Original Article

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Anaesthesia Section

Contributing Factors for Morbidity and Mortality in Patients with Organophosphate Poisoning on Mechanical Ventilation: A Retrospective Study in a Teaching Hospital

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ABSTRACT

Introduction: One of the most common causes of poisoning in agricultural based developing countries like India is due to Organophosphorus (OP) compound. Its widespread use and easy availability has increased the likelihood of poisoning with these compounds.

Aim: To study the morbidity and mortality in patients with acute OP poisoning requiring mechanical ventilation.

Materials and Methods: This was a retrospective study constituting patients of all age groups admitted to the Intensive Care Unit (ICU) with diagnosis of OP poisoning between January 2015 to December 2015. Of 66 OP poisoning cases those patients who went against medical advice, 20 were excluded from the study and thus 46 patients were included. Diagnosis was performed from the history taken either from the patient or from the patient's relatives and presenting symptoms. Demographic data, month of the year, age of patient, mode of poisoning, cholinesterase levels, duration of mechanical ventilation and mortality were recorded. Data are presented as mean ± SD.

Results: A 97.83% (45/46) of cases were suicidal. Out of 46, 9 were intubated and mechanically ventilated. Duration of mechanical ventilation varied from less than 48 hours to more than 7 days. Mortality rate was 50%, 0% and 100% in those who required mechanical ventilation for more than 7 days, 2 to 7 days and <2days respectively. None of the predictors like age, severity of poisoning, cholinesterase levels and duration of ventilation were independent predictors of death and all of them contributed to the mortality. Overall mortality rate in those who required mechanical ventilation was 22.22%

Conclusion: Morbidity and mortality due to OP poisoning is directly proportional to the age, severity of poisoning and duration of mechanical ventilation and inversely proportional to serum cholinesterase level.

Keywords: Atropine, Intensive care unit management, Organophosphorus poisoning, Pralidoxime

INTRODUCTION

Organophosphate Compounds (OPCs) are one of the most common insecticides associated with systemic illness [1,2]. In India, OPCs are the most common insecticides used. Due to their easy availability and low cost, there is abuse of these compounds with suicidal intent [3,4].

Acetylcholine is a neurotransmitter present at the neuromuscular junctions in peripheral and central nervous systems. Acetylcholinesterase (AChE) is an enzyme that normally hydrolyzes and breaks down acetylcholine. OP compounds cause phosphorylation and inactivation of this enzyme leading to the accumulation of acetylcholine [5]. The inhibition of AChE causes accumulation of acetylcholine at synapses with resultant overstimulation of neurotransmission in both central and peripheral nervous system [6].

One of the lethal complications following OP poisoning is the respiratory failure. This may occur due to many reasons, including aspiration of gastrointestinal contents, excessive secretions, neuromuscular involvement, intermediate syndrome, septicaemia, and adult respiratory distress syndrome. Early recognition of respiratory failure, early endotracheal intubation and mechanical ventilation are life-saving in severe OP poisoning [7]. These patients need intensive care management for respiratory and close hemodynamic monitoring due to above-mentioned reasons.

Early diagnosis followed by rapid decontamination and definitive therapy is the key to survival. Management of severe poisoning is difficult, requiring intensive care and use of atropine and oxime cholinesterase reactivators [8].

AIM

To predict morbidity, mortality and survival pattern in patients of OP poisoning, needing mechanical ventilation.

MATERIALS AND METHODS

The study constituted patients of all age groups admitted to the ICU with diagnosis of OP poisoning between January 2015 to December 2015. This retrospective study was done after taking the ethical clearance from the hospital. Confidentiality of the patients was maintained by not mentioning any details of patient's identity.

The diagnosis was made on the basis of history of exposure or contact, characteristic clinical picture and serum cholinesterase levels. Among the intubated patients, 88.89% of patients had serum cholinesterase of <5000 and 66.67% had serum cholinesterase levels of <1000 with mortality rate of 33% [Table/Fig-1].

Treatment was started as per our hospital protocol for managing OP poisoning patients. Clothes were removed and the body was washed thoroughly using soap water. Nasogastric tube was passed and gastric lavage was done. Initial management of all patients with Pralidoxime (PAM) and atropine was done as per the recommended dosage schedule. A loading dose of 3-9mg of atropine was administered depending upon the severity. Once atropinised maintenance dose of 3mg was given every hourly. The target end point of atropinisation was:

(1) Chest clear on auscultation with no wheeze

(2) Heart rate >80/min

(3) Dilated pupils

(4) Systolic blood pressure >80mmHg [9].

PAM was administered with a bolus dose of 2g over a period of 4 hours followed by 1g IV TID.

To the patients with Glasgow Coma Scale (GCS) < 8, hypoxia was intubated and mechanically ventilated. Total number of 12 out of 66 patients were intubated and mechanically ventilated.

