
AUDIT

AUDIT ON ORGANOPHOSPHATE POISONING REQUIRING INTENSIVE CARE UNIT ADMISSION

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Organophosphates (OP) inhibits both cholinesterase and pseudo cholinesterase activities. The inhibition of acetyl cholinesterase causes accumulation of acetyl choline at synapses and over stimulation of muscarinic and cholinergic activities. The mortality rate is 3-25% ⁽²⁾. Early diagnosis and appropriate treatment is life saving. The clinical course of OP is very severe and may require intensive care management.

Materials and methods:

A retrospective audit was performed of Intensive Care Unit (ICU) admissions at General Hospital Nuwara Eliya for a period of six months from 01st of October 2007 to 31st of March 2008. 31 patients were included. The diagnosis was made from the history taken from the patient or from the by-stander. Red cell or serum cholinesterase activity was not measured as facilities were not available. The mainstay of management was administration of intravenous atropine and pralidoxime. 22 patients required ventilator support. Main indications for ventilator support were respiratory failure, depressed conscious level where airway need to be secured and haemodynamic instability. Weaning was performed using spontaneous mode and subsequently T piece trial.

Results:

The total hospital admissions with OP poisoning were 157. The total number of patients admitted to ICU were 31 (19.7%). Male patients were 20 (64.5%) and female patients were 11 (35.5%). Mean age group was 28.6 (16 to 62 years). 25 (80.6%) showed suicidal attempts and 6 (19.4%) were accidental ingestion. 20 (64.1%) patients were married. 18 (58.1%) patients were unemployed. 5 (16.1%) patients had previous history of suicidal attempt. Only 3 (9.6%) patients had induced vomiting at home with coconut milk. The mean time

of arrival to ICU from ingestion of OP was 12.6 hours (6 to 48 hour).

The most frequent signs on admission were miosis 28 (90.3%), bradycardia 29 (93.5%), change in mental status 10 (32.2%), low oxygen saturations (less than 90%) 21 (67.8%) and following convulsions 3 (9.6%), (24) 77.4% needed mechanical ventilation. Intermediate syndrome was observed in 7 (22.5%) patients. Other complications noticed were respiratory failure 24 (77.4%), aspiration pneumonia 7 (22.6%), convulsions 5 (16.1%), cardio-vascular complications 4 (12.9) and electrolyte imbalance mainly hypokalaemia 7 (22.5%). The total number of deaths following admissions were 5 (16.1%).

Discussion:

Organophosphates are ester compounds of phosphoric acids. These are used as pesticides for agricultural usage, insecticides, herbicides, nerve gases and for chemical warfare. The commonly used insecticides include Malathion, Parathion, Diazinon and Fenthion.

Incidence of organophosphate poisoning in USA is 102,750 annually according to the American Association of poison control centre ⁽²⁾. Highest incidence is seen in India ^(2, 12). The incidence in Sri Lanka is 10,000 -20,000 hospital admissions annually ⁽³⁾. Mortality of OP poisoning varies from 3 to 25%. According to WHO estimation there are around 10,000 hospital deaths from OP poisoning world-wide ⁽¹²⁾. Morbidity and mortality are due to inadequate respiratory management, delayed intubation, cardiac complications, aspiration pneumonia, weakness and neuropathy ⁽¹⁾.

Organophosphates are absorbed from gastrointestinal tract, mouth, skin and conjunctiva. The toxicity can occur as accidental ingestion, self poisoning, and occupational exposure. Symptoms usually occur after 12-24 hours after exposure.

Organophosphates cause irreversible inhibition of acetyl choline esterase enzymes. Acetyl choline esterase enzyme regulates the activity of acetyl choline in the synaptic cleft. It hydrolyses acetyl choline to choline and acetic acid. When organophosphates bind to this enzyme, acetyl choline levels increase which produce excessive stimulation of nicotinic, muscarinic and central receptors. Once OP binds to acetyl choline esterase inhibitors, they undergo complete binding and inactivation (ageing), endogenous hydrolysis of phosphorylated enzymes and reactivation by a strong nucleophile as oximes.

The clinical features of organophosphate poisoning:

include the features of muscarinic, nicotinic and central features. Muscarinic features includes excessive salivation, lacrimation, urination, diarrhea, gastro-intestinal cramps, emesis, blurred vision, miosis, bradycardia, wheezing. Muscarinic features are known as SLUDGE and DUMBELS

^(1, 7). Nicotinic features include fasciculation, paresis or paralysis, hypertension and tachycardia. Central receptor features include anxiety, confusion, seizures, psychosis and ataxia. Three types of paralysis are noticed. Type I due to continued depolarization at neuro-muscular junction, type II due to intermediate syndrome and type III due to delayed polyneuropathy.

Features of OP poisoning include three phases. Initial cholinergic phase followed by intermediate syndrome and delayed phase of polyneuropathy.

Cholinergic phase: Medical emergency period. This period may require ICU management. Patients present with weakness, blurred vision, nausea, vomiting, headache, abdominal pain, and dizziness. Examination reveals miosis, salivation, respiratory distress, reduced mental state, muscle fasciculation. It includes cardiac arrhythmias with heart blocks. Deaths during this period are due to cardiac arrhythmias, respiratory failure and depression of vital centre. This period last for 24 to 48 hours ⁽⁸⁾.

