

Retrospective Observational Study of Organophosphate Poisoning in an Urban Malaysian Hospital

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Abstract

Objectives: The objective of this study is to determine treatment interventions that provided the best outcome for patients. Initial treatment interventions performed in the emergency department such as decontamination, antidote administration and intubation will be analysed. Subsequent management in the intensive care unit with complications related to invasive ventilation will be analysed. The risks of aspiration pneumonia for patients who underwent gastric lavage with or without administration of activated charcoal will also be analysed.

Methods: A retrospective observational study was conducted. Study population included all patients presenting to the emergency department of Hospital Tengku Ampuan Rahimah with history of having consumed an organophosphate from the 1st April 2013 to 31st March 2016. The inclusion criteria was all patients with history of ingesting an insecticide containing a suspected organophosphate. The exclusion criteria was patients confirmed not to have ingested an organophosphate from clinical inference and confirmation of actual poison.

Results: A total of 84 patients were sampled with 75 patients fulfilling criteria for study inclusion. A total of 22 cases developed complications during their hospital stay with 13 cases of nosocomial infection, 8 cases of aspiration pneumonia, 2 cases with in hospital cardiac arrest and 1 case of atropine toxicity.

Malathion and chlorpyrifos were the only two identified organophosphates with the remaining 38 having consumed an unidentified organophosphate. Using chi-square test, there appears to be a significant difference between chlorpyrifos and malathion in terms of need for intubation with a p value of 0.017.

Conclusion: Resuscitation of airway, breathing and circulation with close observation for early signs of proximal muscle weakness or paralysis countered with judicious atropine administration is sufficient to ensure good outcome for cases of malathion and chlorpyrifos poisoning which present early to the emergency department.

The risk of aspiration pneumonia is high in patients with organophosphate poisoning outweighing the benefits of performing a gastric lavage. Aspiration of stomach contents with a ryle's tube after endotracheal intubation is an acceptable method of gastrointestinal decontamination for patients who have consumed a large quantity of organophosphate.

Pralidoxime may be beneficial in reducing the period of respiratory paralysis or weakness for chlorpyrifos poisoning but shows no clear benefit for malathion poisoning. The prolonged muscle paralysis seen in malathion poisoning weighs heavily on intensive care resources. Banning the sale of malathion may help reduce morbidity from prolonged ventilation as well as reduce the burden on intensive care resources.

Keywords: Organophosphate; Chlorpyrifos; Malathion; Aspiration pneumonia; Gastric lavage; Intubation; Pralidoxime

Introduction

Insecticide poisoning is commonly seen in developing countries with an agricultural background. Previous studies have shown that organophosphates are the commonest responsible pesticide group causing hospital admissions in this region [1]. Among those admitted to hospital, suicide was the leading cause of acute pesticide poisoning [2]. In Malaysia, most published data are gathered based on occupational poisoning reports or based on individualized health institution reporting [3]. The paucity of data till recent years provides little knowledge on organophosphate poisoning in the Malaysian context.

Organophosphate toxicity gives rise to a spectrum of clinical manifestation by inhibiting the acetylcholinesterase (AchE) activity at the nerve endings. AchE is the enzyme responsible for hydrolysis and breakdown of acetylcholine, a neurotransmitter found mainly at the neuromuscular junctions of the central as well as peripheral nervous system [4]. When this enzyme is inhibited, it can no longer participate in the breakdown of acetylcholine, which leads to an acute cholinergic crisis. Acute cholinergic crisis develops within a few minutes to several hours after exposure, affecting peripheral muscarinic and nicotinic receptors, as well as the central nervous system [5]. The acute

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manifestation of organophosphate poisoning is summarised in Table 1. Following an acute crisis, patients might also develop a constellation of symptoms called intermediate syndrome which is characterised by weakness over the proximal limb muscles, neck flexors, respiratory muscles and motor cranial nerves [5]. It occurs within 24 h and can last up to 2-3 weeks following organophosphate exposure [6]. Patients may develop delayed symptoms called Organophosphate-Induced Delayed Neurotoxicity (OPIDN) 2-3 weeks after the acute exposure. It is characterised by numbness and weakness of the lower extremities followed by progressive ascending weakness of the muscles of the limbs [5]. Among these three presentations, intermediate syndrome has been considered to be the major contributing factor of organophosphate related morbidity and mortality as a consequence of respiratory failure [6]. Early intubation to support ventilation in patients with signs of respiratory failure is a lifesaving intervention in acute organophosphate poisoning [7].

