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Introduction to Poisoning; A Systematic Review

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Review Article

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Introduction

Poison

The term poison was derived from Latin word “potionem” a drink; i.e.,drink, eat, breathe, inject or touch enough of a chemical (also called a poison or toxin) to cause illness or death or poison is derived from Greek word ‘Toxicon’ which means ‘Poison’. A poison is any substance that is harmful to the body when eaten, breathed, injected or absorbed through the skin. Any substance can be poisonous if enough is taken.

Poisoning

Poisoning is an important health problem in every country of the world. Occupational exposure to industrial chemicals and pesticides, accidental or intentional exposure to household to pharmaceutical products and poisoning due to venomous animals, toxic plants and food contamination, all contribute to morbidity and mortality (Lall S.B et al., 2003). The danger of poisoning range from short-term illness to brain damage, coma and death. Some poisons in very small amounts can cause illness or injury. Some poisons cause immediate injury, such as battery acid or household cleaners. Other poisons may take years of exposure to create a health problem, such as heavy metals (lead, arsenic, mercury). The Centers for Disease Control and Prevention (CDC) defines a poisoning that occurs by accident as "unintentional poisoning" and a poisoning that results from a conscious, will full decision (such as suicide or homicide) as "intentional poisoning" Unintentional poisoning includes the use of drugs or chemicals for recreational purposes in excessive amounts, such as an overdose. Unintentional poisoning also includes the excessive use of drugs or chemicals for non-recreational purposes, such as by an infant or child. Intentional poisonings include suicide, such as medication over dosage (B.R. Sharma et al., 2007). Young children are particularly vulnerable to accidental poisoning in the home, as are elderly people, often from confusion. Hospitalized people and industrial workers are also vulnerable to accidental poisoning by drugs errors and from exposure to toxic chemicals, respectively (Tanuj kanchan et al., 2008). The damage caused by poisoning depends on the poison, the amount taken and the age and underlying health of the person who takes it. Some poisons are not very potent and cause problems only with prolonged exposure or repeated ingestion of large amounts. Other poisons are so potent that just a drop on the skin can cause severe damage.

Categories of Poisoning

Poisoning is divided in to 4 broad categories:-

Pharmaceuticals: Paracetamol, Aspirin, Benzodiazepines, Phenytoin, Tricyclic Antidepressants, Barbiturates, Opioids etc.

Insecticides and pesticides:
Organophasphate, Chlorine, Pyrethroids, Superwarfarin, Furadon, Parathion And Endosulphan.

Plants and Animals: Snake or Scorpian bite, Bees or Wasps sting, Insect sting, Oleander, Dhatura and Oduvanthalai.

Chemicals:

- Inorganic: Mercury, arsenic, lead, copper, Sulfur and Hair Dye (Paraphenylenediamine).
- Organic: Rotenone, Pyrethrum, Nicotine and Neem Oil.
- Biological: Bacteria and viruses (Salmonella, Norovirus, Norwalk Virus, Campylobacter, E. coli, Listeria, Clostridium perfringens).

Most of victims of travel related poisoning were businessman (67.56%) rest were normal and domestic travelers (16.21%) and few were service holder (10.81%) (Howlader Mar et al., 2008). Some other victims take poisonous material easily available in the household or at work place like rat killer (superwarfarin), mosquito repellant (pyrethroid) ant killer (gamma hexene), organo compounds (furadon, parathion, endosulphan). They also takes drugs which are available at house (either taken by them or house members) like alprazolam, diazepam, phenytoin, barbiturates, paracetamol, aspirin etc. since all the drugs are easily available over the counter, we also see lot of multidrug over dosage especially combination of antibiotics, analgesics and antihistamines.

Figure 1.1: Multiple tablets (Overdose)

Pesticide poisoning

It is a major public health problem in developing countries particularly in setting in low education and poor regulatory framework. Pesticide usage in South Africa, both agricultural and non agricultural has increased substantially in the past decade and this country is the largest market for pesticides for sub Saharan Africa (Leslie London and Ross Bailie 2001).

