

Study of Clinical Profile of Organophosphorous Compound Poisoning**Dr. Shilpa Anand Hakki***

Associate Professor, Medicine Department, SDMCMS & H Sattur, Dharwad Karnataka, India

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Abstract: Organophosphorus (OP) poisoning leads to high morbidity and mortality. The objective was to study the clinical profile of patients with Organophosphorous Compound Poisoning admitted in community health centre Haliyal. Aim was also to study the prevalence and outcome of patients with Organophosphorus compound poisoning. A prospective study was undertaken in Community Health Centre Haliyal from DEC 2015 to March 2017. All patients with suspicion and definite history of OP poisoning were admitted. Their history and clinical features were recorded. Patients were categorized according to age/sex, the amount of op compound consumed, severity of presentation, duration of exposure, stage of poisoning, intention of poisoning etc. Standard treatment protocol was followed. Intermittent conventional treatment was implemented. Results were recorded and analyzed. The inclusion criteria of the study was definitive history about ingestion of organophosphorus poison from patient self and relatives (when patient not in condition to give history) All patients with clinical signs of op poisoning like Excessive salivation, bradycardia, meiosis, wheezing etc were included in the study. During this one year study period total 51 patients were studied with the diagnosis of OP poisoning. Patients were divided and studied according to different criteria's. Maximum patients were in age group of 14 to 25 yrs. There was almost equal prevalence among males and females. Most common cause of poisoning was suicidal. The most common route of poisoning was oral. According to severity, 21 (41.17%) were of moderate severity while 20 patients (39.21%) were of severe grade with low GCS and 10 (19.60%) patients were of mild severity. Out of 51 patients 20 patients were referred to higher center in view of need of ventilator support. Financial constraint was most important cause in all suicidal attempt cases. Out of 51 patients 8 patients had history of alcohol consumption along with opp. One death occurred in our center. Easy availability of op compounds is main cause of consumption, Also as it occurs more commonly in villages in farmers as they are most commonly available to farmers as pesticides. Though first line of management in form of gastric lavage and atropine is given yet critical patients with respiratory failure who need ventilator support are at risk of losing life due to loss of valuable time in transportation to the higher centre with need of ventilators. In our study non availability of ventilators and ICU set up compelled us to refer high risk patients to higher centre.

Keywords: poisoning, insecticide, organophosphate (OP), carbamates, acetylcholinesterase, oxime, pralidoxime.

INTRODUCTION

Organophosphate compounds are associated with important public health problem. Organophosphate compounds have developed into one of the largest and most versatile group of pesticides in use today. Parathion is the pesticide most frequently used. Not only Suicidal attempts due to easy availability is the problem but, with increasing use of pesticides in agriculture, the agricultural worker as well as those involved in manufacturing are at increasing risk of poisoning.

In India organophosphates as pesticides were introduced in 1960's and toxicity was first reported in 1962. Organophosphate compounds have undoubtedly

contributed to increased yield of agricultural products because of its pesticidal use. But, unfortunately they are also an important cause of suicidal or accidental poisoning. Organophosphate compounds that are widely used in farming in the form of plant protecting preparations, are strong poisons and a source of poisoning. In India, OP poisoning has been steadily increasing since 1963. Most commonest route is oral. Ingestional poisoning is usually suicidal owing to easy availability and accessibility of organophosphorus compound. Poisoning due to exposure is accidental, and occurs in agricultural and industrial workers due to neglect of using protective measures while

spraying. While spraying inhalation is the mode of accidental poisoning.

MATERIALS AND METHODS

Main aim was to study clinical profile of patients with op poisoning.(4) This prospective study was undertaken in Community Health Centre Haliyal ,from December 2015 to March 2017, where total 51 patients were examined . All patients of OPP were included who had definite history of op poisoning. Detailed clinical history and complete physical examination was done. After simultaneously completing the medico-legal formalities, patients were given emergency needful management after thorough gastric lavage.

Patients were categorized according to severity and other parameters like the amount consumed, age/sex, severity of presentation in form of varying GCS, duration of exposure, stage of poisoning, intention of poisoning.(1) GCS level is an important factor in assessing Organophosphate poisoning outcome. All 51 consecutive patients of OPC poisoning admitted during this period were included in this study. All patients were registered medicolegally.