	Area	Effects
Muscarinic	Bronchial tree	Tightness in chest, wheezing suggesting of bronchoconstriction, dyspnoea, increased bronchial secretions, cough, pulmonary oedema, cyanosis
	Gastrointestinal system	Nausea, vomiting, abdominal tightness and cramps, diarrhoea, tenesmus, faecal incontinence
	Sweat glands	Increased sweating
	Salivary glands	Increased salivation
	Lacrimal glands	Increased lacrimation
	Cardiovascular system	Bradycardia, hypotension
	Pupils	Miosis, occasionally unequal
	Ciliary body	Blurring of vision
	Bladder	Frequency, urinary incontinence
Nicotinic	Striated muscle	Muscle twitching, fasciculation, cramp, weakness (including muscles of ventilation)
	Sympathetic ganglia	Pallor, tachycardia, hypertension
CNS		Giddiness, tension, anxiety, restlessness, emotional lability, excessive dreaming, insomnia, nightmare, headache, tremor, apathy, withdrawal and depression, drowsiness, difficulty in concentrating, confusion, slurred speech, ataxia, generalized weakness, coma with absence of reflexes, Cheyne-Stokes respiration, convulsion, depression of respiratory and circulatory centres with dyspnoea, cyanosis, hypotension

Table 1: Acute cholinergic crisis manifestations classified in accordance to the type of acetylcholine activities at the nerve endings as well as central nervous system (CNS) [6].

Patient decontamination in organophosphate poisoning needs to be done simultaneously with resuscitation by removing all contaminated clothes, performing skin and eye irrigation [8]. The efficacy of gastrointestinal decontamination methods such as gastric lavage has now been questioned in acute organophosphate poisoning [9,10]. Atropine, an established antidote for organophosphate [11], is currently the mainstay therapy in acute organophosphate poisoning. Pralidoxime however, has been subject to some scrutiny. It is however still recommended by the World Health Organization (WHO) for the treatment of organophosphate poisoning [11]. In recent years, there has been increasing data on new adjuncts to the treatment of organophosphate poisoning such as magnesium sulphate [12], Nacetylcysteine [13], Iipid emulsion [14] as well as using nanomedicine technology in animal model [15].

Study Objectives

The objective of this study is to determine treatment interventions that provided the best outcome for patients. Initial treatment interventions performed in the emergency department such as decontamination, antidote administration and intubation will be analysed. Subsequent management in the intensive care unit with complications related to invasive ventilation will be analysed. The risks of aspiration pneumonia for patients who underwent gastric lavage with or without administration of activated charcoal will also be analysed.

Methodology and Study Design

A retrospective observational study was conducted. Study population included all patients presenting to the emergency department of Hospital Tengku Ampuan Rahimah with history of having consumed an organophosphate from the 1st April 2013 to 31st March 2016. The inclusion criteria was all patients with history of ingesting an insecticide containing a suspected organophosphate. The exclusion criteria was patients confirmed not to have ingested an organophosphate from clinical inference and confirmation of actual poison. Since this is an observational study, a universal sampling method was used.

The study was conducted in compliance with ethical principles outlined in the Declaration of Helsinki and Malaysian Good Clinical

Practice Guidelines. Critically ill patients and children of all ages will be included in the study. As this study is purely observational there is no risk to these subjects.

This is a retrospective observational study, informed consent is not applicable. Subjects names will be kept on a password-protected database and will be linked only with a study identification number for this research. The identification number instead of patient identifiers will be used on subject data sheets. All data will be entered into a computer that is password protected. On completion of study, data in the computer will be copied to CDs and the data in the computer erased. CDs and any hardcopy data will be stored in a locked office of the investigators and maintained for a minimum of three years after the completion of the study. The CDs and data will be destroyed after that period of storage. There is no conflict of interest to be declared by all investigators. No personal information will be disclosed and subjects will not be identified when the findings of the study are published. Termination of study is not applicable in this study.

Statistical analysis plan was done using SPSS version 20. Descriptive data will be expressed as mean \pm standard deviation (SD) and percentages unless otherwise stated. Categorical data will be analysed using chi-square test. Continous data will be analysed with the ANOVA test. A p value of less than 0.05 is considered statistically significant.

