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Review Paper

Antidotes for Pesticide Poisoning: A Review

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Pesticide poisoning kills hundreds of thousands of people in India each year. The majority are from deliberate self-poisoning with Organophosphorus pesticides (OP), Aluminium phosphide and Paraquat. The current response from a public health, medical and research perspective is inadequate. There are few proven or effective treatments; in addition, very little clinical research has been done to transfer antidotes shown to work in animal studies into clinical practice. The human toxicity of pesticides is poorly studied and better information might inform a more sustained and appropriate regulatory response. Further understanding may also lead to improvement in diagnosis and treatment. The few effective treatments are not being recommended or delivered in an optimal and timely fashion to poisoned patients. A regional approach to facilitate appropriate pricing, packaging and delivery of antidotes is required.

Key words: Antidotes, Atropine, Pesticide, Organophosphorus, Poisoning, Paraquat.

INTRODUCTION

Self-poisoning with pesticides is a major problem. It is estimated that hundreds of thousands of people die each year, the majority from deliberate self-poisoning with organophosphorus pesticides (OP) [1]. Aluminium phosphide and paraquat are also responsible for many deaths in some areas. Although, the number of deaths indicates that this is a major public health problem, of the same order of magnitude as diabetes or HIV in many countries in the region, there is little coordinated effort being applied to improve the medical response to this problem. Only one antidote, atropine for OP poisoning, could be regarded as being of proven effectiveness.

In this article we will describe further the requirements antidotes need to meet in order to be useful in practice and our experience with running clinical trials on pesticide antidotes in India. We will then argue the case for more translational research to progress antidotes that have been shown to be effective in animals into human trials and the need for research and planning for how best to provide and use these antidotes in the resource poor rural areas of Asia where pesticide poisoning is most important[2].

Pesticides, most frequently used in accidental/deliberate intoxication globally; there is a scarcity of information on the magnitude of both intentional and unintentional poisoning, as well as on the relative importance of different pesticides. This information is particularly lacking from most of Africa, and detailed and accurate community-based data on the pesticides responsible for fatal self-harm are not available for most of rural Asia. Sentinel centers, that would need to be identified and supported, could provide this information from across the world. At any rate, it is known that the pesticides that cause most deaths in rural Asia, and in the world, are WHO Class I and II organophosphorus pesticides - causing an estimated 200,000 deaths[3].

At any rate, in rural Asia, the variety of pesticides available in communities for intentional or unintentional poisoning are large, reflecting the pesticides used in local agriculture. Studies from Sri Lanka suggest that less than 20% of pesticides used for self-harm 10 are bought for the purpose; the majorities are freely available in the home or nearby garden. The vast majority of these deaths are intentional; unintentional oral or dermal exposure to WHO Class I OP pesticides can cause severe poisoning, but the doses are usually smaller than with intentional poisoning, resulting in fewer deaths. WHO Class II OPs are generally less toxic in unintentional poisoning. Where Class II OPs are the most commonly used insecticides, unintentional poisoning is generally less likely to cause severe poisoning. Class II OPs are highly toxic in intentional overdose. Other classes of pesticide that are common causes of significant and/or fatal poisoning include carbamate and organochlorine insecticides, the fumigant aluminium phosphide (a significant problem in north India), and the herbicide paraquat. Less common causes of significant poisoning include the herbicides chlorphenoxy acetic acid derivatives and propanil, some pyrethroid insecticides, avermectins, and amitraz[4]. The locally available pesticides will also determine how many poisoned people

