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Approach to Common Poisoning in Punjab

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India is an agriculture based country with Punjab as one of the leading food grain producing states, with increasing burden to feed the growing population. This has led to over-usage of pesticides which on one hand has contributed significantly to increase the crop yield while on the other hand has led to sharp increase in the poisoning cases in the region.

Common poisoning in Punjab are related to most easily available agricultural based products i.e. pesticides, herbicides and preservatives. The nature of the poisoning is more often due to accidental and sprays related and suicidal. In parts of developing world pesticide poisoning causes more deaths than infectious diseases. Organophosphate insecticides account for more than 50% of all acute poisoning in hospital practice; the majority of patients are younger than 30 yrs.[1] In teenagers and adults the poisoning is generally due to suicidal intention although accidental poisoning during spraying can also occur.[2] Mortality ranges from 4% to 38% in Indian studies.

Poisoning as a mode of suicidal death is known from the antiquity. Poisoning among all the age groups and both sexes is seen everywhere and the incidence of Poisoning with reference to insecticides, pesticides and rodenticides has become more common than others in the modern times because of their easy availability, low cost, efficacy of action and rapid death. Also these days because of drug addiction, we see overdose of commonly abused addictions of herione and Smack etc.

COMMONLY USED POISONS

1. Pesticides: Organophosphorous compounds i.e. Dichlorvos DDVD 76%, Chlorpyriphos, Deltamiethin 1% + Trizophos 35%, Monocrotophos 36%, Profenofos 40% + Cypermethrin 4% and Pretilavhlor 50%.
2. Herbicides: Imidachlopride, Beldamycin and Propioconazone 25%.
3. Endosulfan
4. Aluminum Poisoning
5. Corrosives & Others

HOW TO APPROACH

Poisoning is a medical emergency. The patient should be immediately brought to hospital and shifted to ICU or any other high intensity unit of facility. History of inhaled or suicidal intake of poisoning is of paramount importance and maintaining the airway patency is the top priority.

ORGANOPHOSPHOROUS PIOSONING

Organophosphate poisoning results from exposure to organophosphates (OPs),which cause the inhibition of acetylcholinesterase (AChE), leading to the accumulation of acetylcholine (ACh) in the body. It inhibits AChE, causing OP poisoning by phosphorylating the serine hydroxyl residue on AChE, which inactivates AChE. AChE is critical for nerve function, so the irreversible blockage of this enzyme, which causes acetylcholine accumulation, results in muscle overstimulation. This causes disturbances across the cholinergic synapses.

Organophosphate compounds avidly bind to cholinesterase molecules as they share a similar chemical structure. In human beings, the two principal cholinesterases are RBC, or true cholinesterase (acetylcholinesterase), and serum cholinesterase.[3] Intoxication by inhalation and absorption through skin may occur during spraying.

Following absorption, OP compounds accumulate rapidly in fat, liver, kidneys and salivary glands. The phosphorothioates (P=S), for example diazonin, parathion, and bromophos, are more lipophilic than phosphates (P=O), for example dichlorvos, and are therefore stored extensively in fat which may account for the prolonged intoxication and clinical relapse after apparent recovery which has been observed in poisoning from these OP insecticides. OP compounds generally are lipophilic and therefore cross the blood / brain barrier in most cases.[5]

Metabolism

After absorption in skin, GI tract or inhalation, the insecticides and their metabolites gets distributed quickly especially in liver kidneys, adipose tissue and tissues rich in lipids. The plasma half life after a single administration is from few minutes to several hours which depend on type of compound and rate and amount of administration. Metabolism is mainly due to oxidation, by cytocrome-p-450 system and hydrolysis of ester bonds mediated by various esterases or paroxonases. Elimination mainly occurs via urine and faeces. Some compounds remain longer in body like fenthion and Fenithrothion. The biological effects of OP compounds are a result of accumulation of endogenous acetyl choline at sites of cholinergic transmission. Ion binding by which enzyme AChE is inhibited, but eventually progressively phosphorelated by covalent bonding, a process normally takes 24-48 hrs. This process is called “Ageing” and this period is known as the “critical interval” because during this time administration of antidote is still effective in

reversing the process. Once ageing is completed the enzyme cannot be reactivated. Plasma AChE recovers quickly within 4 weeks. Red cell AChE takes longer and may not be restored. Affected AChE recovers at the rate of ~ 1% per day. Restoration of AChE activity occurs by slow denovo synthesis of free enzyme. Ageing has an important bearing on toxicity and treatment outcome.[4]

Three Clinical Phases

Acute Cholinergic Crisis: OP's lead to acute cholinergic crisis in the initial phase.The clinical findings are thereby a mixture of muscarinic effects, nicotinic effects resulting from accumulation of ACh at neuromuscular junctions and consequent depolarization and CNS effects causing initial excitation and subsequent inhibition of all CNS activity.

