methodological aspect of the research. Author A. Alqahtani assisted in literature search and arranging references. Author NAH was responsible in computing results. Author SQ was responsible in assisting writing the discussion, interpretation, in addition to correspondence with the journal, attending to comments of the referees and in addition to rewriting some parts of the manuscript.

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ABSTRACT

Background: Organophosphate (OP) is a chemical component, extensively used as a pest control. It is known to block the action of acetylcholinesterase (AChE), causing accumulation of acetylcholine, resulting in symptoms which tantamount to poisoning. Many reports are published on OP poisoning, however; there is a paucity of literature on poisoning due to OP in Saudi Arabia. Hence, the purpose of our study was to look for OP poisoning, in patients admitted to King Abdul-Aziz Medical City (KAMC) over a period of 12 years ranging from January 2002 to June 2014.
Materials and Methods: This is a retrospective study of patients admitted to KAMC with history of acute toxicity.
Results: The study constituted a total of 82 patients. Eighty five percent of admissions were Saudis. The age range was between 6 months and 91 years. Gender ratio was 1.05:1 female to male. Accidental exposure was 62.2%, followed by 30% suicidal attempts. About 55.41% of the patients ingested the poison orally, 31.08% and 13.51% of the incidents were through skin and respiration respectively. Most of the patients (59.8%) arrived to the hospital within 4 hours of exposure. Majority of the patients (79.27%) arrived by private car. Muscarinic effects had been dominant in these patients. Nausea and vomiting were present in 62% of the cases, followed by pupil dilation (54%) and hyper-salivation (35%). Out of 82 patients, 26.83% showed shortness of breath. During the treatment, 24 patients developed both acute and chronic complications. The rate of mortality was 2.4%.
Conclusion: Poisoning is found common as a suicidal attempt among adult females and those who had a history of psychiatric illness, while children below 6 years are at high risk of accidental poisoning.

Keywords: Accidental; organophosphate; patients; psychiatric; suicidal attempts.

ABBREVIATIONS

OP : Organophosphate.
AChe : Acetycholinesterase.
KAMC : King Abdulaziz Medical City.
ICU : Intensive care unit.
ER : Emergency room.
WBC : White blood cell.

1. INTRODUCTION

Organophosphate (OP) is a chemical component, has been widely used in agriculture and pest control [1]. It inhibits the action of AChE which lead to the accumulation of acetylcholine causing overstimulation of muscles, in addition to the development of toxic symptoms, such as skin itching, headache, sweating, dizziness, fatigue, vomiting, blurred vision and respiratory problems [2,3]. Inhibition of cholinesterase action leading cholinergic hyperactivity, cellular dysfunction, acetylcholine-induced oxidative damage is reported to cause acute toxicity [4]. The severity of symptoms depends on type of substance, route, quantity and the duration of exposure [3].

WHO has an estimated 500,000 cases of acute pesticide poisoning worldwide, most of them are in developing world including Asian countries [5]. The National Poison Data System in United States of America, in their annual report (2011) has shown 2,334,004 incidents of poisoning. Among, approximately 84 thousand were due to poisoning related with pesticides. The reason behind the poisoning has been found to be suicidal, homicidal or accidental exposures. Children under 5 years of age are the most affected group. In the same year, there were about 2500 exposures to OP alone, with 82 being related to intentional use, resulting in 4 deaths [6].

The incidence of poisoning in Arab countries in general and Saudi Arabia in particular is not uncommon. Nevertheless, the prevalence of OP poisoning in Saudi Arabia is yet to capture limelight by published reports [7-10]. Moreover, there is a paucity of definite regulations for dealing with and handling pesticides [11], hence the present study has been conducted on the incidence of OP poisoning reported during past 12 years in the hospital attached to the King Saud bin Abdul- Aziz University, National Guards, Riyadh.

2. METHODOLOGY

2.1 Study Design

This is a retrospective medical record review for all OP poisoning patients who were admitted to

KAMC through Casualty between January 2002 and June 2014. The modified protocol of Sawalha et al. [12] was used. The study included both adults and children who were diagnosed with acute OP poisoning and required admission to Intensive Care Unit (ICU) and/or general ward. Acute OP poisoning was considered based on the following criteria: (a) history of confirmed contactor exposure to OP (b) patient presented with cholinergic symptoms (c) Improvement of patient's signs and symptoms after treated with atropine and oximes.