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survive to hospital presentation. In areas where highly toxic, fast acting WHO Class I organophosphorus (OP) pesticides are used, the onset of poisoning can be so fast that many people die before they can be taken to hospital. By contrast, where slower acting pesticides are used, more patients will survive to reach hospital and medical care. The case fatality for different pesticides also varies markedly, from around 70% for both aluminium phosphide and paraquat, to close to 0% for many of the newer lower toxicity pesticides[5]. Therefore, hospital statistics, whether from primary or secondary hospitals, must be interpreted in light of this difference. More than half of global deaths from pesticide poisoning occur in China, where currently, the WHO Class I OP pesticides are the major problem, but where five Class I OPs (methamidophos, methylparathion, parathion, monocrotophos, phoxim) have been recently banned. This was expected to reduce the number of poisoning deaths in China, and has since been associated with a possible 10-15% fall in overall suicide rates in women. In China, some deaths occur from pesticides that are considered to be generally safe in poisoning. More recently developed pesticides are generally safer than the older pesticides still used widely in low- and middle income countries. While the main international pesticide industry would be keen to sell the newer pesticides, it is likely that the generics and black market industry that is particularly active in low- and middle income countries would not change their sales[6].

Signs and Symptoms of Pesticide Poisoning: General

Pesticide poisoning can mimic the signs and symptoms of other common diseases. It is important to find out exactly what happened. Pesticide poisoning is likely only when a person is known to have had recent exposure to pesticide. The person may be wearing soaked clothing or known to have swallowed pesticide, either accidentally or deliberately. All cases should be seen by a doctor as soon as possible. It will be important for the doctor to know the pesticide to which the person has been exposed. If the container is available, send it to the poisoned person for the doctor to see. Otherwise, copy the trade and approved names of the pesticide from the label. The label may include important notes on the treatment of poisoning, which should be followed[7].

- Pesticide poisoning can affect the body in two ways: it can cause a local reaction when a pesticide comes into contact with exposed parts of the skin or eye, or it can be absorbed into the body and cause a systemic reaction. Local reactions vary from direct irritation following a single contact to allergic reactions, usually after multiple contacts with the same compound. Pesticide poisoning is the appearance of systemic reactions[8].
- Always check first if the poisoned person is breathing and has a pulse. If necessary, start resuscitation immediately, and do not waste time getting the information above. However, someone else should be asked to find the name of the pesticide, as it is important that proper antidotes be used for some types of pesticide poisoning[9].

Signs and Symptoms of Organophosphorous Poisoning

Poisoning by organophosphorous insecticides is the commonest form of pesticide poisoning, and needs immediate treatment.

ONSET: 1/2 - 24 hours after exposure

At first:

- The person feels sick
- Complains of headache
- General weakness or tiredness

Then:

- The person begins to sweat and salivate (water in the mouth), may vomit and have diarrhea
- Complains of stomach cramps
- Pupils (of the eyes) become very small
- The person may mention blurred vision
- Muscles twitch, and hands shake
- Breathing becomes bubbly
- The person has a fit and becomes unconscious

Signs and Symptoms of Carbamate Poisoning

Carbamate insecticides have the same action as the organophosphorous compounds, but they are much faster in onset, and recovery is much faster. If a person is applying these compounds and does not take the proper precautions, symptoms will occur very quickly and work stoppage. Soon after exposure ends, the person will start to feel better, unless still absorbing pesticide from contaminated skin or clothing[10].

ONSET: Sometimes at work - 3 hours after exposure

At first:

- The person feels sick and may vomit
- Complains of headache and dizziness
- Tiredness and tightness in chest

Then:

- The person may begin to sweat and salivate
- May mention blurred vision
- Muscles may twitch
- Rarely, a person may have a fit and become unconscious

The management of pesticide poisoned patients at various levels of health care

In putting together the following elements of guidance for health care workers at different levels of the health care system, the experts who participated in the meeting considered previously released guidelines, some of which were produced by WHO, literature reviews, publications, and their extensive experience and expert knowledge in this area. Basic elements Respiratory failure is the primary cause of death following the ingestion of pesticides, either due to specific anti-cholinesterase effects of OP and carbamate poisoning, or - for all pesticides - the non-specific complications of aspiration. Also, much aspiration results from poor initial care of the patient and/or unsafe gastric decontamination. Therefore, the two basic elements of the clinical management of acute intoxication with pesticides are airway management and antidote administration[11].