A Protocol of treatment of OP poisoning:

- Immediate gastric lavage
Gastric sample for analysis sent to the forensic laboratory
- Activated charcoal through Ryle's tube q 4hours
- Thorough washing of the skin with soap and water twice
repeated sponging and change of clothing and sheets every 4 hours.
- Inj. Pralidoxime 1 gm stat F/B 500mg Bd
- Inj. Atropine 2 to 4 mg intravenous stat followed by 0.5 to 2 mg every 10-15 min till full atropinisation is achieved [8].
- Withholding NG feeding for at least 96 hours

Following five important parameters were monitored every 15 minutes and gradually increased to 1/2/3 hourly.

- Chest auscultation for wheeze
- Heart rate
- Pupil
- Skin
- Blood pressure

TREATMENT

Atropine forms the main stay of treatment of organophosphate and carbamate poisoning. Atropine is given 2 to 4 mg intravenous stat followed by 0.5 to 2 mg every 10-15 min till full atropinisation is achieved [8]. In our study we treated patients with this conventional intermittent therapy.

Clinical features of atropinisation are; drying of bronchial and mucus membrane secretions, dilated pupils, tachycardia (to maintain pulse rate between 110-120/min) and raised skin temperature. Atropine is a muscarinic receptor antagonist and is ineffective for nicotinic effects of organophosphates. Atropine has little effect on CNS toxicity of organophosphates. The duration of atropine administration is variable, but on an average it is required for 4 to 7 days. 500- 1000 ml of Normal saline (10-20 ml/kg) over 10-20 min should be given to compensate fluid loss due to sweating, diarrhoea and cholinergic hyper-secretion[9].

Atropine can also be used as continuous infusion. The continuous infusion of high doses of atropine also significantly reduces the mortality in organophosphate poisoning as against the conventional intermittent administration of atropine[3].

Pralidoxime Oximes (such as pralidoxime, obidoxime, and HI-6) reactivate AChE inhibited by OP poisoning. Reactivation is limited by ageing of the ACh E and high concentrations of pesticides. The chemical name of pralidoxime is 2-formyl-1-methylpyridinium. Pralidoxime Chloride (2-PAM) is the most commonly used pralidoxime. Others are pralidoxime iodide and pralidoximemethylsulfonate. The principle action is to reactivate cholinesterase (mainly outside the central nervous system). Pralidoxime also slows the process of "ageing" of phosphorylated enzyme. Pralidoxime is most effective if administered immediately after poisoning [12]. In our study patients received 1gm loading dose of PAM followed by 500 mg twice a day for 3 days.

Observations

The important above five parameters were monitored every 15 minutes initially which can be gradually increased to 1-2-3 hours depending on the state of atropinisation. Close observation and monitoring plays not only a vital role in the management but also can contribute to the learning process by gathering new symptoms and signs and can anticipate recurring cholinergic crisis which may occur with little notice. Close monitoring of patient is main important aspect of managing op poisoning cases.

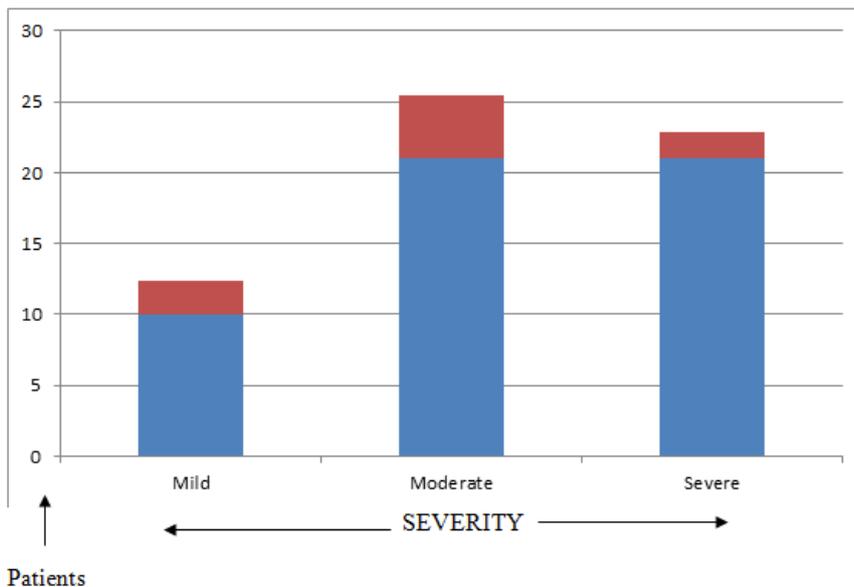
Atropine toxicity: - Signs such as Confusion, agitation, hyperthermia, tachycardia etc would suggest over atropinisation and necessitate reduction of atropine dose. Slowly tapering and discontinuation of the atropine treatment/ infusion, followed by frequent observation is important aspect in managing such cases. Duration of maintenance of tapering doses of atropine in conventional intermittent therapy depends on the severity and response to therapy. Usually it is maintained for 24- 48 hrs or longer in severe cases, and gradually withdrawn over 3-5 days. Frequent observation is required to detect early signs of intermediate syndrome.