Figure 1.2: Insecticides and Pesticides

Organophosphate Poisoning

It is one of the commonest poisons consumed, as it is easily available. Among the organophosphorous compound, methyl parathion (metacid) is the most commonly used the other compound is Dichlorovos (nuvan) (Bhattarai MD et al., 2006). Organophosphorus poisoning occurs very commonly in southern India, where farmers form a significant proportion of the population who commonly use Organophsphorus compound like Parathion as Insecticides. Thus, due to the easy accessibility of these compounds, a large number of suicidal cases are encountered in this region (Subhash Vijay Kumar et al., 2011).

Figure 1.3: OPC Poisoning Substances

Most toxic compounds are Endosulphan, methyl parathion, malathion, oleander seeds (in higher doses), Dhatura, Zinc sulphide and Phosphide. Less toxic compounds are Gammahexene, Pyrethroids and Superwarfarin.

Figure 1.4: Oleander Seed and Dhatura Fruit

Snakes

These are found all over the world except in the arctic, New Zealand and Ireland and are more commonly distributed in temperature and tropical

countries. Snakes are most likely to bite human beings when they feel threatened, startled or provoked and have no means of escape cornered. The Deccan plateau, with its agricultural land and hot, dry climate provides an ideal environment for cobras, kraits and vipers (Inamdar et al., 2010).

Figure 1.5: Snake poison

The most common symptoms of all snakebites are overwhelming fear, which may cause symptoms such as nausea and vomiting, diarrhea, vertigo, fainting, tachycardia and cold, clammy skin. Dry snakebites and those inflicted by a non-venomous species, can still cause severe injury. There are several reasons for this snake bite area may become infected with the snake's saliva and fangs sometimes harboring pathogenic microbial organisms, including Clostridium tetani. Infection is often reported with viper bites whose fangs are capable of deep puncture wounds. Bites may cause anaphylaxis in certain people. Most snakes bites, whether by a venomous snake or not, will have some type of local effect. There is minor pain and redness in over 90 percent of cases, although this varies depending on the site. Bites by vipers and some cobras may be extremely painful, with the local tissue sometimes becoming tender and severely swollen within five minutes. This area may also bleed and blister and can eventually lead to tissue necrosis. Other common initial symptoms of pit viper and viper bites include lethargy, bleeding, weakness, nausea and vomiting. Symptoms may become more life-threatening over time, developing into hypotension, tachypnea, severe tachycardia, severe internal bleeding, altered sensorium, kidney failure and respiratory failure. Snakebite is a common acute medical emergency faced by rural population in tropical and subtropical countries with heavy rainfall and humid climate. 35,000-50,000 people die each year from snake bite which is a common cause of morbidity and mortality in India (Subhash Vijay Kumar et al. 2011). Snake bite is a large problem of the rural area, where basic health facilities are poor and as a result death is common. The four families of venomous snake's atractaspididae, elapidae, hydrophidae and viperdae contain some 500 species; whereas the fifth family, the colubridae contain 40 species venomous to humans. Less than 200 species have caused clinically severe envenoming, ending in death or permanent disability (Atta Muhammad chandio, 2000). There are some 300 species of land snakes in Pakistan out of which 40 are poisonous. The commonest poisonous snake in Pakistan is cobra, viper and krait (Atta Muhammad chandio, 2000).

Figure 1.6: Snake bite

Food poisoning

It is defined as an illness caused by the consumption of food or water contaminated with bacteria and their toxins or with parasites, viruses or chemicals. The most common pathogens are Norovirus, Escherichiacoli, Salmonella, Clostridium perfringens, Campylobacter and Staphylococcus aureus.