Intermediate syndrome: Presents with proximal muscle weakness. Muscle weakness includes muscles of respiration and cranial nerve palsies. The onset of this phase is within 1 – 4 days. The complete recovery occurs within 4-18 days. This phase is due to excessive cholinergic stimulation. The complications during this period include arrhythmias and infection ^(10, 11).

Delayed polyneuropathy: presents with peripheral weakness. This is due to toxic axonopathy. The onset is usually 7-14 days.

Other features include: dystonia, cog wheel rigidity, Parkinsonism features, optic neuropathy, retinal

degeneration, myopia, ototoxicity, Guillen Barre like effect ⁽¹²⁾.

The differential diagnosis includes poisoning of carbamate, nicotine, neostigmine, pilocarpine, mushroom, myasthenia gravis, Guillen Barre syndrome, botulism and Eaton Lambert syndrome.

The diagnosis of organophosphate poisoning is essentially clinical. The choline esterase levels can be useful. But most of the centres do not have the facilities to perform this investigation. Chest X Ray may show pulmonary oedema. Electro Cardiogram shows prolonged QT interval, ST elevation and T inversion.

Management of these patients include:

First aid and initial resuscitation.

Medical management.

Surgical intervention if any association of trauma or burns.

Counseling and psychiatric referral.

First aid and initial resuscitation include removal from contaminated environment, removal of contaminated clothes, washing the skin with soap and water, assessment of breathing and circulation, resuscitation if necessary, control of convulsions if any, assisting vital functions and monitoring vital parameters like pulse, blood pressure, oxygen saturation and Glasgow coma scale.

Medical management includes use of atropine, pralidoxime, and benzodiazepine.

Atropine:

Physiological antidote at muscarinic receptor. No effects at neuro muscular junction. It does not cross blood brain barrier. Initial dose of 2mg followed with boluses every 5 to 10 minutes or as infusion until signs of atropinisation occur. That includes heart rate more than 80/minute and dilatation of initially constricted pupil. Contra-indications for atropine include previous hypersensitivity and narrow angle glaucoma ⁽¹⁾.

Pralidoxime:

Choline esterase reactivator. The mechanism of action includes reactivation of acetyl choline esterase enzyme, detoxification of unbound OP molecules and endogenous anticholinergic effect. Effective concentrations of oximes improve reactivation of anticholine esterase (AChE). Beneficial effects are shown by starting oximes and continuing for several days. Reactivation mainly occurs at neuromuscular junction. It does not cross the blood brain barrier since it is ionized. Adult dose is 1-2g IV followed by 0.5g/hour infusion. For children, the dose is 20-50mg/Kg intermittent

dose⁽¹⁾.

The side effects of pralidoxime include tachycardia, laryngospasm, muscle rigidity, dizziness, diplopia, impaired accommodation, headache, hyperventilation, muscle weakness. It is not safe in pregnancy and lactation. Needs caution in renal failure and myasthenia gravis since it can precipitate myasthenic crisis.

Benzodiazepines:

Useful for sedation while the patient is on the ventilator. It reduces the distress and anxiety.

It can be given as an infusion or intermittent boluses. There are various new modalities involved in the management which is being tested on animals and humans. They include use of fresh frozen plasma, clonidine, NMDA antagonists, and magnesium sulphate. Trials are extensively done on use of activated charcoal, gastric lavage and use of some form of emesis at home.

The use of fresh frozen plasma can dilute the toxins and increase the plasma choline esterase levels⁽⁸⁾.

Clonidine inhibits the release of acetyl choline from the post synaptic cleft^(2, 1). NMDA antagonists prevent the neuronal death and improve the EEG activity. It also can cause bronchodilatation which will antagonize the bronchoconstriction effect of OP poisoning⁽²⁾. Magnesium sulphate inhibits the release of acetylcholine from the CNS, peripheral nervous system and autonomic nervous system (ANS). It also augments the hydrolysis of the poison⁽⁵⁾. The other modalities like activated charcoal, gastric lavage neutralizes the toxin⁽³⁾.

Medico-legal pitfalls in the management:

Delay in recognition of respiratory distress.

Failure to optimize oxygenation.

Patient need to be monitored for a symptom free period of a minimum of 48 hours before discharging from hospital because of delayed neurological effects.

Recommendations:

Early referral from medical wards for patients who require ICU admissions. Needs aggressive management with atropine and PAM either in the form of infusions or boluses. Early recognition of respiratory failure and ventilator support is always mandatory. Need careful weaning from ventilation. Recognition of intermediate syndrome and other complications are important in the proper management. A team approach is always necessary with physician, anaesthetist and micro-biologist. Proper nursing care and good physiotherapy is also required.

Conclusions:

OP poisoning is a serious condition that needs rapid diagnosis and treatment. Since respiratory failure is the main reason for mortality, careful monitoring, appropriate treatment and early recognition of complications may decrease mortality rate among these patients.

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