RESULTS

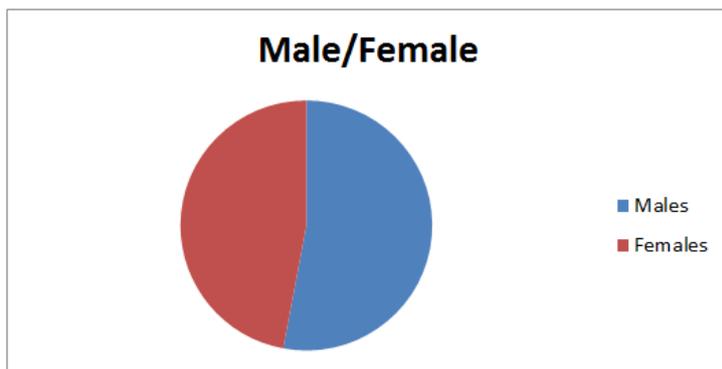
The most common cause of poisoning was suicidal in 49 cases out of 51. Financial constraint was most important cause in all suicidal attempt cases. The precipitation factors in the suicide attempts were social stress with strained lifestyle and stressful relations [2]. One patient consumed accidentally while one got exposed while spraying opp in fields. The exact type of opp c poison consumed varied with each individual

patient. During the period of study 51 patients were studied with the diagnosis of OP poisoning. They were divided and studies according to following criteria's [7].

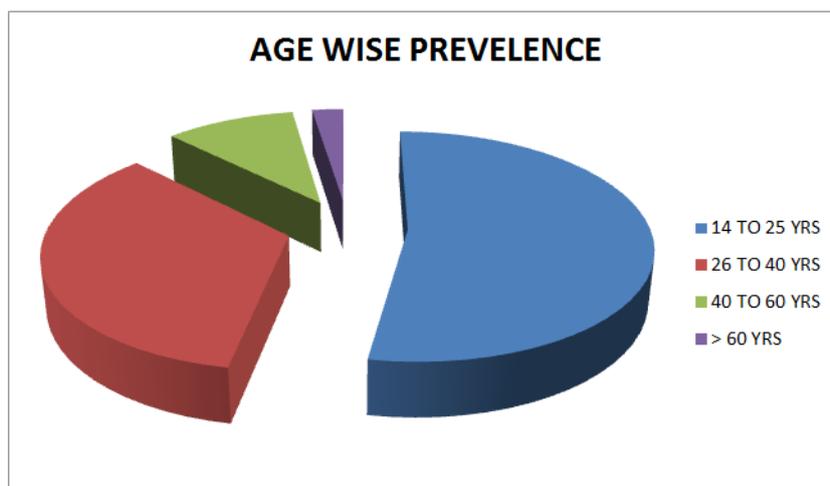
According to severity
 10 (19.60%) patients were of mild severity,
 21 (41.17%) were of moderate severity, and
 20 (39.21%) were of severe grade with low GCS.



- According to their age max patients were in age group between 14 to 25 yrs
- According to their sex there was almost equal ratio between males and females. Males were 27 (53%) and females were 24 (47%)



- **According to the route of poisoning**
 The most common route of OP exposure was ingestion 50 (98%), followed by inhalation and dermal absorption while spraying in 1 patient (2%).
- According to the clinical features as hyper salivation, meiosis, wheezing and depressed mental status were present in all 51 cases(100%)
 Lacrimation/sweating 51 (100%), bradycardia 20 (39.21%), hypotension 24 (47%), chest crepitations 51 (100%), vomiting 51 (100%), Respiratory failure 20 (39.21%), seizures in 0 (0%), Pulmonary edema in 20 (39.21%)
- 20 (39.21%) patients were intubated and referred to higher center with inotropic Support. Out of 51 patients 8 patients had history of alcohol consumption along with opp
- Financial constraint was most important cause in all suicidal attempt cases[4]

