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Pesticide Poisoning as a Pediatric Emergency

by

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Abstract

There are branches in medicine where knowledge of the average physician is deficient, such as in pollutional problems, industrial medicine and diseases caused by agricultural chemicals. Many of these involve the toxicology of substances rarely met with in medical practice.

A multidisciplinary agro-medical and industrio-medical approach is esential to understand the management including precautionary and legislative measures that have to be taken. This will involve not only medical personnel but also engineers, chemists, agronomists, ecologists and many others.

Poisoning with agricultural chemicals most often involve O.C. and O.P. compounds. In adults these cases have been typified by self-poisonings and through neglect of safety measures prescribed by the factory. In children poisonings almost always have been associated with accidents. Here the most important factor is also negligence of parents to keep away dangerous pisticides from the reach of children.

There are quite a few potent antidotes available in pesticide-poisoning, notably atropine for O.P.'s and carbamates, vitamin K for warfarin, and dimercaprol for arsenics. There are also chemicals like paraquat and pentachlorophenol for which no antitode is available and they present great problems in treatment.

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Introduction

Poisoning has always been an emergency in children as well as in adults. In children it is more often an accidental type of poisoning. In some emergency hospitals, poisoning could constitute up to 20% of emergency cases. A survey in 11 Jakarta hospitals (Darmansjah et al., 1974) showed, however, that the ratio of poisoning-admissions was only 34 per 10.000 and that pesticides-poisoning had an incidence rate of 6%. In the Department of Child Health of the Cipto Mangunkusumo General Hospital, Jakarta, poisoning-admissions were 47 in 1971, 28 in 1972 and 18 in 1973. Of these only two were due to pesticides. There is reason to believe, however, that the real incidence of poisoning is much greater. Jo Kian Tjay et al. (1971) listed 6 pesticide poisoning cases during the years 1963 — 1968 in Medan and reported 157 cases of arsenic poisoning in children living in two orphanages at an outbreak in 1969 (Jo Kian Tjay and Djohan Aziz, 1971).

There are doubt that poisoning by pesticides could pose a problem in diagnosis and treatment, and that more pediatric cases could be anticipated when pesticides are being used more abundantly in house and garden.

Organochlorine compounds (O.C.)

These are chlor-substituted hydrocarbons and are represented as DDT, dieldrin, aldrin, BHC, thiodane, endrin, chlordane, isodrin and kelthane. Endrin is by far the most toxic of the series with an $L.D._{50}$ of about 7 mg/kg. It has been the cause of death in many cases of suicidal as well as accidental poisoning. O.C. insecticides are less and less used now in Indonesia and are largely replaced by organophosphorus which in itself is equally toxic if not more. Problems of persistence are however less intense with the last mentioned.

Clinical picture

All O.C. compounds have the same action in man, primarily on the central nervous system where supraspinal stimulation resulting in tremors and convulsions dominates the entire clinical picture of poisoning.

About half to three hours after ingestion or absorption through the skin, tremors are manifested which will proceed into convulsions with shorter and shorter intervals and if severe, a state of continuous convulsion will be reached. Coma often accompanies severe poisoning and fever may be present. At this stage diagnosis can only be made if there is an indication of O.C. ingestion or absorption of its only solutions through the skin.

Differential diagnosis should be made against all convulsive disorders.

Laboratory findings

The only laboratory proof of O.C. poisoning is the demonstration of its presence in the blood. It is convenient to use a thin layer chromatography technique, which is able to detect at least 1 ppm DDT in the blood or DDA in urine.

A two and a half year old child who ingested a spoonful of DDT by mistake was admitted in the Pediatric department last year and had a bloodlevel of 15 ppm. four hours after ingestion. Severe convulsions were noted but treatment brought complete recovery.

Treatment

There is no specific antidote for O.C. insecticide poisoning, but symptomatic treatment of convulsions and anoxia may be lifesaving.

a. *General measures :* All clothes soaked with the insecticide should be removed from the body and the skin washed with soap and lots of water. After oral ingestion, the insecticide should be removed from the stomach by gastric lavage or vomiting. Great care should be taken in these procedures because of the danger of aspiration, especially in children. The patient should be placed on his left side with the head in a downwards position using a large enough gastric tube. Lukewarm tap-water can be used for stomach-washing, repeating the procedure 20-30 times. In general, gastric lavage is still useful if the agent has not been more than 4 hours in the stomach.