The muscarinic symptoms are diarrhea, lacrimation, salivation, bronchorrhoea, bronchospasm, bradycardia, urination and miosis. Patient may have hypertension and tachycardia occurring due to nicotinic actions rather than hypotension and bradycardia. The nicotinic receptors activated during acute intoxication lead to muscle paralysis. Fasciculations are seen and are a reliable sign of poisoning. Progression of paralysis may occur and the muscles of respiration may get affected. Severe intoxication may cause emotional irritability, mental obtundation, cognitive impairment, coma and convulsions because of CNS effects.

Intermediate Syndrome: Wadia et al first described this syndrome as type II paralysis.[5] The term intermediate syndrome was coined by Senanayake and Karalliedde L. in 1987.[6] This term is derived from the fact that it arises between the period of early cholinergic syndrome and the late onset peripheral neuropathy. This syndrome is commonly associated with OPs like diazinon, dimethoate, methylparathion, methamidaphos, monopcrotophos, fenthion and ethylparathion. It develops 12-96 hrs after exposure and reflects a prolonged action of acetylcholine on the nicotinic receptors and is characterized by muscular weakness in the ocular, neck, bulbar, proximal limb and respiratory muscles. The sensory functions characteristically remain normal and full recovery is evident in 4-18 days.

Organophosphate Induced Delayed Polyneuropathy (OPIDN): OPIDN is common following exposure to OPCs which have weak anticholinesterase activity. OPCs have been found to be neuropathic eg. Mipafox, merphos, leptophos, DEF, EPN, cyanophos and trichloronat.

Treatment

If the insecticide was in contact with skin or eyes, these should be thoroughly washed. Dirty clothes should be removed, patient cleaned and redressed in ICU gown. On admission to ICU, maintaining respiratory airway clearance is a top priority. Oxygen, Endotracheal intubation and ventilation if required. A nasogastric tube inserted & Stomach Wash with 3-4L of saline needs to be done after securing clearance of respiratory passages.

PAM-Pralidoxime (1 ampoule -20ml contains 500mg): In the cholinergic phase, the use of oximes as rejunevators of the enzyme cholinesterase has found favour. The beneficial effects of oximes is exerted through the reactivation of enzyme cholinesterase by cleavage of the phosphorylated site and by a direct detoxifying effect on the unbounded organophosphorous compound.

Dosage: Adults: 30 mg/kg (1-2 g), administered by intravenous infusion therapy over 15–30 minutes. Dosage may be repeated 60 minutes later and then 500 mg at 6 hourly interval for next 3 days. It can also be given as a 500 mg/hr continuous IV infusion in severe cases.

Children: 20–50 mg/kg followed by a maintenance infusion at 5–10 mg/kg/hr. Intravenous infusions can lead to respiratory or cardiac arrest if given too quickly.

Atropine: Atropine was administered in the dose of 0.6mg/min infusion, till the patient is fully atropinised and signs of toxicity appear i.e. Tachycardia, dryness, dilated pupils, and urinary retention. Once atropinised, a maintenance dose of 1-3 mg was given hourly. The target end point of atropinisation was: dry and clear chest on auscultation with no wheeze, heart rate >80/min, dilated pupil, dry axilla and systolic blood pressure >80 mmHg.

Atropinisation, once achieved, should be maintained for 3-4 days, with low dose of atropine. Atropinisation is evidenced by pupillary dilation, drying up of secretions and pulse rate >100. Tafuri and Roberts have shown beneficial effects of infusion of atropine 0.02-.08 mg/kg hourly. Sedation if required and analgesia was obtained administering midazolam and lorazepam.

Ventilatory support: Patients requiring ventilatory support were intubated and put on ventilator and managed accordingly.

Caution

Morphine, theophyline, aminophyline, succinycholine, reserpire and phenothiazine-type transquilizers should be avoided in patients with OP poisoning.

ENDOSULFAN POISONING

Endosulfan is a pesticide belonging to the organochlorine group of pesticides. It was introduced in the 1950's as a leading broad spectrum pesticide. World Health Organisation (WHO) classifies endosulfan as a Highly Hazardous in category II.

Endosulfan has now been banned in India, following the Supreme Court interim order on May 13, 2011, in a Writ Petition in the backdrop of the large no. of suicidal incidents reported in Kasargode, Kerala.