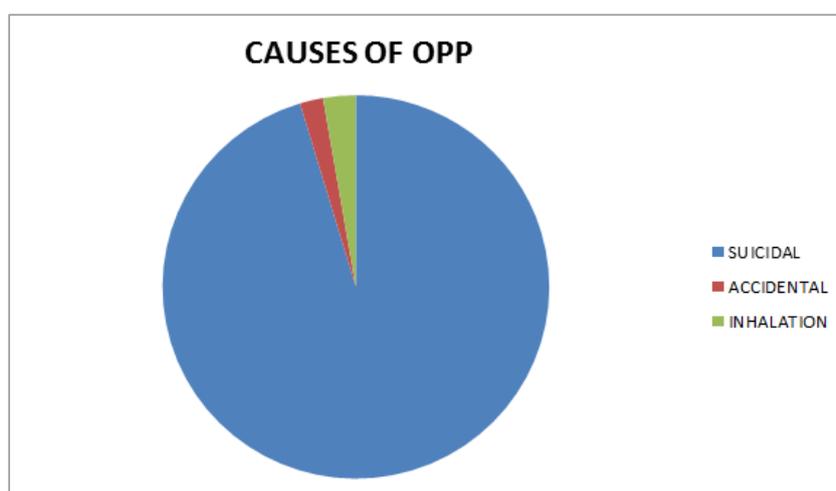


Final outcome in patients of OP poisoning

The final outcome or mortality in OP poisoning depends on the severity, type of the OP compound consumed, and amount of compound and duration of poisoning, low levels of serum ChE, development of respiratory failure and other complications. These can be considered the predictors of mortality in op poisoning cases [6].

Mortality and morbidity are directly proportionate to the lag time in initiation of treatment and/or amount of OP substances consumed, clinical severity (single/multiorgan failure) and duration of ventilatory support. Mortality is also higher in patients who immediately develop acute complications like

severe bradycardia and severe acute renal failure. Although each predictor that is age, lag time, severity of poisoning, amount of organophosphate consumed, organ failure, acute kidney injury and duration of ventilation is associated with mortality, death due to organophosphate poisoning results from overlapping contribution of these factors. No single factor is independently responsible for mortality in these patients. Therefore, the importance of rapid diagnosis, early and effective treatment should not be overlooked because patients who receive early and effective treatment generally do better and have less complications and decreased morbidity and mortality rate. Good supportive and ICU care cannot only reduce the frequency of acute or chronic complications, but will also decrease mortality rate in these cases.



Final outcome

- Out of 51 patients 18 patients were intubated for acute respiratory failure.
- patients were intubated in the emergency room due to a low GCS
- 1 patient had an acute respiratory arrest and succumbed to death.

- Above total 20 Intubated patients were transferred to higher center for further magement who needed ventilator support.

DISCUSSION

OPCs are irreversible inhibitors of the enzyme acetylcholinesterase (AChE), binding to the esteric site

of the enzyme. The mechanism of action is inhibition of both cholinesterase and pseudo-cholinesterase activity. The inhibition of acetylcholinesterase causes accumulation of acetylcholine at synapses. This results in overstimulation of neurotransmission. The clinical features are due to excess acetylcholine at the muscarinic and nicotinic receptors which leads to initial stimulation and eventual exhaustion of cholinergic synapses. The mechanism of action of paralysis is persistent depolarization of the neuro end-plate eventually leading to desensitization.

There are three distinct phases

- Acute cholinergic crisis
- Intermediate syndrome (IMS);
- Delayed polyneuropathy (OPIDN).

Acute Cholinergic Crisis

The symptoms are due to stimulation of the muscarinic and nicotinic receptors: Nicotinic manifestations include increased or decreased muscle power and skeletal muscle fasciculations. Muscarinic manifestations include excessive salivation, miosis, diarrhea, bronchorrhoea, bronchospasm, bradycardia, urination. Other signs include vomiting, respiratory distress, and abdominal pain, depressed level of consciousness, muscle fasciculations and muscle paralysis. Progression of paralysis may affect the muscles of respiration necessitating ventilatory support.

The cholinergic phase usually passes off within 48-72 hours but complete clinical recovery from all the effects may take up to a week. Treatment is supportive with oximes, atropine and mechanical ventilation, in addition to gastric lavage and decontamination.