Figure 1.7: Food poisoning

Hair dye poisoning

It is an emerging as one of the important causes of intentional self-harm in the developing world. Hair dyes contain paraphenylenediamine and a host of other chemicals that can cause rhabdomyolysis, laryngeal edema, severe metabolic acidosis and acute renal failure (J Emerg Trauma Shock. 2009 May-Aug). Hair dye and its constituent paraphenylenediamine (PPD) have been reported as accidental and intentional causes of poisoning

from developing countries in Africa and Asia. Ingestion of Super-Vasmol33 (Trade Mark), a common, inexpensive, emulsion based hair dye has been increasingly used for deliberate self-harm in India. The constituents of this dye are PPD, resorcinol, propylene glycol, ethylene-diamine-tetraacetic acid (EDTA) sodium, liquid paraffin, cetostearyl alcohol, phenol, sodium lauryl sulphate, herbal extracts, preservatives and perfumes. The combined effect of the individual toxicants results in significant morbidity and mortality (Augrah Chrispal et al., 2010).

Figure 1.8: Hair Dye Poisoning

Common Causes of Poisoning

- Pain killers
- Cosmetics or personal products
- Household cleaning products
- Sedatives, hypnotics and antipsychotics medicine
- Foreign bodies, toys and other objects

How to Poison Proof Your Home

Medicines: Keep medicines in their original containers, properly labeled and store them appropriately.

Carbon Monoxide (CO) Detector: Have a working carbon monoxide detector in your home. The best places for a CO detector are near bedrooms and close to furnaces.

Household Products: Keep products in their original containers. Do not use food containers like cups or bottles to store antifreeze, household cleaners or other chemicals or products.

Arts and Crafts: Some art products are mixtures of chemicals which should be kept in their original containers. They can be dangerous if not used correctly. Make sure children use art products safely by reading and following directions. Do not eat or drink while using art products. Wash skin after contact with art products. Clean equipment; wipe tables, desks and counters.

Kitchen: Wash hands and counters before preparing all food. Store food at the proper temperatures. Refrigerated foods should not be left out at temperatures above 400 F (50C). Use clean utensils for cooking and serving.

Outdoors: Know what poisonous snakes live in your area and wear proper attire (boots etc.) when hiking outdoors. Check the label on any insect repellent, most contains N-Diethyl meta Toluamide or Diethyltolumide (DEET), which can be poisonous in large quantities. Be sure that everyone in your family can identify poisonous mushrooms and plants. (U.S. Department of Health and Human Services).

The causes and type of poisoning vary in different parts of the world depending upon the factors such as demography, socioeconomics, status, education, local belief and customs. Many-civilian and industrial, accidental and deliberate (Budhathoki et al. 2009). The problem is getting worse with time as newer drugs and chemicals are developed in vast numbers. Today there are more than 9 million natural and synthetic chemicals, and the list keeps growing inexorably. However, less than 3000 of these cause more than 95% of the reported cases of poisoning. Some drugs causes poisoning were classified in one of eight categories as follows: medical drugs, corrosives, alcohol, organophosphate, insecticides, rat poison (superwarfarin), carbon monoxide (CO) and mushroom. The medical drugs were categorized in to eight subgroups as psychoactive drugs, analgesics, antibiotics, cardiovascular drugs, antiemetic, multiple drugs, others (hormones, vitamins, minerals, antidiabetics, anticholinergics and antihistamincs) or unknown (Ferruhniyazi et al., 2009).

Mechanism of Toxicity

There are several specific acting modes of toxic action:

Uncouplers of oxidative phosphorylation: Involves toxicants that uncouple the two processes that occur in oxidative phosphorylation i.e. electron

transfer and adenosine triphosphate (ATP) production.

Acetyl-cholinesterase (AChE) inhibitors: AChE is an enzyme associated with nerve synapses that is designed to regulate nerve impulses by breaking down the neurotransmitter Acetylcholine (ACh).When toxicants bind to AChE, they inhibit the breakdown of ACh. This results in continued nerve impulses across the synapses, which eventually cause nerve system damage. Examples of AChE inhibitors are organophosphates and carbamates, which are components found in pesticides.

Irritants: These are the chemicals that cause an inflammatory effect on living tissue by chemical action at the site of contact. The resulting effect of irritants is an increase in the volume of cells due to a change in size (hypertrophy) or an increase in the number of cells (hyperplasia). Examples of irritants are benzaldehyde, acrolein, zinc sulphate and chlorine.

