ORGANOPHOSPHORUS INSECTICIDE POISONING

Pages with reference to book, From 27 To 31

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Abstract

A review of 755 cases of Organophosphorus Insecticide Poisoning, admitted to the department of Intensive Care at the Jinnah Postgraduate Medical Centre between 15th January, 1976 to 31st December 1985, has shown that these insecticides form a majority of the cases of acute poisoning and are associated With a comparatively higher mortality rate. Of 1900 cases, 755 were cases of organophosphorus insecticide poisoning forming 39.7% of the total poisoning cases and 16% of the total admissions to the Unit. Being easily accessible, these insectidides are frequently used as suicidal agents specially by uneducated housewives. They are highly toxic and their management is very complicated. Of 108 deaths from poisoning in the last 10 years 73 (67.6%) were due to Organophosphorus Insecticide Poisoning. This being such a common mode of poisoning in our country, we have presented here our experience of the clinical features and management of these cases (JPMA, 39:27, 1989).

INTRODUCTION

Organophosphorus insecticide" poisoning formed more than one third of the total poisoning cases and 16% of the total admissions to the department of Intensive Care over a ten years period. This poisoning has a typical presentation, requires specific management and is attended by a comparatively high mortality. We describe here our experience of the management of such patients. Insecticides are classified into five groups as shown in Table—I.

1. CHLORINATED INSECTICIDES:

Such as Diccophane (Dichlorodiphenyl trichlorethane), Gammabenzene-Hexachloride (Gammaxene). These are absorbed through the respiratory tract, gastrointestinal tract and skin, and the absorption is increased by oily substances. They affect, mainly, the central nervous system. Symptoms inplude vertigo, giddiness, tremors, convulsions and coma, and pulmonary oedema may occur. They potentiate the metabolism of testosterone, steroids and barbiturates.

Treatment is symptomatic. Milk and oily substances are not given and adrenaline is avoided as it may precipitate cardiac arrythmias.

2. ORGANOPHOSPHORUS COMPOUNDS:

a) Malathion (trade name khatmaleen) is the least toxic as it is rapidly detoxicated by aliesterase.

b) DDVP (Dichlordivinyl) phos) is highly toxic and rapid acting, having direct inhibitory effect on acetyl and non-specific cholinesterase and is rapidly absorbed by any route. It is present in Finis, Typhon, Dingo, Sheltox, Kaltox, Vapona.

c) Metriphenate is used as an agricultural insecticide and as a veterinary anthelmintic.

d) Parathion, a poor inhibitor of cholinesterase, is rapidly metabolised in the liver to form Paraxon[1] which is a very effective inhibitor of cholinesterase and, therefore, its onset of action is delayed.

These compounds are absorbed through the respiratory tract, gastrointestinal tract and skin, are highly toxic and even 300mg mity be dangerous. Symptoms may occur immediately or upto 8 hours after exposure. The signs and symptoms may vary in severity according to the compound used and depend on their anticholinesterase activity resulting in increased parasympathomimetic tone. Toxic Effects — Acetylcholine accumulates at the autonomic synapses and at the endings of the post-ganglionic para-sympathetic and skeletal efferent nerves. Their toxic effects resemble those of physostigrnine and

neostigmine but with some compounds may be much more persistent, lasting for a day or two rather than hours. [2]

Muscarine Effects of Acetylcholine:

Miosis, increased salivation, abdominal cramps, vomiting, diarrhoea, bronchospasm and pulmonary oedema, increased lacrimation, blurring of vision; bradycardia.

Nicotinic effects: Muscular twitchings, fasciculations, weakness, flaccid paralysis.

3. CARBAMATES

Sold under the trade name of "Baygon Dust," these have a mode of action similar to Organophosphorus Insecticides but since their anti-cholinesterase activity is reversible, their fatality rate is not so high. Cholinesterase reactivators are contraindicated as the action of carbamates is reversible. [3]

4. DINITROPHENOLS

They are cumulative poisons and increase the metabolic rate which may cause death in a manner like heat-stroke. Treatment is symptomatic. Atropine and thiopentone anaesthesia are contraindicated, the latter because of its synergistic action on cellular respiration. Barbiturates should be given in diminished doses.

5. PYRETHIUM FLOWER

Is the dried flower head of Crysanthemum. Its action is due to two active ingredients - pyrethrum 1 acinerin. It is an agricultural and domestic insecticide. It is not commonly used here as it is expensive (Table-I).