2.2 Data Collection

Saudi patients attending emergency were identified through a computerized search of an electronic database using the search code ''organophosphate'' or the ICD-10 code T60.0 of ER database from January 2002 to June 2014. Only patients who required admission were included in the study. The data retrieved from charts were: Demographic information including exposure time, place of admission, clinical presentation, disposition information, besides conduction of hemodynamic parameters, course in the hospital and treatment were given. Complications and mortality were also reported in our study.

2.3 Statistical Analysis

All raw data collected from medical records were compiled using Excel sheet after ensuring the removal of confidential information. All coded data were imported from Excel sheet to SAS (a software company in the USA), version 9.2 for analysis. Descriptive statistics was used to describe frequencies and percentages for categorical data. The continuous variables were compared using Independent sample t-test. Results reported were in terms of mean difference, standard error, 95% confidence interval, and p-value. Chi-square test and Fisher Exact test were run to show if there is any relationship between some demographic factors and the OP poisoning. A p-value <0.05 was considered to be statistically significant.

2.4 Ethical Clearance

The ethical consideration in the study was approved by experts in the King Abdullah International Medical Research Center, Riyadh, Saudi Arabia.

3. RESULTS

The typical toxidrome in OP poisoning includes hyper-salivation, shortness of breath, lacrimation, diaphoresis, pinpoint pupils, seizures, urination, defecation, gastric cramps, and emesis symptoms. Although most symptoms occurred within minutes or hours, the delayed onset of symptoms caused after the minor indications following acute exposure may influence treatment and time to discharge.

3.1 General Analysis

An analysis of a total of 82 cases of OP poisoning admitted to KAMC emergency department during 12 years showed overall female to male ratio was 1.05. The mean age of cases was 20.10±2.29, majority of them were found to be children below 6 years of age (35.37%), followed by adults above 30 years old (26.83%). The accidental and intentional cases of OP poisoning were 62.2% and 30.49% respectively, whereas among 7.32% patients, it was not clear whether they were intentional or by mistake. Majority of the cases (79.27%) arrived to ER by their families or relatives by private conveyance. Others were brought either by ambulance (14.63%) or transferred (6.10%) from other facility (Table 1). Most of the cases ingested the substance orally (55.41%), absorption through skin came in second place (31.08%) and the least (13.51%) were by inhalation. Oral ingestion was dominant in adults (78.38%) with significant p-value (<.0001). While dermal absorption was the most common way in pediatric patients (54.05%) (Table 2).

Table 1. Demographic and baseline characters

Variables	N (%)
Age (Mean)	20.10±2.29
<6	29 (35.37)
6-12	12 (14.63)
13-30	19 (23.17)
>30	22 (26.83)
Gender	
Male	40 (48.78)
Female	42 (51.22)
Ingestion cause	
Intentional	25 (30.49)
Accidental	51 (62.19)
Admission source	
Ambulance	12 (14.63)
Private car	65 (79.27)
Transferred from other hospital	5 (6.10)

3.2 Intentional and Accidental Poisoning

The cases who tried to commit suicide were 30.49 per cent. All of them ingested OP orally. However, 62.2% of cases were accidental, Majority of them were expose through skin. Mean age in accidental exposure was 13.46 years. In the Intentional poisoning, there was an increase in the age to 31.2 years. Although female account 64% intentional group, that was not enough to yield a significant p-value. Eight cases of intentional group reported to have a history of psychiatric disease, including depression, while three cases had a prior attempt of suicide (Table 3).