Patients requiring ventilatory support were initially put on Synchronised Intermittent Mandatory Ventilation (SIMV) then weaned off to pressure support ventilation (CPAP) based on the improvement in GCS levels and Muscle power. Patients were extubated using Spontaneous Breathing Trial (SBT) as the extubation criteria.

For the present study the parameters recorded were: age, sex, demographic data, month of the year, mode of poisoning, reason for ingestion/poisoning, serum cholinesterase levels and duration of mechanical ventilation and mortality.

RESULTS

During the study period, 66 patients reported with history of acute OP poisoning. Twenty patients went against medical advice, hence, were excluded from the study group.

Out of 46 patients, 31 (67.39%) were males of whom 3 (9.68%) patients died and 15 (34.78%) were females of whom none died [Table/Fig-2]. A 43/46 of patients were aged less than 50 years out of which 2 died. A 3/46 of the patients were aged ≥50 years, out of which 1 died. A 9/46 was intubated and mechanically ventilated of which 2 died [Table/Fig-3]. The mean (SD) age of all the patients was 30.19 ± 10.86 years and of males 32.03±11.55 and that of females was 26.04±8.41. The mode of poisoning was suicidal in 45 patients of whom 3 patients died and 1 accidental of whom none died [Table/Fig-2]. A total of 9 patients required intubation [Table/Fig-3].

The mean±SD duration of ventilation in all patients who required endotracheal intubation and mechanical ventilation was 4±2.24 days and of males 4.43±2.37 and that of females 2.5±0.71. Majority (6/9) of the patients required mechanical ventilation for a period of 2 to 7 days. A 2/9 required ventilation for more than 7 days. Mortality was 50% (1/2) in patients who required mechanical ventilation for more than 7 days, 0% (0/6) in those who received mechanical ventilation for 2 to 7 days and 100% (1/1) in those who received mechanical ventilation for <2days [Table/Fig-4] [10].

Ser. Cholinesterase (Units /Ltr)	No. of patients intubated	Survived	Died
>5000	1	1	
3000-5000	None		
1000-3000	2	2	
<1000	6	4	2

[Table/Fig-1]: Serum cholinesterase levels in mechanical ventilated patients.

	Total patients	Gender		Age		Mode of poisoning	
		Male	Female	<50	>50	Inhalation	Suicidal
Survived	43(93.48%)	28	15	41	2	1	42
Died	3(6.52%)	3	0	2	1	0	3
Total	46	31	15	43	3	1	45

[Table/Fig-2]: Demographic data.

	Total intubated patients	Gender		Age	
		Male	Female	<50	>50
Survived	7(77.77%)	5	2	7	0
Died	2(22.23%)	2	0	1	1
Total	9	7	2	8	1

[Table/Fig-3]: Intubation data.

DISCUSSION

This retrospective study showed that OP poisoning was predominantly suicidal, affected males, aged less than 50 years.

Total patients	Severity			Duration of mechanical ventilation		
	Mild	Moderate	Severe	<2 days	2-7 days	>7 days
Survived	12(26.09)	22(47.83)	9(19.57)		6(66.67)	1(11.11)
Died	0	1(2.17)	2(4.35)	1(11.11)		1(11.11)
Total	12	23	11	1	6	2

[Table/Fig-4]: Severity of poisoning and duration of mechanical ventilation using modified Dreisbach's classification [10].

Most of the patients who were intubated, required mechanical ventilation for 2-7 days and mortality rates were high in those who required mechanical ventilation for less than 2 days and more than 7 days.

OP compounds are used worldwide in agriculture as well as in household gardens [11,12]. This easy availability of the compounds has resulted in a gradual increase in accidental and suicidal poisoning, mainly in developing countries. OP poisoning due to self-poisoning or suicidal poisoning accounts for at least 40-60% of all cases in some African countries [12].

Organophosphate and carbamate compounds inhibit the enzyme. AChE is found primarily in erythrocyte membranes, nervous tissue and skeletal muscle. Plasma cholinesterase (pseudocholinesterase or butyrylcholinesterase) is found in the serum, liver, pancreas, heart and brain. Inhibition of cholinesterase leads to acetylcholine accumulation at nerve synapses and neuromuscular junctions, resulting in overstimulation of acetylcholine receptors. This initial overstimulation is followed by paralysis of cholinergic synaptic transmission in the central nervous system, in autonomic ganglia, at parasympathetic and some sympathetic nerve endings (e.g., sweat glands) and in somatic nerves. Organophosphate compounds bind irreversibly to AChE, thus inactivating the enzyme through the process of phosphorylation. Aging is a term describing the permanent, irreversible binding of the OP compound to the cholinesterase. The time to aging is highly variable with different agents and can range from minutes to a day or more. Once aging occurs, the enzymatic activity of cholinesterase is permanently destroyed and new enzyme must be resynthesized over a period of weeks before clinical symptoms resolve and normal enzymatic function returns. Antidote agents must be given before aging becomes effective [13,14].