TABLE I [4]

GROUP	ABSORPTION AND MODE OF ACTION	TOXIC EFFECTS	MANAGEMENT
Chlorinated Insecticides Dichlorodiphenyl Trichlorethane (Dicophane) Gamma Benzene Hexachloride (Gammaxene)	Skin, Respiratory tract, G.I.T. Action is direct on CNS stimulation. Absorption increased by oily substances	Mainly on Central nervous system parasthesia, vertigo, giddiness, tremors, convulsions, coma, pulmonary oedema rare. No miosis and muscular twitching Potentiates metabolism of barbiturates steroids testosterone.	Symptomatic. Avoid Atropine and Adrenaline as they may precipitate cardiac arrhythmias. Avoid milk and oily substances
Organophosphorus Compounds	Skin, Respiratory tract, G.I.T. 1. Action direct on CNS 2. Inhibition of Cholinesterase resulting in accumulation of Acetyl Choline. Onset of action may be immediate or 8 hours after exposure.	CNS R.C. Depression, Coma convulsions rare Muscarine effects of Acetyl Choline. Miosis, increased salivation, abdominal cramps, vomiting, diarrhoea, bronchospasm and pulmonary oedema increased lacrimation, blurring of vision, Nicotine effects Muscular twitching, fasciculations, weakness, flaccid paralysis.	Atropine blocks CNS and Muscarine effects of Acetyl Choline but not Nicotinic effects. Cholinesterase reactivators also reverse Nicotinic effects.
Carbamates Baygon dust, Dimeton Mactacyl	Mode of action like Organophosphorus Insecticide Poisoning but the Acetyl Choline effects are reversible.	Same but less toxic. Since the anticholinesterase activity is reversible, their mortality rate is not so high	Atropine.Cholinesterase reactivators are contraindicated.
Dinitrophenols	Act by increasing Metabolic rate. Cumulative Poisons	Like heat stroke.	Symptomatic
Pyrethium		Not used as expensive	

PATIENTS AND METHODS

Clinical data of 755 patients of Organophosphorus Insecticides Poisoning was recorded and their clinical features noted on a separate proforma. The patients were classified into accidental and suicidal cases. The insecticides used by the patients were Finis, Khatmaleen, Typhon, Dingo, Sheltox and Kaltox.

RESULTS

Of 1900 cases of poisoning seen in the department of Intensive Care over a ten years period, 755 (39.73%) were of Organophosphorus insectiside Poisoning. The frequency of this poisoning has increased at an alarming rate from 33.75% in 1976 to 47.34% in 1981 to 62.9% in 1985 giving an overall frequency of nearly 40%. The majority of cases (8 1%) were between ages 11—30 years. Females predominated over males in the ratio 3: 2. Nearly 80% of the cases belonged to the low income group (Income below Rs. 1500/-) and 20% to the high income group (Income over Rs. 1500/-). Four hundred and five (53.64%) cases were unmarried and 350(46.35%) were married. Poisoning was more frequent in unmarried males and married females. This mode of poisoning was very common among the housewives to whom these insecticides are easily accessible and nearly half of our cases belonged to this category. The cause of poisoning was suicidal in 480 (63.5%), and accidental in 265 (35%) cases. However, the latter could be a false hgh figure as the patients and their relatives often give wrong statements for fear of prosecution and disrepute. Organophosphorus Insecticide Poisoning as an occupational hazard occurred in 40 (5.29%) cases. These were mainly fumigators and porters. The portal of entry into the body was by ingestion in 717 (95%) and by inhalation and absorption from the skin in 38 (5%) cases. The clinical features of organophosphorus insecticides depend on their irreversible anticholinesterase activity resulting in increased parasympathetic tone (Table II).

TABLE II

	Sign and Symptoms	No. of Cases	%
1.	Miosis	732	(97)
2.	Unconsciousness	642	(85)
3.	Anorexia Nausea and Vomiting	566	(75)
4.	Bronchorrhea, Bronchospasm and Excessive Salivation	559	(74)
5.	Excessive sweating	528	(70)
6.	Respiratory distress and acute pulmonary oedema	464	(61.5)
7.	Restlessness	464	(61.5)
8.	Muscular twitching	453	(60)
9.	Abdominal cramps	453	(60)
10.	Blurring of vision	355	(47)
11.	Cyanosis	355	(47)
12.	Bradycardia	340	(45)
13.	Giddiness	340	(45)
14.	Excessive Lacrimation	241	(32)
15.	Tremors	76	(10)
16.	Convulsions	60	(8)
17.	Diarrhoea	60	(8)
18.	Involuntary defecation & Urination	45	(6)

The signs and symptoms of toxicity are usually anorexia and mental confusion with a sense of unreality. Vomiting, abdominal cramps, excessive cold sweating and salivation follow. Giddiness and restlessness may be noticeable. Constriction of the pupils is not always present. As poisoning progresses, muscular twitchings occur initially in the eyelids, tongue, face and the neck. Generalised twitchings with muscular weakness and convulsions occurs in severe cases. Other symptoms include diarrhoea, tenesmus, involuntary defecation, pulmonary oedema with bronchoconstriction. Respiratory

centre depression and coma may finally occur. Sometimes it is difficult to differentiate between the toxic effects of Chlordana (Flit) and organophosphorus insecticides. Two points of diagnostic importance in organophosphorus insecticide poisoning when present are:
1. Miosis
2. Muscle Twitching and Fasciculations
These two are not seen with Flit (2% chlordane with kerosene). Further therapeutic improvement with Atropine Sulphate in cases of organophosphorus insecticides is diagnostic. Maximum duration of unconsciousness was between 4-5 hours, the interval was, in 60% of cases, within 1-2 hours and in 30% if cases, 2-6 hours and 10% between 6-12 hours.