Acute Effects

Endosulfan is highly toxic and can be fatal if inhaled, swallowed or absorbed through the skin. It directly affects the central nervous system and recurrent epileptic seizures are reported. Symptoms of poisoning include hyperactivity, excitement, dyspnea (breathing difficulty), apnea, salivation, loss of consciousness, diarrhea, anemia, vomiting, insomnia, blurred vision, cyanosis, tremor, dry mouth, lack of appetite, irritability, headache, decreased

respiration, loss of memory, haematuria, albuminuria, confusion, dizziness, imbalance and lack of coordination.[7] Autopsy examination of an intentional ingestion (suicide) case has revealed damage to liver, lung and brain.

Discussion & Treatment

Convulsions are a common and severe manifestation. Endosulfan is also toxic to the liver, kidney and lung and can cause rhabdomyolysis in higher doses. Liver function tests are abnormal in the form of deranged AST or ALT. Severe poisoning results in death due to status epilepticus that can lead to asphyxia, and rhabdomyolysis leading to renal failure.

Treatment is symptomatic and supportive. Early termination of convulsive status epilepticus by aggressive treatment is the best way to prevent mortality. Refractory seizures requires more aggressive treatment as it is associated with higher mortality and morbidity.

ALUMINUM POISONING IN PUNJAB

Aluminium phosphide poisoning (ALP) is a large problem, particularly in the Indian subcontinent. It is readily available as a cheap solid fumigant for storing cereal grains. It is sold under various brand names such as QuickPhos and Celphos and is highly toxic, especially when consumed from a freshly opened container. Unfortunately this has become the most common chemical agent used for the self poisoning.

Death results from profound shock, myocarditis and multi-organ failure.[8] Aluminium phosphide has a fatal dose of between 0.15 and 0.5 grams (0.0053 and 0.0176 oz).[9] It has been reported to be the most common cause of suicidal death in North India. Deaths have also been reported in Iran, Thailand and Southeast Asia.

Mortality Rate

The mortality rates 40 to 80 percent. The actual numbers of cases may be much larger, as less than five percent of those with AP eventually reach a tertiary care center. Since 1992, when aluminium phosphide became freely available in the market, it had, reportedly, overtaken all other forms of deliberate poisoning, such as organophosphorus and barbiturate poisoning, in North India. In a 25-year-long study on 5,933 unnatural deaths in northwest India, aluminium phosphide poisoning was found to be the major cause of death among all cases of poisonings.[10]

Mechanism of Toxicity

The toxicity of aluminium phosphide is attributed to the liberation of phosphine gas, a cytotoxic compound that causes free radical mediated injury, inhibits vital cellular enzymes and is directly corrosive to tissues. The following reaction releases phosphine when AlP reacts with water in the body:

$AlP + 3\ H_2O \rightarrow Al(OH)_3 + PH_3$

$AlP + 3\ HCl \rightarrow AlCl_3 + PH_3$ (stomach)

Signs, Symptoms & Diagnosis

After ingestion, toxic features usually develop within a few minutes. The major lethal consequence of aluminium phosphide ingestion is profound circulatory collapse, is reportedly secondary to these toxins generated, which lead due to direct effects on cardiomyocytes, fluid loss, and adrenal gland damage. The signs and symptoms are non-specific, dose dependent and evolve with time. The dominant clinical feature is severe hypotension refractory to dopamine therapy. Other features may include dizziness, fatigue, tightness in the chest, headache, nausea, vomiting, diarrhoea, ataxia, numbness, paraesthesia, tremor, muscle weakness, diplopia and jaundice. If severe inhalation occurs, the patient may develop acute respiratory distress syndrome (ARDS), heart failure, arrhythmias, convulsion and coma.

Treatment & Management

Detailed history need to be taken regarding number of tablets, freshness of tablets, reason and mode of ingestion-whether dissolved in water/ liquid or ingested as such.

All patients of suicidal AlP intake needs to be shifted to ICU without any delay. Garlic odor in the breath is to be noticed and nasogastric tube put in and aspirate the contents. It is recommended not to do gastric lavage with water. Liquid paraffin/Coconut oil may be instilled through NG tube to give a protective coating over the mucosa and accelerate the excretion of aluminium phophide and phosphate.Some authors recommend gastric levage with potassium permagnate (1:10000) to reduce the absorption of phosphine. Permagnate oxidizes PH_3 to form non-toxic phosphate.