To hasten passage through the gut, a solution of an appropriate concentration of magnesium sulfate can be left in the stomach. Oily laxatives are contraindicated since they may promote absorption of the insecticide from the gut.

b. *More specific measures :*

(1) Convulsions in general cause anoxia, so that oxygen is needed. No mouth to mouth breathing is allowed.

(2) Anticonvulsive therapy is essential when frank convulsions occur or for prevention when hyperexcitability exists. Pentothal sod. or diazepam i.v. can be used to control status convulsivus immediately, but care should be taken to administer only a dose sufficient to stop the convulsions. Phenobarbital can be administered to control further convulsions and has the advantage that it is an enzyme inducer and thus enables the liver to metabolize DDT at a faster rate.

(3) Morphine is contraindicated because of the danger of respiratory depression.

(4) Epinephrine or other vasoconstrictors may not be given to combat possible shock, because these can cause arrhythmia of the heart

due to sensitization by organochlorines.

(5) All cases must be hospitalized for at least 48 hours after convulsions have ceased and phenobarbital oral treatment should be extended for a longer period. This must only be withdrawn gradually.

Organophosphorus compounds (O.P.)

Starting off as chemicals meant to kill man in war, these phosphate esters were further developed to serve mankind in the struggle against food-shortages and disease. Its deadly characteristic against the human race is, however, retained.

Available in Indonesia are among others: Malathion, Dimecron, Bazudin, DDVP, and Diazinon. Pharmacologically they all act by the same mechanism, inhibiting cholinesterases (ChE) persistently and hereby leaving acetylcholine (Ach) unhydrolized. This results in accumulation of Ach at all sites where cholinergic transmission is physiological.

To summarize, the actions of Ach in the body are stimulations of:

(1) muscarinic receptors (smooth muscles and exocrine glands)

(2) nicotinic receptors (autonomicganglia and striated muscles)

(3) adrenal medulla (secretion of epinephrine)

(4) synapses in the brain.

The high fat-solubility of these O.P. compounds allows free absorption through all mucous membranes and the intact skin.

Clinical picture

A pure clinical diagnosis of O.P. poisoning can be made when we combine history with the presence of cholinergic effects. Each history of contact with O.P. compounds must lead to suspicion of poisoning when symptoms arise.

The first manifestations will be notable within a few minutes to two hours after exposure.

Signs and symptoms can be divided into central and peripheral, beginning with non-specific ones like vomiting, feeling of weakness, headache, visual disturbances and ataxia.

These quickly pass into the following important muscarinic signs: hypersecretion of saliva, sweat, nasal and bronchial mucus, colic of the gut with diarrhea, myosis and bradycardia or tachycardia.

Nicotinic signs are generally biphasic: first twitchings and convulsions of voluntary muscles occur, followed by paresis or paralysis.

Central signs include: ataxia, diminished reflexes, difficulty in speech, respiratory depression, cyanosis and coma.

The cause of death at the beginning of poisoning is airway obstruction, when no measures are taken to

remove mucus from the upper respiratory tract. Later on central and peripheral respiratory depression or brain damage may lead to lethal complications.

Hypersecretion of exocrine glands are important indices although sweating might not be prominent in air-conditioned rooms.

The occasional presence of mydriasis sometimes misleads diagnosis. This might be due to apprehension associated with poisoning (sympathetic stimulation) or as a result of paralysis of the constrictor muscles of the iris (overstimulation).

Laboratory findings

Leucocytosis, slight proteinuria and glycosuria may be found. The ChE level of the blood is greatly reduced. Normal ChE levels are 75-100% of a man's statistical preexposure value. Liver insufficiency can cause lowering of these figures.

The reserve capacity of ChE is of such a magnitude that symptoms only occur when there is less than 30 — 35% in the red blood cells.

The prognosis of patients with practically zero ChE activity is by no means poor when vigorous treatment is started as quick as possible.

Treatment

(1) Artificial respiration preferably with a mechanical respirator is life saving, including clearing of the airway passage by suction. Mouth-to-mouth breathing is prohibited. A serious poisoning has occurred to a doctor who applied mouth-to mouth breathing in a case of parathion poisoning.

(2) If O.P. has been spilled on the skin, wash immediately with soap and water.