Central nervous system (CNS) seizure agents: CNS seizure agents inhibit cellular signaling by acting as receptor antagonists. They result in the inhibition of biological responses. Examples of CNS seizure agents are organochlorine pesticides.

Respiratory blockers: These are toxicants that affect respiration by interfering with the electron transport chain in the mitochondria. Examples of respiratory blockers are rotenone and cyanide.

Mechanism of Organophosphates

These compounds are based on the irreversible inhibition of acetylcholinesterase (AChE) due to phosphorylation of the active site of the enzyme. This leads to accumulation of acetylcholine and subsequent over activation of cholinergic receptors at the neuromuscular junctions and in the autonomic and central nervous systems. The rate and degree of AChE inhibition differs according to the structure of the Organophosphate (OP) compounds and the nature of their metabolite. In general, parathion compounds are not significant inhibitors in their original form and need metabolic activation (oxidation) in vivo to oxon form. For example, parathion has to be metabolized to paraxon in the body so as to actively inhibit AChE. The toxic mechanism of OP pesticides differs from that of carbamates which inhibit the same enzyme reversibly and are sometimes useful as medicines (neostigmine, pyridostigmine) as well as insecticides (carbaryl). After the initial inhibition and formation of Acetylcholine esterase organophosphate (AChE-OP) complex two further reactions are possible: Spontaneous reactivation of the enzyme may occur at a slow pace, much slower than the enzyme inhibition and requiring hours to days to occur. The rate of this regenerative process solely depends on the type of OP compound. In general, AChE dimethyl OP complex spontaneously reactivate in less than one day whereas AChE diethyl OP complex may take several days and re-inhibition of the newly activated enzyme can occur significantly in such situation. The spontaneous reactivation can be hastened by adding nucleophilic reagents like oximes, liberating more active enzymes. These agents thereby act as an antidote in organophophate poisoning. With time the enzyme-OP complex loses one alkyl group making it no longer responsive to reactivating agents. This progressive time dependent process is known as ageing. The rate of ageing depends on various factors like pH, temperature and type of OP compounds dimethyl OPs have ageing half-life of 3.7 hours whereas it is 33 hours for diethyl OPs. The slower the spontaneous reactivation greater the quantity of inactive AChE available for ageing. Oximes by catalyzing the regeneration of active AChE from enzyme-OP complex reduce the quantity of inactive AChE available for ageing. Since ageing occurs more rapidly with dimethyl OPs, oximes are hypothetically useful before 12 hours in such poisoning. However, in diethyl OP intoxication they may be useful for many days.

A mode of toxic action is a common set of physiological and behavioral signs that characterize a type of adverse biological response. A mode of action should not be confused with mechanism of action, which refers to the biochemical processes underlying a given mode

of action. Modes of toxic action are important, widely used tools pollutants in eco-toxicology and aquatic toxicology because they classify toxicants or according to their type of toxic action. There are two major types of modes of toxic action: non-specific acting toxicants and specific acting toxicants. Non-specific acting toxicants are those that produce narcosis, while specific acting toxicants are those that are non-narcotic and these produces a specific action at a specific target site (Poadyal BP, 2008).

Physical Examination

- A physical examination usually includes:
- Inspection (looking at the body)
- Palpation (feeling the body with fingers or hands)
- Auscultation (listening to sounds)
- Percussion (producing sounds, usually by tapping on specific areas of the body)
- A complete physical examination should be performed to detect complications and to help with the diagnosis.
- Specific attention should be paid to vital signs, mental status (depressed or agitated), respirations (depressed, evidence of pulmonary edema or aspiration), pupils (size, reactivity, presence of nystagmus), skin (diaphoresis or abnormally dry, blisters), bowel sounds (increased or decreased).

Based on findings from physical examination, the clinician should specifically consider the presence of a Toxidrome (Guideline of Investigation of the poisoned patient, 2006).

Diagnosis

Consideration of poisoning in patients with altered consciousness or unexplained symptoms

- History from all available sources
- Selective, directed testing
- Identification of the toxin involved is based on history, physical examination and clinical course as well as selected diagnostic tests.
- Specific drug levels (as discussed below) may be helpful in confirming the diagnosis and in making management Decisions (Guideline of Investigation of the poisoned patient, 2006).