On arrival in the ICU, the vital parameters are monitored-pulse, BP, SaO_2 ,ABG, respiratory rate, and urine output. Resuscitate the patient on the line of breathing and circulation. Order Immediate investigations of arterial blood gases, Na^+ , K^+ , and ionized Ca^{++}. Establish I/V access and given normal saline guided by CVP (apprx. 12cm of water).

Low dose dopamine (4-6 ug/kg/min) to combat shock. Oxygen is given for hypoxia. ARDS may require mechanical ventilation. All types of arrthymias esp. atrial fibrillation are seen in these patients,and the management has to be done accordingly. Magnesium sulphate used both high and low dose did not improve survival in controlled clinical trials. Hence Siwach et al do not recommend its use. Metabolic acidosis are corrected by intravenous sodium bicarbonate, requirement of which are guided by base excess.

$NaHCO_3$ required (meq) = 0.6 x body weight (kg) x Base Excess

Total requirement of sodium bicarbonate are given immediately (full correction) and arterial blood gases are estimated after one hour and sodium bicarbonate was given accordingly. After that, arterial blood gas analysis are done again at one-hour intervals till two consecutive readings of arterial blood pH above 7.4 are obtained. Following which, ABG analysis is done at 2-, 4-, or 6-hourly intervals, according to requirement. Associated electrolyte imbalances are treated accordingly.

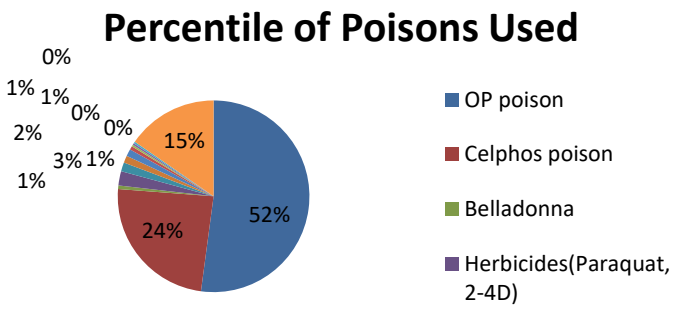

Fig. 1: Percentile of Poisons used

All the patients are given injection hydrocortisone 200 mg IV on arrival and then 150 mg at 8 – hourly intervals. Inotropic support is given with injections dopamine and noradrenalin

The outcome correlates with the severity of the hypotension the patient develops. The average time interval between intake of poisoning and death is 3 hrs with range o1-48hrs.Even with most aggressive management the survival rate is 10 to 40%.

Continuous Veno-Venous Hemofiltration (CVVH)

Continuous veno-venous hemofiltration (CVVH) in the early stages of AP poisoning may be beneficial before the development of multiple organ failure because AP causes metabolic acidosis and hypotension resistant to medical treatment.

CORROSIVES

Many poisons other than the strong acids and alkalis listed below have corrosive effects on the gastrointestinal tract. They include iron salts, paraquat, phenol, oxalic acid and mercuric chloride.

Strong acids	Strong alkalies
Hydrochloric acid	Ammonia
Nitric acid	Lye
Sulphuric acid	Potassium hydroxide
	Sodium hydroxide

Poisoning with strong alkalies and strong acids is uncommon. Ingestion of strong acids and alkalies produces almost immediate burning pain in the lips, mouth, throat, substernal region and epigastrium. Vomiting occurs very rapidly and may recur repeatedly. Hypersalivation is common. Shock and melena may develop in severe poisoning. The patient may look pale and burns may be visible on the hands and face.

Development of oesophageal or gastric necrosis depends on whether acid or alkali is ingested. Alkalies commonly produce oesophageal burns but only 20% have gastric lesions. Oesophageal mucosa is relatively resistant to acids whereas gastric mucosa particularly in the antrum is vulneralble. Oesophageal necrosis may be present in about 15% without buccal abnormalities. Oesophagus may perforate leading to mediastinitis but this is more likely to be a complication of oesophagoscopy. The major long term complication is oesophageal stricture formation and oesophageal carcinoma may develop at such sites after 20-30 years. Gastric damage due to acids can be equally severe with haemorrhage, gangrene (which may involve the whole stomach) and peritonitis.

Management of Ingestion

Every case should be referred to hospital for assessment. First aid management is given to help neutralize the corrosive but in severe cases the patient is unlikely to be able to retain it. Gastric emptying by any means is contraindicated. Analgesics and intravenous fluids or blood are often required and metabolic acidosis should be sought and treated appropriately. Oxygen and endotracheal intubation may be required if the larynx is involved.

Corticosteroids- no convincing evidence in limiting the damage or preventing long term sequelae i.e oesophageal strictures.