Results

A total of 84 patients were sampled with 75 patients fulfilling criteria for study inclusion. By gender, 42 were female (56%) and 33 were male (44%). The youngest patient was one year old, whereas the eldest patient was 63 years old. Majority of these patients were aged between 11-40 years old. The racial demographic showed 57 patients were of Indian origin (76.0%), followed by Malay 7 (9.3%), and Chinese 5 (6.7%). The remaining 6 (8%) were foreigners from India, Nepal and Bangladesh. By intent, 88% patients took the poison intentionally (Figure 1).



Estimation of the amount taken was difficult with 20 cases showing missing data. Twenty four patients claimed to have ingested more than 100 mls of poison. By time of ingestion to emergency department

presentation, 10 cases presented in less than an hour, 29 cases presented between 1-2 h post ingestion with the remaining 31 more than 2 h post ingestion. There were 5 cases with missing data. Time of poison ingestion to emergency department presentation ranged from 10 min to 1680 min with a median value of 120 min and a mean value of 218 min.

Majority of patients arrived at hospital with their own transport. Only 17 cases were brought in by ambulance. Commonest symptoms on presentation was vomiting followed by excessive secretions and diarrhoea. Patients presenting with vomiting numbered 50, 26 patients presented with excessive secretions and 24 with diarrhoea. No patients presented with seizures (Figure 2).

On initial clinical assessment, 18 patients had lung secretions while 24 patients were noted to have pin point pupils. One patient arrived at the emergency department dead on arrival. Only 4 patients presented with a mean arterial pressure (MAP) of less than 80. A total of 6 patients required inotropic support of which 4 were intubated. No patients presented with bradycardia which was taken as a heart rate of less than 60 per minute. Excluding the patient who was dead on arrival, 38 (51%) patients presented with a heart rate of more than 100 per minute while 36 (49%) patients presented with a heart rate of 60-100 per minute. A total of 7 patients presented with a Glasgow Coma Scale (GCS) of 3/15, 11 presented with a GCS of 9-14/15 while the remaining 57 patients had a full GCS on presentation to the emergency department.



A total of 14 cases had a gastric lavage with 10 of these cases eventually requiring intubation. Of these 10 cases, 6 developed aspiration pneumonia. From theses 6 cases, 4 were intubated on arrival as they were already comatose or stuporous suggesting that aspiration pneumonia may have already occured prior to arrival to the emergency department. Gastric lavage was performed after intubation in these patients. The remaining 2 cases were intubated 2 to 3 h after arrival to the emergency department with lavage done prior to intubation. Lung findings on arrival for one case was clear but the other patient already had lung crepitations on arrival. Charcoal decontamination was given to 28 patients, 9 of them required intubation with the same 6 who had gastric lavage developing aspiration pneumonia.

A total of 30 patients were intubated. Of these, 11 patients were intubated immediately upon arrival as they were already stuporuos or comatose with excessive lung secretions. Another 5 patients were

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intubated for excessive lung secretions from 2 to 96 h post arrival to the emergency department. Another 11 cases were intubated for respiratory paralysis 2 to 168 h post arrival to the emergency department. The remaining 3 were intubated as they were restless and agitated 11-18 h post arrival to the emergency department. Patients with pin point pupils showed a higher affinity for intubation compared to patients without pin point pupils. There was a significant difference using chi-square test with a p value of less than 0.001.

Out of 75 patients, 50 patients received atropine infusion, 5 received loading dose only, while another 20 patients did not receive any atropine. A total of 19 patients who were not intubated were on atropine infusion ranging from a minimum of 4 to 192 h. Only one patient was noted to have atropine toxicity. This patient was not intubated and was noted to have consumed chlorpyrifos. For intubated cases atropine infusion ranged from a minimum of 84 to 257 h. The patient with the longest duration of atropine infusion was only intubated at 168 h post arrival to the emergency department. This patient also received the longest duration of pralidoxime infusion at 90 h. The type of organophosphate consumed by the patient was not specified. This patient was on mechanical ventilation for 96 h followed by tracheostomy for a further 11 days.

Pralidoxime was started for all patients requiring atropine infusion. Most patients were only given pralidoxime for 24 to 48 h. There was no standardization between continued infusion or intermittent dosing. Pralidoxime was administered by infusion over 1 h even for intermediate dosing. No bolus administration was allowed. Out of 75 patients, 50 patients received pralidoxime, 6 patients received only a loading dose of pralidoxime, 41 patients had continous infusions after loading dose and 3 had intermittent dosing after loading dose. Patients were oftened changed to intermittent dosing in the intensive care unit or ward depending on the managing physicians preference. All patients who were intubated received at least 24 h of pralidoxime.