The ABC of supportive care - Airway, Breathing, and Circulation - is crucial. It is not possible to over-emphasize the

need to apply the basic treatment correctly, to tailor treatment to the patient, to evaluate the need for gastric decontamination, and to give antidotes early. In emergency medical treatment the initial management is pivotal, yet, in spite of a great variation in initial management, with no standardization, the basic principles of initial resuscitation and assessment are often applied only after gastric decontamination for which there is currently no evidence of benefit (American Academy of Clinical Toxicology and European Association of Poison Centre's and Clinical Toxicologists, 2004 a, b[12].

Information on safe airway management and intubation should be part of the basic training of any health worker and included in any document on management of emergencies published by health agencies and authorities. Gastric lavage the importance of iatrogenic deaths as shown by the number of deaths occurring after ingestion of low toxicity pesticides needs to be emphasized13. The role of inappropriate gastric decontamination in these deaths is important. There is a need to tailor treatment to the poison and the patient; for example, if a person has ingested a low toxicity pesticide 12 and does not show clinical features of poisoning, it may be best to only observe and support the patient rather than carrying out gastric decontamination and giving antidotes[13].

There is much discussion about the use of gastric lavage or forced emesis compared to activated charcoal in pesticide poisoned patients. Recent studies indicate that single or multiple doses of activated charcoal are safe in pesticide poisoned patients, including patients receiving appropriate amounts of atropine. By contrast, both forced emesis and gastric lavage have potential serious complications if performed in nonconsenting patients or unconscious patients without airway protection However, in light of the absence of direct data showing the benefits of charcoal over other forms of gastric decontamination, it is difficult to make a strong recommendation. Overall, if a patient presented within one hour to a health care facility, the administration of activated charcoal should be considered if the patient is conscious and gives consent. The patient should not be forced to accept the charcoal. Forced emesis is not recommended. Oral fluids should not be given[14].

Pesticide poisoning and suggested therapies

Some common brand name chemicals containing organophosphate compounds include Bidrin, Thimet, Orthene, Dursban, and Guthion. Common chemical names for organophosphate active ingredients include methyl parathion, ethyl parathion, malathion, and chlorpyrifos. Organophosphate insecticides affect people in much the same way they affect insects -- the nervous system is damaged and breathing becomes difficult. Symptoms of acute organophosphate poisoning usually appear within 4 hours of the exposure. Common, early symptoms may include headache, nausea, and dizziness. The victim may also appear anxious and restless. The later symptoms of a worsening condition are muscle twitching, weakness, abdominal cramps, and vomiting. Sweating, salivation, and tearing are often seen. Dark or blurred vision and constricted pupils are other symptoms that may occur. Tightness of the chest and coughing may lead to respiratory depression, or the lungs may fill with fluid. Either way, without immediate medical attention, the victim may die. Two antidotes doctors use for treating organophosphate poisonings are atropine and 2-PAM. Large doses of the antidote may be needed for a severe poisoning, and follow-up doses may need to be given for several hours to several days[15].

Ingredients in LBAM butylated hydroxytoluene (World Health Org)

Butylated hydroxyanisole (E 320) & Butylated hydroxytoulene (E 321) are two antioxidants listed as possible cancerogenic substances, according to WHO's cancer research tricaprylyl methyl ammonium chloride, Potential Acute Health Effects: (from MSDS data) Extremely hazardous in case of skin contact (irritant), of eye contact (irritant), of ingestion, of inhalation (lung irritant). Hazardous in case of skin contact (corrosive, permeator). Inflammation of the eye is characterized by redness, watering, and itching. Skin inflammation is characterized by itching, scaling, reddening, or, occasionally, blistering. polyvinyl alcohol: (MSDS data) Potential Acute Health Effects: Slightly hazardous in case of skin contact (irritant), of eye contact (irritant), of ingestion, of inhalation. Sodium phosphate, immediate effects: Inhalation of this product may be irritating to the nose and throat, causing coughing and choking. Ingestion of large amounts may cause diarrhea, nausea, vomiting and cramps. It may cause eye and skin irritations. Potential health effects: Primary Routes of entry: Inhalation, ingestion or skin absorption. Signs and Symptoms of Overexposure: Dermatitis may develop from repeated or prolonged skin contact. Eyes: Irritating. Skin: Irritating. Ingestion: Nausea and vomiting. Inhalation: Irritates the nose and throat and may cause coughing and chest discomfort. Chronic Exposure: Dust may aggravate existing pulmonary conditions and/or asthma. A Chemical Listed As Carcinogen Or Potential Carcinogen[16].