Endoscopy

Upper GI endoscopy in acute phase is hazardous but is necessary and should only be performed by an experienced endoscopist using a thinner instrument than usual. It is done to establish the severity of oesophageal and gastric burns. Circumferential burns have higher chances for perforation and even causing mediastinitis.

Laporatomy

It including resection may be necessary if serious haemorrhage from the stomach. The chronic sequelae i.e the oesophageal and pyloric strictures can be managed by repeated endoscopic dilatations and retrievable oesophageal stents. Accidental poisoning in children is most frequent and deliberate self-poisoning is common.

KEROSENE POISONING

Kerosene is an oil used as a fuel for lamps, as well as heating and cooking.The harmful effects from swallowing or breathing in kerosene.

Symptoms

Poisons ingredients like hydrocarbons lead to difficulty in breathing, throat swelling, pain in eyes and ears, abdominal pain with bloody stool, low BP - develops rapidly, unconsciousness, Drowsiness and skin burns.

Data Collected at Sidhu Hospital, Doraha (Figure 1)

In a retrospective study done in a rural setting at Sidhu Hospital Doraha Punjab, we analyzed the data of patients from the past 6 years who were admitted with poisoning. A total of 341 patients, 244 (72%) males and female 97 (28%) were admitted to hospital from 2010 till November 2015. The most predominant poisonous agent used was Organophosphorus (52%)(Malathion, Parathion, Thimit, Baygon etc) followed by Celphos (aluminium phosphide 24%) and others like belladona, carbamates, rat poisons (zinc phosphide), herbicides (Diquat, Paraquat, 2-4d, Glyphosate- Roundup), acid poisoning, kerosine oil, phenyl tablets. Hospital has received appx. 20 cases of heroine & smack overdose with severe respiratory depression.

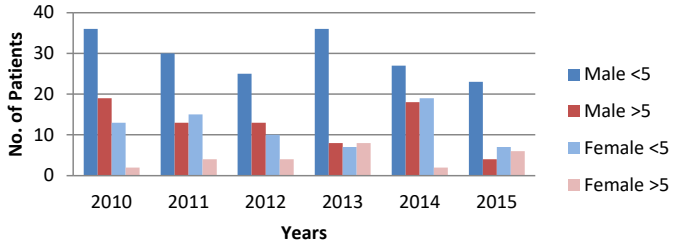

Fig. 2: Duration of Stay

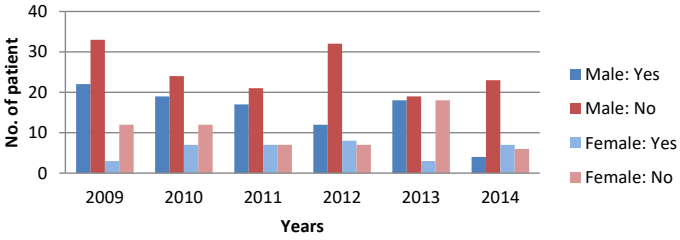

Fig. 3: Requirement of Ventilation

According to the study, 90% of cases where suicidal poisonings. In the rural area, the insecticides are lying freely in the fields, in the motor pump sheds making them very easily available. The study has shown an increased prevalence of incidence in males (72%), especially in the less than 35 years age group(52%), making them twice as likely to consume poison as compared to females.

The duration of the hospital stay on an average was less than 5 days (73%), but patients who were more sick and needed ventilatory support stayed for more than 5 days (Figure 2). The duration of hospital stay in 248 (73%) patients was less than 5 days and 93(27%) patients stayed for more than 5 days.

Out of the total 173 (51%) patients of OP poisoning, only 127 (73%) patients needed ventilator support (Figure 3).

OP poisoning had the least number of deaths as compared to Celphos poisoning having a 98% survival rate (Figure 4).

RECOMMENDATIONS

Prevention is better than cure. It is recommended that these insecticides should be rationed and not freely available and farmers using them should be made aware to dispose them completely after spraying in the fields, so that poisonings can be prevented.

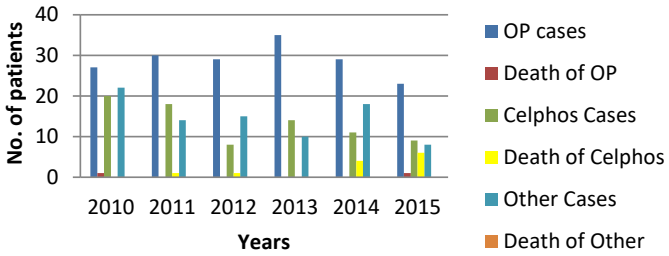

Fig. 4: Deaths from Poisoning

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