Out of 30 patients who were intubated, 12 were reported to have difficult extubation where 8 eventually required tracheostomy. The remaining 4 were reintubated and subsequently successfully extubated after 48-72 h. Of the 12 patients, 5 were confirmed to have taken malathion while the remaining 7 were categorised as having ingested an unspecified organophosphate. Patients were on tracheostomy for a period ranging from 11 to 20 days. Only 7 cases required atropine infusion post extubation of which one case required reintubation.

A total of 22 cases developed complications during their hospital stay with 13 cases of nosocomial infection, 8 cases of aspiration pneumonia, 2 cases with in hospital cardiac arrest and 1 case with atropine toxicity. As discussed earlier 6 cases of aspiration pneumonia had a gastric lavage performed. The remaining 2 cases were not lavaged. One patient arrived to the emergency department with a GCS of 3/15 suggesting the aspiration probably occured prior to arrival. The second case had an in hospital arrest which most likely caused the patient to aspirate.

Three patients developed cardiac arrest requiring cardiopulmonary resuscitation. Of the three, one patient presented to the emergency department dead on arrival. Return of spontaneous circulation was achieved after 25 min of cardiopulmonary resuscitation but the patient died on the second day of admission. The remaining two patients went into cardiac arrest while in the emergency department. Return of spontaneous circulation was achieved after 5 min of cardiopulmonary resuscitation. Both cases developed aspiration pnuemonia but subsequently recovered with full neurologic function. One patient was successfully extubated at day 5 and the second after 19 days with 14 days on tracheostomy.

All but one patient who survived was discharged home neurologically intact. This patient presented to the emergency department with a GCS of 3/15, was ventilated 24 days of which 11 days was on tracheostomy. The patient was noted to have confused speech.

The median length of stay was 5.5 days whereas the mean was 7.8 days. The longest duration of admission was 30 days. Out of 75 patients sampled, 25 (33.3%) were admitted to the emergency department observation ward, 19 (25.3%) were admitted to the medical ward and 26 (34.7%) were admitted to the intensive care unit.

There were 6 patients with co-ingestion, four of them required invasive ventilation. Ethanol was the only co-ingestion noted. Out of 75 patients, 13 patients ingested malathion, 24 patients ingested chlorpyrifos, while the remaining 38 patients ingested an unspecified type of organophosphate.

Of the 13 patients who ingested malathion, 7 patients required invasive ventilation. Atropine infusion was administered to 10 patients. Of the 24 patients who ingested chlorpyrifos, 3 patients were intubated. Atropine infusion was administered to 11 patients with 3 patients requiring bolus 1.0 mg dose only. Of the 38 patients who ingested an unspecified type of organophosphate, 20 were intubated. Atropine infusion was administered to 27 patients with 3 patients requiring bolus 1.0 mg dose only. Using chi-square test, there appears to be a significant difference between chlorpyrifos and malathion in terms of need for intubation with a p value of 0.017 (Figure 3).





There were 40 patients with plasma cholinesterase level of less than 500 U/L. Of these, 19 required intubation, 11 were given an atropine infusion with 3 cases given initial bolus 1.0 mg of atropine. Of the remaining 7 an observation period of 2-3 days was carried out where patients remained asymptomatic and were discharged home with no further complications or return visits to the emergency department. Of these 7 cases, 5 were noted to have consumed chlorpyrifos while the remaining 2 had ingested an unspecified type of organophosphate.

There were 16 patients with plasma cholinesterase level ranging from 500-4000 U/L. Of these, 8 required intubation and 6 required atropine infusion only. There were 18 patients with plasma cholinesterase level of more than 4000 U/L. Of these, 4 patients required intubation. One patient received atropine infusion which was stopped after a few hours and another was given only bolus of 1.0 mg atropine. Patients who were ventilated showed a decreasing plasma cholinesterase level with one case dropping to a value of 478 U/L.

Discussion

HTAR had the highest number of organophosphate poisoning cases in Malaysia in 2014 and 2015. The largest percentage of patients who consumed organophosphates were Malaysian Indians. There may be a social factor affecting suicide behaviour among Malaysian Indians. Further studies will be required to analyse this better. The Department of Statistics Malaysia shows population estimates in Malaysia for 2016 as 68.6% Malay, 23.4% Chinese, 7% Indian with the remaining 1% made up of other races.