Diagnosis of OP poisoning depends mainly on history, characteristic clinical presentation of muscarinic effects like salivation, lacrimation, urination, vomiting, increased sweating, bronchorrhea, cough, bradycardia and hypotension and CNS effects like restlessness, confusion, tremors [15-17] and is supplemented by decreased levels of serum cholinesterase levels [15,18,19].

Intermediate Syndrome (IMS) develops 24-96 hours after exposure and reflects a prolonged action of acetylcholine on the nicotine receptors. The clinical features are muscular weakness in the ocular, neck, bulbar, proximal limb and respiratory muscles. The risk of mortality is due to the associated respiratory depression. Most patients with intermediate syndrome develop respiratory failure, which requires mechanical ventilation [20]. Reported frequency of intermediate syndrome varies from 8% to 49% [20,21].

Organophosphate-induced delayed neuropathy occurs 1 to 3 weeks after acute poisoning. This mixed sensorimotor syndrome is due to the inhibition of neuropathy target esterase which may begin with leg cramps and may progress to weakness and paralysis. Treatment of OP poisoning should be started immediately and must not await the results for serum cholinesterase levels. Treatment of OP poisoning includes decontamination and reversal of effects of compound by administering atropine and oximes. Atropine acts competitively at the peripheral and central muscarinic receptors and antagonises the parasympathetic effects of excess AChE at these sites and is administered in doses of 2mg every 5 to 10 minutes. Delay or inadequate atropine can result in death from central respiratory depression, bronchospasm, excessive bronchosecretion, severe bradycardia, and hypotension [22].

PAM, compound which regenerates and reactivates AChE from the OP cholinesterase complex, is used as an antidote to treat OP poisoning. Although it works at nicotinic, muscarinic, and central nervous system receptors, its main therapeutic effect is predicted to be the recovery of neuromuscular transmission at nicotinic synapses. It should be administered as soon as possible to prevent ageing [23]. Stomach decompression was carried out in all patients with nasogastric tubes.

The estimated mortality from OP ingestion ranges from 10% to 20% [24]. According to Kumar et al., the effective number of cases is approximately up to 76,000 annually [23]. In our study, the incidence of suicidal poisoning was 97.83%, probably because it is cheap, easily available over the counter and used as a major pesticide in agricultural farming throughout India. In the study by Aziza et al., 76.92% cases were suicidal and 23.07% were accidental [25]. The present study, the incidence of poisoning was higher in males than in female. Similarly, in a study by Srinivas et al., the males outnumbered females (57% vs. 43%) with all types of pesticides including OP compounds [26]. Also, in a study by Aziza et al., and Safdar et al., incidence was higher in males than in females [25,27]. In our study, the incidence was highest in male patients aged less than 50 years.

The overall mortality following OP poisoning varies between 4% to 30% [28]. In a study by Safdar et al., 4% of patients who received mechanical ventilator support ultimately died [27]. Aziza et al., reported 8% mortality in patients who received mechanical ventilation [25]. In the present retrospective analysis, the overall mortality was 6.52% and mortality in those who required intubation and mechanical ventilation was 22.22%. All the patients who were on ventilator for less than 2 days died. The mortality was also high in patients requiring mechanical ventilation for more than 7 days (50%). The duration of mechanical ventilation in our patients was 4.00 ± 2.24 days.

There was no statistically significant association with death and age, lag time, severity of poisoning and duration of ventilation independently. This signifies that death due to OP poisoning is not dependent on a single predictor as age, severity of poisoning, serum cholinesterase levels and duration of mechanical ventilation etc., Death in OP poisoning is rather due to overlapping of all these factors [29]. In this study rate of mechanical ventilation was inversely proportional to serum cholinesterase levels (lesser the cholinesterase levels, higher the rate of mechanical ventilation and mortality) and moratlity in OP poisoning was directly proportional to age, duration of mechanical ventilation and severity of OP poisoning.

LIMITATION

Sample size was small. The levels of serum cholinesterase which was considered in this study was done only at the time of admission.

CONCLUSION

Due to their low cost, rapid action and easy availability OP compounds are most commonly used for suicidal purposes. Since respiratory failure is the major reason for mortality, careful monitoring, appropriate management and early recognition of this complication may decrease the mortality rate. Mortality is directly proportional to the age, severity of poisoning, delay in starting PAM, duration of mechanical ventilation and inversely proportional to serum cholinesterase level. No single factor is independently responsible for mortality in these patients.

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