Oximes (effective in the early phase) are clinically important reactivators of acetylcholinesterase that can prevent degenerative effects of insecticide intoxication.

Intermediate Syndrome (Ims)

After the acute cholinergic phase, a second stage of weakness occurs 1 - 4 days later with or without a symptom-free interval, and, if left unrecognized, can lead to fatal respiratory depression[5].

Delayed Organophosphate Induced Polyneuropathy

Organophosphate induced delayed neuropathy (OPIDN) is an uncommon clinical condition. It occurs in association with the ingestion of large amounts of organophosphate and manifests as limb weakness persisting long after the acute cholinergic symptoms have subsided. The clinical picture is characterized by a distal paresis in lower limbs.

CLASSIFICATION

Pesticides are chemicals or mixtures of chemicals, which are used for destroying, repelling,

mitigating or reducing pests. Modern pesticides are in general, organic chemicals i.e. compounds which contain carbon. The organic pesticides are further subdivided into organophosphates, carbamates, organochlorines, organomercurials, thiocarbamates, ureasetc[10].

MECHANISM OF ACTION

Organophosphates by irreversibly inhibiting carboxylic esterase enzyme, true cholinesterase and pseudo-cholinesterase, result in accumulation of acetylcholine at muscarinic, nicotinic, and central nervous system synapses. True cholinesterase is chemically acetylcholinesterase (AChE) and is present in the grey matter of central nervous system, sympathetic ganglion, myoneural junctions and erythrocytes. Pseudocholinesterase is chemically butyrylcholinesterase and is present in white matter of central nervous system, plasma, pancreas, liver and intestinal mucosa. The inactivation of acetylcholine occurs by binding at two different sites on cholinesterase enzyme. Anionic site of cholinesterase enzyme binds with quaternary nitrogen atom of acetylcholine and esteratic site binds with the carboxyl group of acetylcholine. This results in formation of acetylcholine-cholinesterase complex. There is release of choline and cholinesterase is acetylated, the latter is regenerated.

The turning over time of acetylcholinesterase is very short. After OP poisoning the phosphate radical of organophosphate compound binds firmly to the active (esteratic) site of the acetylcholinesterase, resulting in the formation of inactive phosphorylated enzyme. In the absence of acetylcholinesterase, there is continuous and prolonged excess of acetylcholine in the autonomic, neuromuscular and central nervous system synapses, hence the various clinical manifestations.

Hydrolysis of this inactive phosphorylated enzyme is a slow process, which may take days to weeks before new cholinesterase is synthesised, if not treated. Rapid reactivation is possible with help of pharmacological agents like oximes. The exact mechanism how organophosphate affect central nervous system is unclear. There is another esterase in the brain and spinal cord called neurotoxic esterase (NTE). Organophosphates cause phosphorylation of the NTE. Depressed levels of this enzyme are believed to lead to delayed neurotoxicity. A high level of inhibition (70%-80%) of NTE is possibly necessary for the neurotoxicity. Next step is "aging" of the phosphorylated enzyme complex. Compounds that do not "age" do not cause polyneuropathy. The amount and type of organophosphate consumed determine the development of the polyneuropathy [10].

CONCLUSION

Easy availability of op compounds is main cause of consumption, Also as it occurs more commonly in villages in farmers as they are most commonly available to farmers as pesticides. Though first line of

management in form of gastric lavage and atropine is given yet critical patients with respiratory failure who need ventilator support are at risk of losing life due to loss of valuable time in transportation to the higher centre with availability of ventilators. In our study non availability of ventilators in ICU set up compelled us to refer high risk patients and intubated patients to higher centre. In our study follow up could not be done in patients who were referred to higher center.

Though large dose of atropine are given in some units, 3-10 mg may be the loading dose, depending on severity. Once atropinized, a maintenance dose at 1-3 mg 1/2 hourly is usually sufficient. Also different studies have different outcomes. Continuous infusions of high dosage of atropine have good results in some studies [3]. Even titrated incremental atropine as loading dose and slow infusion for maintenance studies were also found effective[11].

GCS level is an important factor in assessing Organophosphate poisoning outcome[1]. However, early aggressive medical therapy with antidotes and intensive care management are the keys to prevention of morbidity and mortality associated with OPP. Last but not the least prevention is always better. We as a collective body, should strive for a ban on the hazardous forms and restriction on use of a number of pesticides.

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