Majority of poisonings were intentional with a few accidental poisonings involving work place incidents and pediatric patients. The insecticides used were mostly household insecticides which were produced locally.

In this study we focused on the insecticides containing an organophosphate compound. Organophosphate compounds exhibit different levels of toxicity. The World Health Organization's classification of pesticides classifies pesticides including organophosphates into 5 groups based on comparative rat oral LD50 data of the active ingredients. Different organophosphates have different lipid solubility, rate of activation, rate of aging and reactivation.

Organophosphates sold in the market are formulated, typically emulsified concentrates in which an active ingredient is mixed with an organic solvent or surfactant [16]. Aspiration pneumonia seen in patients may be due to the solvents and surfactants added. Aspiration pneumonia adds significant morbidity and in many cases prolonging the need for invasive ventilation beyond intermediate syndrome. Out of 8 cases which developed aspiration pneumonitis 6 had a gastric lavage. While only 2 cases were identified to have possibly aspirated because of the lavage procedure, the risk for aspiration pneumonia outweighs the benefits of performing the lavage. Gastric lavage is not performed at this hospital anymore. Instead, aspiration of stomach contents via ryle's tube is carried out after intubation for cases requiring mechanical ventilation. Charcoal administration as routine has been discontinued. Skin decontamination as well as removal of soiled clothes immediately is still performed. There were no reports of nosocomial poisoning among any healthcare staff during the study period (Table 2).

	Chlorpyrifos (n=24)	Malathion (n=13)	Unspecified OP (n=38)	P value
Age	27.8 ± SD 13.1 (1-63)	27.5 ± SD 9.9 (15-51)	29.8 ± SD 14.2 (1.7-63)	0.800
BP (MAP)	95.4 ± SD 10.6 (81-120)	97.1 ± SD 13.8 (79-120)	98.5 ± SD 22.2 (0-144)	0.810
HR	101.7 ± SD 19.9 (72-152)	97.9 ± SD 21.6 (70-139)	100.5 ± SD 27.9 (0-160)	0.901

GCS	14.9 ± SD 0.3 (14-15)	12.9 ± SD 4.5 (3-15)	12.7 ± SD 4.1 (3-15)	0.052
Time of poison ingestion to presentation	230.2 ± SD 316.9 (15-1560)	141.4 ± SD 198.8 (10-720)	235.5 ± SD 331.6 (15-1680)	0.667
Cholinesterase level	1977.8 ± SD 3175.3 (100-9929)	2456.9 ± SD 2971.3 (315-10505)	2058.5 ± SD 2895.6 (110-9673)	0.898
Atropine infusion	11	10	27	0.184
Intubation	3	7	20	0.004
Duration of intubation (SD)	3.0 ± SD 1.0 (2-4)	9.0 ± SD 4.6 (1-14)	8.7 ± SD 8.2 (1-26)	0.426
Pralidoxime	7	10	29	0.043
Gastric Lavage	2	5	7	0.090
Activated charcoal	8	7	13	0.399
Nosocomial infection	1	4	8	0.086
Aspiration Pneumonia	0	3	5	0.074
Atropine tox	1	0	0	0.341
LOS(SD)	5.0 ± SD 4.1 (1-13)	10.2 ± SD 8.9 (1-30)	8.7 ± SD 8.2 (1-28)	0.080

Table 2: Demographics, clinical presentation and treatment data for all organophosphates.

In this study, patients were noted to have suffered significant organophosphate poisoning if they were intubated and required ventilatory support for at least 24 h. Patients suffering from significant organophosphate poisoning had good outcome provided they arrived at hospital before cardiovascular collapse as well as received appropriate care and monitoring in the emergency department. Two patients who developed cardiorespiratory arrest in hospital both had return of spontaneous circulation after 5 min of resuscitation and were subsequently discharged home neurologically intact. Reinforcing monitoring for early signs of respiratory failure as well as monitoring for proximal muscle weakness prevented further incidents in the emergency department.

Atropine was used judiciously for all patients. Atropine boluses and infusion at 5.0-10.0 mg per hour were given initially until drying of secretions was observed after which the rate of atropine infusion was reduced to 0.5-1.0 mg per hour. This proved sufficient to control oral and tracheal secretions which persisted beyond 24 h in most patients.