3.3 Clinical Presentation and Interventions Recorded on Arrival

Thirty eight patients (46.34%) were hemodynamically unstable at the time of admission. Majority (58.54%) of these were adults (p-value, 0.026). Most of the patients were presented with nausea and recurrent vomiting (62.2%), without significant difference between adults and pediatric patients (p-value= 0.494). The incidence was followed by constricted pupils (53.66%) and increase of saliva (41.47%) among adults. Sixty one percent of adults were on mechanical ventilation, compared with twenty percent of pediatric patients, p-value was 0.0001. Both groups received Atropine and Oximes, however; more adults received Oximes than pediatric patients (80% vs. 56.1%), with statistically significant p-value (0.021). Most commonly observed complication was pneumonia (14.63%) in 12 cases, 11 of them were adults (p-value=0.0018), followed by 8 cases of seizure (9.76%), and 6 % cases each of brain injury and cardiopulmonary arrest. Other complications include: sepsis, renal injury, Parkinsonism, vocal cord paralysis and quadraparesis. Overall, majority of complications were noticed among adults. The rate of mortality was observed to be 2.44%, one of them was pediatric and other one adult (Table 4). Overall, there were no statistically significant differences in between accidental and intentional groups in clinical presentations, complications and outcomes. Seventy nine per cent of accidental group presented to the hospital with Glasgow coma scale 14-15. Whereas 33.3 per cent of those who take OP intentionally showed the Glasgow coma scale as between 3 and 8 with a significant p-value (Table 4).

3.4 Length of Treatment

Mean length of mechanical ventilation was 175.8±59.6 hours for both pediatric patients and adults. The average stay at ICU and hospital was 6.48 and 13.85 days respectively, adults tend to have a longer time at ICU and hospital compared with pediatric patients, which showed a statistically significant p-value (0.0009, 0.0001). The mean time between consuming OP and admitting to the hospital was 4.44±1.47 hours, although pediatric patients tend to be admitted to hospital faster than adults (2.87 vs. 6.51 hours). The difference was statistically insignificant (Table 5).

Table 2. Route of exposure

Variables	Overall N= 82	Pediatric patients<12 N= 41	Adults ≥ 12 N= 41	P-value
Ingestion route				
Oral	41(55.41%)	12(32.43%)	29(78.38%)	
Inhalation	10(13.51%)	5(13.51%)	5(13.51%)	**<.0001**
Dermal	23(31.08%)	20(54.05%)	3(8.11%)	

Table 3. Demographic and baseline characters between Intentional and Accidental cases

Variables	Overall* (N=82)	Accidental (N=51, 62.2%)	Intentional (N=25, 30.49%)	P-value
Age (Mean)	20.10±2.29	13.46±2.75	31.20±2.54	**<.0001**
Gender				
Male	40(48.78%)	26(50.98%)	9(36.0%)	0.218
Female	42(51.22%)	25(49.01%)	16(64.0%)	
History of suicidal attempt	3(3.66%)	0.0	3(12.0%)	**0.033**
Positive psychiatric history	9(10.98%)	0.0	8(32.0%)	**<0.0001**

4. DISCUSSION

Infants and toddlers constitute a high proportion of all admissions followed by adults above 30 years of age, which correlated with different studies worldwide [5,8,13-16]. Children at this age tend to be active and driven by curiosity, where they end up putting every substance or object into their mouth as sort of exploration. That increases the risk of children poisoning, especially when it associate with poor storage setting, or close to toddlers reach. The incidence of OP poisoning in pediatric patients was 35.37% and 14.63% in the age groups of <6 and 6-12 respectively. This is almost equivalent as compared to 23.17% and 26.83% in the age groups of 13-30 and >30 respectively. Literature reports suggest an increased number of morbidity and mortality due to pesticide exposure among pediatric patients. Nevertheless, the magnitude of the problem is masked by inadequate notification with the relevant health authorities. For example; In a recent study, O'Reilly and Heikens [17] reported the case of a 12-day-old infant girl who was admitted with increasing lethargy and respiratory distress. Initial treatment was for pneumonia but deterioration despite appropriate treatment prompted review of her diagnosis and consideration of OP poisoning as there was a brisk response to atropine. The reports of poisoning experienced by newborns, infants and toddlers are unlikely to be recorded accurately. Their experience of ingesting toxicant can be felt but cannot be diagnosed.