(3) If needed and the patient is conscious, induce vomiting or gastric lavage.

(4) Administer atropin sulfate 0.04 mg/kg B.W. intravenously and repeat every 10-15 minutes until complete atropinization is accomplished, which includes flushing of the face, tachycardia, dry skin, diminished bowel-sounds, decreased secretion of saliva, and mild midriasis.

When atropinization is adequate, coma and labored breathing will usually be overcome. The patient should be watched constantly, as within a few hours the signs may reappear and further atropinization may be required. There is no maximum dose for atropine, dosage should be guided by reappearance of signs and symptoms. Atropine will restore respiration, muscarinic and central signs; while convulsions or paralysis are not affected.

(5) Some oximes have the ability to regenerate the phosphorylated ChE. There are: 2-PAM iodide (2-pyridine-aldoxime-methiodide) or Protopam or pralidoxime iodide; dia-

cetyl monoxime (DAM) and 1,1-trimethylene-bis-(4-formyl pyridinium bromide) dioxime (TMB-4).

Pralidoxime is the most widely used, in conjuction with atropine. The dose is 10-20 mg/kg B.W. administered slowly intravenous. This dose may be repeated several times at 20-minute intervals when paralysis is not adequately affected. There is no benefit if pralidoxime is administered after more than 36 hours because of a dealkylation process which is called "aging".

Carbamates

Carbamate insecticides (such as Carbaryl) resemble prostigmin in structure and are reversible ChE — inhibitors. Unlike prostigmin, they are very well absorbed through the intact skin, inhalation or digestive mucosa.

All the actions and toxic properties are like those of the O.P.'s, but are usually of more sudden onset and less prolonged. Because ChE-depression is not persistent there is less danger of cumulative effects.

Blood- cholinesterase determinations are of little use as the carbamylated enzyme very rapidly dissociates. Treatment consists of the measures taken for O.P.'s with the exception that 2- PAM is **not** required. Atropinization is reached with a smaller total dose and relapse after atropinization occurs less frequently.

Warfarin

Warfarin, a hydroxycoumarin derivative is a slow-killing rodenticide used as bait. It acts by inhibition of prothrombin formation and capillary damage. The ingestion of about 1-2 mg/kg bodyweight per day for about 15 days has resulted in serious illness of 14 persons of whom 2 died.

Finished bait usually contains 0.025% active material.

Clinical picture

The inhibition of prothrombin only becomes apparent if the reserves in the body are consumed. Owing to this fact bleedings occur after repeated ingestions or a single massive dose, usually after a few days or weeks. When massive doses are ingested abdominal pain is evident directly.

Bleedings usually start as epistaxis, intestinal bleeding and petechial rash. These become worse and involve larger areas like in ecchymosis or hematomas and massive bleedings especially at the elbows, knees and buttocks. Hematuria may be present. Complicating phenomena are cerebral hemorrhage and hemorrhagic shock.

Laboratory findings

The principal detectable change is the demonstration of reduced prothrombin activity in plasma. The blood-clotting time and bleeding time

may be prolonged, but not necessarily. Also blood may be demonstrated in urine and feces.

Treatment

Vitamin K is a specific antidote and should be given 1 mg/kg B.W. three times on the first day of treatment. Afterwards smaller doses should be continued until prothrombin time becomes normal.

Shock should be treated by frequent small transfusions with fresh whole blood.

Any bruises or other trauma must of course be avoided, to minimize bleeding.

Paraquat

Paraquat is a weedkiller, marketed under different names, like "Gramoxone", "Gramixel" and "Weedol". The fluid-concentrate contains 20% paraquat and is extremely toxic, while the 5% granular form is considerably less toxic. It has an unpleasant taste, so that if ingested accidentally it will almost immediately be rejected. In spite of this, deaths have been reported, indicating the high toxicity of the concentrated product.

Clinical picture

A burning sensation in the mouth and abdomen is immediately felt and ulceration of the mucous membranes occurs within a few days. A few days to a week after ingestion an irreversible proliferative alveolitis and bronchiolitis become evident clinically, while X-ray of the lungs reveals granular patches. Renal failure may develop during the course of the intoxication as well as hepatic parenchymal jaundice.

Treatment

So far most forms of treatment have been failures with the exception of peritoneal dialysis which has had some limited success. Early forced diuresis may be tried before renal failure ensues, but seemingly the lung-changes develop at the first passage of paraquat through the lungs. Cortisone has been shown not to be effective.