Miosis or pin point pupils was a common clinical muscarinic finding which suggested a significant organophosphate poisoning. Out of 24 patients who presented with pin point pupils 19 were subsequently intubated.

Patients who were intubated electively retained their conscious level once sedation was tapered off but remained in respiratory and muscle weakness from days to weeks. Decision for extubation was initially based on muscle power and resolution of proximal muscle weakness but this proved insufficient. A few patients required reintubation

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Aspiration

Pneumonia

Atropine tox

LOS(SD)

0

1

5.0 ± SD 4.1 (1-13)

within hours of extubation as they developed apnea or respiratory distress. It was noted by the managing physicians that these patients often had intentional tremors suggesting residual neurologic dysfunction. Nevertheless, some patients were successfully extubated in spite of having intentional tremors. For some patients tracheostomy had to be performed first with eventual weaning and removal of tracheostomy tube done over a period of 1-2 weeks.

The only laboratory testing available at the hospital for organophosphate poisoning was butyrylcholinesterase or plasma cholinesterase level. All patients with significant organophosphate poisoning requiring intubation demonstrated a rapid fall in plasma cholinesterase levels. Plasma cholinesterase levels were monitored for patients who were ventilated and corresponded well with clinical status. Plasma cholinesterase levels showed an increasing trend once patients muscle power and strength improved but was still not a reliable indicator for extubation.

There were 7 patients who consumed chlorpyrifos with a plasma cholinesterase level of less than 500 U/L on initial presentation but did not develop significant toxicity other than vomiting in the first 3-4 h after poison ingestion. This group of patients were observed for 2-3 days without atropine or pralidoxime. These patients did not develop further signs or symptoms of organophosphate poisoning. All patients who had consumed malathion with plasma cholinesterase levels of less than 500 U/L on initial presentation developed significant organophosphate poisoning requiring invasive ventilation.

Case fatality from organophosphate poisoning varies according to the type of insecticide commonly used in the region. Depending on the type of organophosphate, amount ingested and access to emergency services some patients may develop cardiac arrest before reaching the nearest health care facility [17]. During the study period, only one patient arrived to hospital in cardiac arrest. Despite return of spontaneous circulation after 25 min resuscitation he eventually died from multiorgan failure.

As chlorpyrifos and malathion are the only two organophosphates identified in this study we are able to provide a comparison of these two organophosphates (Table 3). Only 37 patients were confirmed to have consumed one of the two poisons. The remaining 38 cases were suspected to have consumed a type of organophosphate which was not identified.

Malathion is categorised as class III which is slightly hazardous with a LD50 of c2100 mg/kg. Chlorpyrifos is classified as Class II moderately hazardous with a LD50 of 135 mg/kg [18]. Malathion and chlorpyrifos are both classified as Group 4 multiple constituents organophosphates. Malathion has a dimethoxy leaving group while chlorpyrifos has a diethoxy leaving group. Chlorpyrifos has more relative lipophilicity than malathion with a larger volume of distribution suggesting that it is more toxic. Malathion inhibits butyrylcholinesterase (BuChE) more than acetylcholinesterase (ACheE) compared to chlorpyrifos which has equal inhibition for both BuChE and ACheE [17,18]. ACheE inhibition is considered to be a better marker of toxicity whereas BuChE inhibition is a more sensitive marker of exposure because it is inhibited more effectively than ACheE by most organophosphates including chlorpyrifos and malathion [19]. Plasma BuCheE activity which constitutes 99% of human plasma Besterase activity [20] can be inhibited at exposures below those required to inhibit red blood cell AChE but no adverse biological effects are causally associated with the inhibition of plasma BuChE

	Chlorpyrifos (n=24)	Malathion (n=13)	P value
Age	27.8 ± SD 13.1 (1-63)	27.5 ± SD 9.9 (15-51)	0.922
BP (MAP)	95.4 ± SD 10.6 (81-120)	97.1 ± SD 13.8 (79-120)	0.684
HR	101.7 ± SD 19.9 (72-152)	97.9 ± SD 21.6 (70-139)	0.588
GCS	14.9 ± SD 0.3 (14-15)	12.9 ± SD 4.5 (3-15)	0.035
Cholinesterase level	1977.8 ± SD 3175.3 (100-9929)	2456.9 ± SD 2971.3 (315-10505)	0.668
Atropine infusion	11	10	0.159
Intubation	3	7	0.017
Duration of intubation (SD)	3.0 ± SD 1.0 (2-4)	9.0 ± SD 4.6 (1-14)	0.061
Gastric Lavage	2	5	0.073
Activated charcoal	8	7	0.300
Nosocomial infection	1	4	0.042

[21]. Malathion needs to be converted to malaoxon to become an active anticholinesterase agent [22].