Allopathic recommendations for pesticide poisoning

Skin decontamination is accomplished with a shower using soap, large amounts of water, and shampoo. Skin folds, areas underneath fingernails, ear canals, and other portions of the body that may trap chemicals should be inspected and cleaned carefully. Contact lenses should be removed, so the eyes can be inspected and irrigated thoroughly if exposure is suspected. Contaminated clothing should be removed, bagged, and laundered carefully. Leather items usually cannot be decontaminated and should be bagged and treated as hazardous waste. – Gastric lavage Consider if the patient presents within 60 minutes of ingestion. Insert orogastric tube.

Attempt aspiration first, followed by 100 to 200 ml normal saline, then aspiration. Relatively contraindicated in hydrocarbon ingestion it is indicated only when the potentially life-threatening amount of poison is ingested and the procedure can be done within 60 minutes of ingestion. Cathartics used only in combination with activated charcoal Sorbitol (1 to 2 ml/kg or 70 percent solution in adults, 1.5 to 2.5 ml/kg of 35 percent solution in children) Single dose only Not recommended in poisonings that produce diarrhea (organophosphates, carbamates, heavy metals in particular) or those that produce ileus (paraquat and diquat) If it is used, it should be as a single dose. Numerous contraindications: absent bowel sounds, abdominal trauma or surgery, intestinal perforation or obstruction, volume depletion, hypotension, or ingestion of a corrosive substance[17].

First Aid Treatments

If the poison has been inhaled, as in the case of toxic fumigants, the patient should be removed to the open air and given artificial respiration. If the poison has been spilled on the skin, it should be washed off immediately with large amounts of

warm soapy water, scrubbing the skin thoroughly. Drop or particles in the eyes should be removed by flushing with large quantities of plain water[18].

If the poison has been swallowed, the stomach of the affected person should be emptied as soon and as completely as possible. After this has been done, a demulcent such as raw eggs, milk or a thin flour paste can be given. These serve to absorb the poison, and to soothe the irritated membranes. If the specific poison is known, the following emergency treatments could be given.

Acids

Limewater or milk of lime, milk of magnesia should be given, arsenic Compounds. After emptying the stomach, raw eggs, milk, lime water, flour, and water, or sweet oil should be given.

Benzene Hexachloride

Tea or coffee and gypsum salts may be given after the stomach has been emptied. Chloroans, same treatment as benzene hexachloride. The same treatment as for benzene hexachloride

Mercury Compounds

Raw egg and milk should be given immediately.

Nicotines

After emptying the stomach, stimulants such as hot tea or coffee should be given. Parathion after emptying the stomach has a physician administer 1/30 to 1/60 grain of atropine sulfate at hourly intervals, until pupils dilate.

Tetraethyl Pyrophosphate

The same treatment as recommended in the case of parathion may be given. The following information will also be useful in this connection.

IS: 4015 (Part I) 1967:

Provides information with regard to the first aid measures that are necessary to be taken in cases of pesticide poisoning before a physician attends the case.

IS: 4015 (Part II) 1967:

Outlines the basic information intended for the use of physicians with regard to the symptoms, differential diagnosis and treatment in relation to poisoning due to different types of pesticides and their formulations during their use in a laboratory, field or a factory.

Pesticide Disposal

There are a number of methods available to tackle the problem of disposal of surplus pesticides, but they are not always satisfactory for all types of materials. The methods, presently in practice, include thermal decomposition, chemical neutralization, burial and biological degradation.

Thermal Decomposition

This method requires exposure of the pesticide to a high temperature (900-1000 °C) for varying periods of time. This method is satisfactory enough as it degrades about 98% or even more of most of the commercial pesticide formulations[14]. The exposure time should be sufficient so as to ensure complete decompositions, and care must be taken to remove air pollutants before the gases are discharged into the atmosphere.