Table 4. Clinical presentation, at arrival

Variables	Overall N= 82	Pediatric patients<12 N= 41	Adults ≥ 12 N= 41	P-value
Shortness of breath	22(26.83%)	11(26.83%)	11(26.83%)	1.00
Hypersalivation	29(35.37%)	12(29.27%)	17(41.47%)	0.248
Abdominal pain	16(19.51%)	4(9.76%)	12(29.27%)	**0.028**
Nausea and vomiting	51(62.20%)	24(58.54%)	27(65.85%)	0.494
Lacrimation	13(15.85%)	4(9.76%)	9(21.95%)	0.126
Diaphoresis	10(12.20%)	2(4.88%)	8(19.51%)	**0.043**
Pinpoint Pupils	44(53.66%)	23(56.10%)	21(51.22%)	0.658
Wheeze	12(14.63%)	4(9.76%)	8(19.51%)	0.212
Diarrhea	9(10.98%)	2(4.88%)	7(17.07%)	0.154
Seizure	8(9.76%)	3(7.32%)	5(12.10%)	0.712
Hemodynamic stability				
Unstable	38(46.34%)	14(34.15%)	24(58.54%)	**0.026**
Interventions				
Intubation	33(40.24%)	8(19.51%)	25(60.98%)	**0.0001**
Medications				
Atropine	67(82.72%)	32(78.05%)	35(87.50%)	0.261
Oximes	55(67.90%)	23(56.10%)	32(80.0%)	**0.021**
Morbidity				
Seizure	8(9.76%)	3(7.32%)	5(12.20%)	0.712
Pneumonia	12(14.63%)	1(2.44%)	11(26.7083%)	**0.0018**
Cardiac arrest	5(6.10%)	1(2.44%)	4(9.76%)	0.359
Sepsis	3(3.66%)	0.0	3(7.32%)	0.241
Acute Renal Injury	3(3.66%)	0.0	3(7.32%)	0.241
Pulmonary Embolism	1(1.22%)	0.0	1(2.44%)	1.000
Brain Injury	5(6.10%)	2(4.88%)	3(7.32%)	1.000
Parkinsonism	1(1.22%)	0.0	1(2.44%)	1.000
Quadraparesis	1(1.22%)	0.0	1(2.44%)	1.000
Vocal cord paralysis	1(1.22%)	0.0	1(2.44%)	1.000
Mortality				
Death	2(2.44%)	1 (2.44%)	1 (2.44%)	0.002
Glasgow coma scale				
3-8	16(19.75%)	3(7.32%)	13(32.50%)	0.005
9-13	13(16.05%)	5(12.20%)	8(20.0%)	
14-15	52(64.20%)	33(80.49%)	19(47.50%)	
Missing	1	-	-	
pH (mean)	7.32±0.02	7.35±0.01	7.30±0.0	0.043

Table 5. Comparison of treatment length between pediatric and adult patients

Variables (Mean)	Overall N= 82	Pediatric patients<12 N= 41	Adults ≥ 12 N= 41	P-value
Length of mechanical ventilation (hours)	175.84±59.57	216.64±164.50	162.79±60.76	0.077
ICU stay (days)	6.48±1.58	4.26±2.51	7.97±2.01	**0.0009**
Hospitalization (days)	13.85±4.76	5.07±2.47	22.63±9.04	**0.0001**
Time between ingestion and admission (hours)	4.44±1.47	2.87±0.47	6.51±3.36	0.295

Overall, there was no variation between adults and pediatric patients, nor male and female. However things slightly change when the etiology is related to ingestion. While accidental poisoning tend to be at young age, suicidal poisoning is more likely to occur among adults, especially among those who have psychiatric illness or history of suicidal attempt. Although 64% of the suicidal attempts were committed by females, but this was statistically insignificant in our study. This finding is relatively small when it is compared to the study conducted at King Khalid Hospital in Riyadh where females account to about 72% of cases [6].

The typical toxidrome in OP poisoning includes hypersalivation, shortness of breath, lacrimation, diaphoresis, pinpoint pupils, seizures, urination, defecation, gastric cramps, and emesis symptoms. Exposure to insecticides also showed skin itching, headache, coughing, sweating, difficult breathing, fatigue, blurring of vision, dizziness and changes in mood, sleeplessness and vomiting, besides forgetfulness and memory disorders [11].