 Table 3: Demographic, clinical and treatment data comparing chlorpyrifos and malathion.

3

0

10.2 ± SD 8.9 (1-30)

Out of 13 patients who ingested malathion, 7 required intubation with a period of ventilation ranging from 1 to 14 days. For chlorpyrifos, out of a 24 patients only 3 required intubation with a period of ventilation ranging from 2-4 days. Both groups of patients were given pralidoxime for at least 24 h as either continuous infusion or intermittent dosing.

Intermediate syndrome developed in both chlorpyrifos and malathion poisoned patients. Not all patients were affected perhaps due to a lower exposure to the toxin. We report 2 cases which developed intermediate syndrome less than 24 h after acute poisoning where there appeared to be complete resolution of muscarinic symptoms. Intermediate syndrome was first defined as occuring 24 to 96 h after acute organophosphate poisoning and following resolution of the cholinergic crisis [23]. A later study by Eddleston noted that it can occur before 24 h and after 96 h [24]. Pralidoxime was started for all patients who required repeat dosing of atropine or atropine infusion concurrently. Pralidoxime was continued for at least 24 h after initiation for both chlorpyrifos and malathion poisoning. Chlorpyrifos is reported to respond well to oxime therapy [25]. However, pralidoxime has shown unsatisfactory therapeutic effects for malathion poisoning [26]. Pralidoxime given as an infusion either continously or intermittently did not cause any adverse effects for patients in this study.

0.037

1 000

0.023

when malathion was compared to chlorpyrifos for duration of mechanical ventilation with a p value of 0.061. In spite of this, the maximum duration of ventilation for malathion was 14 days compared to 4 days for chlorpyrifos. The number of cases were probably too small to provide a proper comparison. The larger group of unspecified organophosphate poisoning probably contained both malathion and chlorpyrifos specimens but the exact compound could not be confirmed.

There was a significant difference in need for mechanical ventilation

Looking at severity of poisoning in terms of respiratory failure or intermediate syndrome requiring ventilatory support malathion appears to be more toxic. The prolonged muscle paralysis seen in malathion poisoning weighs heavily on intensive care resources which is a heavy burden for developing countries. Banning malathion in Malaysia may help reduce mortality and morbidity from prolonged ventilation as well as reduce the burden on intensive care resources. Banning of the most toxic organophosphorus insecticides in Sri Lanka resulted in a 50% decrease in total suicides [27].

Limitations

Citation:

Confirmation of the type of organophosphate consumed was from the label of the bottle containing the poison. Unfortunately most patients arrived to hospital without the bottle of poison. In these situations, identification of the poison was from clinical inference and history. These cases were subsequently labeled as unspecified organophosphates. Serum concentration of the possible toxin was not measured. The amount of poison consumed was based purely on history.

Pralidoxime was administered either as continous infusion or intermittent dosing based on the managing clinicians preference. Pralidoxime was often discontinued after 24-48 h based on clinicians preference. There was however no difference in administration of pralidoxime for the different types of organophosphates. Pralidoxime administration may have prevented or shortened the effect of intermediate syndrome for patients who had consumed chlorpyrifos.

Conclusion

Resuscitation of airway, breathing and circulation with close observation for early signs of proximal muscle weakness or paralysis countered with judicious atropine administration is sufficient to ensure good outcome for cases of malathion and chlorpyrifos poisoning which present early to the emergency department.

The risk of aspiration pneumonia is high in patients with organophosphate poisoning outweighing the benefits of performing a gastric lavage. Aspiration of stomach contents with a ryle's tube after endotracheal intubation is an acceptable method of gastrointestinal decontamination for patients who have consumed a large quantity of organophosphate.

Pralidoxime may be beneficial in reducing the period of respiratory paralysis or weakness for chlorpyrifos poisoning but shows no clear benefit for malathion poisoning. The prolonged muscle paralysis seen in malathion poisoning weighs heavily on intensive care resources. Banning the sale of malathion may help reduce morbidity from prolonged ventilation as well as reduce the burden on intensive care resources.

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