A wet scrubber and filtration through a porous clay bed and carbon filter, with lagoon treatment of the waste water, are suggested. Mercury, arsenic, lead and similar toxic compounds should not be incinerated unless special residue handling and disposal facilities are available.

Chemical Neutralization

This is feasible for most of the organophosphates and carbonate insecticides, but not for the chlorinated hydrocarbons. Various chemicals used to destroy the pesticides are nitric acid, sulfuric acid, ammonium hydroxide, sodium hydroxide, chlorine compounds, peroxides or other types of active chemicals. Calcium hydrochloride seems to have the broadest application. A strong acid or alkaline hydrolysis does not provide complete treatment[19].

Burial

Burial is susceptible to contamination of waters and ground waters from leaching and run off on pesticides. Careful shallow burial with 18 inches of earth for small quantities of pesticides in clay soil is generally acceptable until a better method is developed.

The location should be well above ground water level, downgrade, and several hundred feet from any source of water supply and they should also be beyond the reach of children and animals. The burial of pesticides in sandy soils is not recommended as it has greater possibility of leaching into surface water or ground water[20].

Biological or Natural Degradation

This method is satisfactory for short lived materials while for other more persistent materials, the rate of degradation is too slow. The persistence of some pesticides in soils is given in proper facilities are available, surplus pesticides and containers should be disposed of as described above.

Lead, Copper, Arsenic Dieldrin, BHC, DDT insecticides Triazine herbicides Urea herbicides Benzoic acid herbicides 2, 4-D: 2, 4, 5-T Herbicides Organophosphorous insecticides Carbamate (Carbaryl) insecticides[21-22].

Conclusion

As stated earlier, in spite of the short term advantages of pesticides, they may create serious health hazards to human beings in the long run. The fourth report of the Council of Environmental Quality of the USA, published in 1972, has virtually banned the use of DDT because this chemical, being highly persistent, enters the food chain of innumerable forms of life which results in a total dislocation of the balance of nature[13, 26].

Unfortunately, the use of DDT is increasing in India, day by day. Total consumption of pesticides per year is given in at present, about 4000 tonnes of DDT are manufactured in India

and an equal quantity is imported, mainly for malaria control. Apparently the malaria carrying mosquito, Anopheles culcifacious, has become resistant to many kinds of insecticides[18, 23].

The universe of cultivated crops often overlaps the habitats of insects responsible for transmission of human diseases. This is particularly true in the case of the mosquito popu-lation, which breeds in diverse water bodies in all types of situations. Repeated application of different pesticides ensures exposure of genera of these insects of speedy selection for resistance to the pesticides used. Increase in malaria during the last few years has obviously made it necessary to plan for a much greater use of DDT. Attempts are being made to find alternatives to DDT like Methaxsichlor, which, unlike DDT, is quickly degradable. An ideal pesticide is Pyrethrum which is extracted from the flowers of a plant grown widely in India. Pyrethrum is most effective, and being a natural insecticide, is completely harmless to the environment. Attempts are being made to grow Pyrethrum in Kashmir and Tamil Nadu, but, as yet, the output is very limited[24, 25].

Biological control is, of course, the best way of dealing with pests. This involves the use of bacteria, virus and other pathogens which attack or by the use of predators or parasites or both. A lot of work is yet to be done in this field, and according to the Indian Council of Agricultural Research, there has been considerable success in some fields. The most suc-cessful of these was the almost total eradication of the prickly pear, opuntia spp which had, like many toxic plants, proliferated widely over the countryside in India, and was a great menace for many years.

The Indian station of the Commonwealth Institute of Biological Control situated in Bangalore is attempting to find natural enemies of a number of pests, but this work is at a very early stage. The extensive use of pesticides could have an adverse effect on soil fertility and on crops.

The growing requirement for the use of pesticides is obvious. But the harmful effects of pesticides with higher persistence suggest the necessity for development of pesticides which are biodegradable[25].

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