DIAGNOSIS

Diagnosis was based on history, typical clinical signs such as miosis, increased salivation and sweating, bronchospasm, muscular twitching, bradycardia, examination of the stomach contents and containers brought by the relatives. A further very important therapeutic test that helped us was lack of Atropinisation with 1—2mg of Injection Atropine Sulphate. Blood levels to determine cholinesterase activity were done in a few cases from private laboratories.

MANAGEMENT

In general management, special attention was paid to maintaining a clear airway and adequate pulmonary ventilation (Table III).

TABLE III. General Management.

1.	Observation of vital parameters	Half hourly BP and TPR, neurological
2.	Respiratory failure	status chart, ECG monitoring intake, output chart, Patent airway, suction, endotracheal intubation. Artificial respiration-C_2 therapy, respiratory stimulants. Mouth to mouth breathing, Ambu Resuscitator.
3.	Shock	Parenteral fluid therapy sympathomimetics
4.	Secondary infection, Nutrition	Antibiotics, Hypertonic glucose I.V. every six hourly.
5.	Care of bladder and bowel	Nasogastric feeding with milk, juice, soup, three hourly.
6.	Prevention of bed sores	Change posture three hourly.

The mainstay of specific management were Atropine and Cholinesterase Reactivators. Injection Atropine was given in a dose of 1-2mg every ten to fifteen minutes till Atropinisation occurred instead of 2-4mg[5]. The average dose of Atropine required in 24 hours was 100—200mg and maximum we have given in 24 hours was 400mg. The maximum total dose given was 1900mg in 120 hours. Atropine blocks the effects of anticholinesterase agents at muscàrinic receptor sites but has no effect on the neuromuscular junction and autonomic ganglia where accumulation of ACh causes weakness and eventually paralysis of skeletal muscular including those of respiration. [6]. Injection Toxogonin (Pralidoxime) was given in 50 patients of which 47 survived. It is given immediately after the first injection of Atropine in the dose of 250mg I.V. repeated every two hours for 1—2 doses. it is not used in poisoning due to carbamate group as their action is reversible, injection Toxogonin effects are not prominent as the skeletal neuromuscular junctions and muscle weakness and fasciculation improved within 10 minutes; little effect was seen at autonomic receptor sites, Paralidoxirne reactivates

phosphorylated cholinesterase and forms an inert complex with the organophosphate. As the phosphorylated cholinesterase enzyme undergoes a process of aging within second hours it becomes resistant to reactivation by Toxogonin, hence not more than 2 doses of the latter are given (Table IV).

TABLE – IV. Specific Management of Organophosphorus Compound Poisoning.

Removal of prevention of absorption	Anticholinergic drug	Cholinesterase Reactivators injection
Externally	Injection Atropine Sulphate Initial dose 2–3mg I.V. Stat	Toxogonin 250 mg I.V. 4–5 minutes after first administration of Atropine. If required repeat once or twice at 2 hourly intervals. Do not use if more than 24–48 hours have elapsed.
Wash skin with water and spirit		Injection Pralidoxime, Initial dose 1gm I.M. or I.V. repeated by 1 gm in 3–4 hours.
Gastric	Do not delay atropine administration	Injection Bispropane dibromide (Not used).
Conscious Induced emesis	Maintenance 1–2mg I.M. I.V. every 10–15 minutes until atropinization. Total average dose 100–200mg in 24 hours	Especially important if patient has not responded to 10mg atropine sulphate or general condition deteriorates because of by convulsions or respiratory centre depression. Not very effective if used 12 hours after the onset of symptoms.
Unconscious Stomach wash No milk No Castor Oil	Maximum dose given 400 mg in 24 hours, 1900mg in 120 hrs. Average duration of treatment 3–7 days. Contraindication Cyanosis as it may cause ventricular fibrillition.	

MORTALITY RATE

Of the 755 cases, 682 (90.33%) recovered and 73 (9.6%) expired. The cause of death was acute respiratory failure coupled with acute pulmonary oedeina. Some cases relapsed into secondary respiratory failure after improvement[7]. The mortality rate though high has gradually reduced from 20.7% in 1976 to 7.14% in 1981 to 5.35% 1985. Comparing the mortality rate of Organophosphorus Insecticide Poisoning with those of poisoning in general, the figures show that the mortality rate of Organophosphorus Insecticide Poisoning is twice as high (3.8%) as the mortality rate from all other poisons excluding Organophosphorus Insecticide (1.8%). The latter figure compares favourably with results from Western studies. [8]

DISCUSSION

The number of patients of Organophosphorus Poisoning is alarmingly high and is expected to rise each year, unless, some form of restriction is placed on the sale of these highly toxic agents. Cases of poisoning with these agents are not very common in the studies reported for the developed countries where, under stresses and strains of life, people resort to self poisoning with tranquilisers, hypnotics and sedatives. [8] Not only are the organophosphorus insecticides highly toxic but their management is complicated and more often requires specialised forms of treatment such as artificial ventilation which require highly sophisticated and costly units. To reduce mortality and cost of management of poisoning cases it is all the more important that simple aspects of prevention be practiced. [9] In view of the data presented, it is recommended that certain restrictions be put on the sale of these highly toxic products.

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