A lung transplant has been tried, but the patient died two weeks later, probably because paraquat was still circulating in the blood after the successful operation. An attempt may be made to inactivate unabsorbed paraquat by administering orally Fuller's earth as a 30% suspension or bentonite as a 6-7% suspension.

Arsenicals

There are two forms of oxides of arsenic, the trioxide and the pentoxide. Both form acids with water and produce their corresponding salts. Applications of arsenicals in agriculture are as rodenticides

(As_2Q_3), and herbicides (arsenite and arsenate). The use as insecticidal baits are not populer.

All arsenical pesticides are general protoplasmic poisons and act by binding sulfhydryl groups. Enzymes like pyruvate oxidase and phosphatases are hereby inhibited and impair tissue respiration. It is an irritant to the mucous membranes of the digestive tract regardless of its site of absorption, whether from oral ingestion or inhalation.

Damage to the capillaries is a pronounced manifestation, causing dilation and increased permeability. These in turn will cause congestion of blood, trombosis, ischemia and finally necrosis of tissues affected.

The fatal dose is around 1 mg/kg B.W. of arsenic trioxide; finer dispersion will cause greater absorption and toxicity.

Clinical picture

Arsenic pesticides-poisonings are almost always acute and often involve children. Abdominal pain, vomiting and diarrhea resembling cholera are the most important signs. Dehydration is the result of profuse fluid-loss.

If the patient survives, usually after 3-14 days, exfoliative dermatitis and polyneuritis with transverse bands on the nails are found as sequels. Liver and renal degeneration may be noted, and rarely cardiac involvement.

Laboratory findings

Although normal people have arsenic in their body and excrete it in their urine (as high as 0.17 ppm as As_2O_3), poisoning cases definitely show a higher concentration in urine, blood or tissue levels. Urinary arsenic concentrations in poisoning are in the order of 4-6 ppm per day.

Liver and renal function tests may show abnormality and the urine may contain albumin and hemoglobin.

Treatment

As with all types of acute poisoning, gastric lavage is indicated when the poison is ingested not more than 4 hours previously and the patient is not unconscious.

Symptomatic treatment should be mainly instituted towards dehydration with saline infusions. Dimercaprol (BAL) as 10% solution in oil is a specific antidote and acts by chelating As into a more soluble complex, so that excretion through the kidney is enhanced. BAL is given intramuscularly at the following schedule:

first 2 days: 3 mg/kg B.W. every 4 hours.

third day: 3 mg/kg B.W. every 6 hours.

there after: 3 mg/kg B.W. twice daily until recovery.

Pentachlorophenol

Pentachlorophenol (PCP) is soluble in various fat solvents, but the sodiumsalt which is more often used, is freely soluble in water. Applications in agriculture are as weedkiller, defoliant and wood-preservative. The last mentioned is applied in Kalimantan for preservation of very inferior sorts of wood. The dipfluid consists of :

5 kg sod. pentachlorophenate 26%
1 kg Lindane 26%
1½ kg borax
} in 200 1 water

Of these ingredients PCP is by far the most toxic. It has a lethal dose of about 5-50 mg/kg B.W. Poisoning has occurred through absorption by the skin, inhalation or ingestion.

The main action in man is the uncoupling of oxidative phosphorilation so that the metabollic rate is increased markedly, resulting in a rise of body temperature. So far all PCP intoxications were either suicidal or occupational and for this reason involve only adults. Pediatric cases however could show up as an accident or the involvement of children in such work.

Clinical findings

The onset of critical illness is acute and the course progressive. Cumulation however can preceed this sudden illness without other warning than aspecific symptoms like weakness, anorexia and headache.

Tightness in the chest, sweating and dehydration may be marked and the temperature frequently goes up very high which differentiates this condition against O.P. poisoning. Since PCP resembles phenol, acidosis is a prominant finding. Coma occurs very early in severe poisoning.

Laboratory findings

Nothing conclusive could be detected in the ordinary laboratory investigations. PCP can be detected in urine and blood and in fatal cases urine levels have ranged from 55 — 96 ppm.

Treatment

Treatment is purely symptomatic directed towards fluid and electrolyte balance and the lowering of body temperature with ice packs. Atropine is contra-indicated.

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