Although most symptoms occur with minutes or hours following acute exposure, delayed onset symptoms occurring after a period of minimal or mild symptoms, may influence treatment and timing of the discharge following acute exposure. Pharmacologically, the mode of action of OP is on an inhibition of cholinesterase, which results in complications such as cardiovascular, respiratory, renal failure, neurological manifestations, and coma necessitating mechanical ventilation and prolonged hospital stay, following morbidity and mortality [18].

Muscarinic symptoms were dominant in both children and adults. Similar to other studies [13,14,19-21], pinpoint pupils, emesis and increased salivation were prominent among other presentations. Compared with children, about 58% of adults were hemodynamically unstable at admission. That associate with notable decrease in Glasgow Coma Scale and mean pH was 7.30. This more likely a consequence of determinant factor corresponded with adults. Sixty percent of adult ingestion was suicidal attempts; all of them were ingestion via oral route. Organophosphate poisoning, heavy metal intoxication, organic solvent and semiconductor agent poisonings causes the most common neurotoxic diseases. Due to its high metabolic rate, the nervous system is known to be susceptible to toxic agents and organophosphates are no exception. The brain damage caused by OP- induced brain damage is reported to result from inhibition of AChE which causes cholinergic neuronal excitotoxicity and dysfunction. These changes are apt to delay the secondary neuronal damage in the cholinergic regions of the brain. This might be largely responsible for persistent neuropsychiatric and neurological impairments (memory, cognitive, mental, emotional, (r and sensory deficits) in the victims of OP poisoning [22].

Mortality due to OP agents is attributed to respiratory dysfunction, including central apnea. Cholinergic circuits are integral to many aspects of the central control of respiration; however it is unclear which mechanisms predominate during acute OP intoxication [23]. Organophosphates are insecticides associated with associated with different types of cardiac complications including cardiac arrest, arrhythmia and cardiac injury [24]. Concern about the effects of OPs on human health has been growing as they are increasingly used throughout the world for a variety of agricultural, industrial and domestic purposes. Although the neurotoxic effects of OP poisoning are well established, the impact of low-level exposure is still controversial. The meta-analysis of 14 studies on low-level occupational exposure to OP found a significant association between even the low-level exposure to OP and impaired neurobehavioral function is consistent [25].

Complication in this study correlate with other studies [13,19,20], despite that it was not common. Complication ranged between aspiration pneumonia, seizure, renal injury to

neurological deficits and cardiac arrest. About 29% of the total admissions developed complications, without clear relationship between age, poisoning cause or time elapsed until seeking medical advice. All patients received supportive care and appropriate intervention as the protocol used on anticholinergic poisoning. In contrast to many studies [20,26-29] conducted in different countries (Turkey, Pakistan, Singapore, Taiwan, and China) where the rate varied between 7.3 to 34.1 percent of all OP poisoning. Mortality rate in our study was 2.43%. This figure appears to be too meagre (82) in comparison to the global incidence of OP mortality, which is reported to be 250,000 deaths per year [23] Results of our studies on OP poisoning are comparable to the investigation by Al-Sarar [11] on health effects of pesticides in Riyadh Municipality workers. These authors found a significant decrease in AChE activity, while no significant differences were detected in haematological parameters, except WBC count, the liver and kidney functions also increased slightly in the exposed group.

5. CONCLUSION

The intensity of toxidrome in OP–related poisoning influence more serious medical conditions, including cardiovascular, respiratory, renal failure, neurological manifestations, and coma necessitating treatment including mechanical ventilation and prolonged hospital stay, morbidity and timing of discharge and mortality. Infants and toddlers constitute a high proportion of all admissions. This is almost equivalent as compared to adults. The incidence of OP poisoning observed during a period of twelve years is found very less as compared to the global incidence of OP poisoning. However, the reports of poisoning experienced by newborns, infants and toddlers are unlikely to be recorded accurately. Their experience of ingesting toxicant can be felt but cannot be diagnosed accurately. Moreover, the incidence of suicidal poisonings among females might not be brought to the hospitals and the knowledge of authorities to avoid, perhaps, disrespect to the families.

CONSENT

It is not applicable.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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