Diagnostic Tests

- Laboratory evaluation is indicated in the following cases:
- Any intentional ingestion
- When the ingested substance is unknown
- When the toxin has the potential to produce moderate to severe toxicity
- The patient has more than minimal symptoms

Additional Tests for an Intentional Overdose Include the Following:

- An electrocardiogram as a screen for poisoning with tricyclic antidepressants or other cardiotoxic agents (Tricyclics antidepressants cause widened QRS intervals and tachycardia).
- Chest radiographs are useful to detect pulmonary damage in patients with suspected aspiration, non-cardiogenic pulmonary edema or other lung injury.
- Abdominal radiographs are useful screening tools in patients who may have ingested radio opaque material such as lithium, iron, lead and other heavy metals. Drug packets and enteric coated compounds may also be detectable on plain films (Guideline of Investigation of the poisoned patient, 2006).

General management of poisoning

The general management of these cases is anticipatory and supportive and the importance of assessing airway, breathing and circulation cannot be over emphasized. If the airway can be protected, activated charcoal may be indicated to decrease absorption if the patient presents within 1 hour of ingestion. Whole bowel irrigation is rarely performed and occasionally endoscopic retrieval may be indicated for body stuffers. Urgent surgery may be required for body packers or stuffers and these cases should be discussed with surgeons early.

For any patients admitted with poisoning first their vitals has to be stabilized like protecting the

- Airway (oropahryngeal or nasopharyngeal airway)
- Breathing (nasal prong or face mask with venture or intubation and mechanical ventilation)
- Circulation (inotropes)

Any acute problem has to be treated like giving antiepileptic medication for patients with seizures in endosulphan poisoning. All patients should be given gastric lavage (except for corrosive poisoning with sulphuric acid, kerosene, paraffin and diesel). All patients irrespective of the time of intake of poison should be given activated charcoal for prevention of absorption of the drug and magnesium sulphate for increasing the motility and fastening the excretion.

Treatment goals

The basic goals for treatment of acute poisoning assess patient condition, symptoms and prognosis to study treatment pattern of poisoning. Assist an improvement in drug therapy and better patient care to analyze the patients admitted due to the poison with respect the socio-demographic profile, etiological agents used clinical aspects and outcome. The treatment of acute poisoning can be summarized in four points: life support, which involves common measures to treat any urgent and serious pathology, reducing absorption of toxin, increasing its elimination and the use of specific antidotes (Raquel Aguilar Salmeron et al., 2009).

Managing Common Complications

Complications of poisoning are relevant to clinical toxicologists for two reasons:

Organ toxicity affecting major organs such as the heart, respiratory tract, kidneys and liver present problems in assessment and management on a regular basis in poisoned patients.

Complications of poisoning may assist the clinician as poisons may produce specific syndromes based on their Pharmacological properties. Common complications of poisoning include depressed mental status, Coma and altered conscious state, seizures, delirium and agitation, hypotension, bradycardia and vomiting. Most of these can be treated empirically without knowl¬edge of the toxin involved and without specific antidotes. Management of these complications occurs with history, physical examination and specific laboratory tests (Guideline of Investigation of the poisoned patient, 2006).

Antidotes

An antidote is a substance which can counteract a form of poisoning. The term ultimately derives from the Greek “antididonai” i.e. "given against". The antidotes for some particular toxins are manufactured by injecting the toxin into an animal in small doses and extracting the resulting antibodies from the host animal’s blood. This results in an antivenom that can be used to counteract poison produced by certain species of snakes, spiders and other venomous animals. A number of venoms lack available antivenom and a bite or sting from an animal producing such a toxin often results in death. Some animal venoms, especially those produced by arthropods (e.g. certain spiders, scorpions, bees, etc.) are only potentially lethal when they provoke allergic reactions and induce anaphylactic shock; as such, there is no "antidote" for these venoms because it is not a form of poisoning and anaphylactic shock can be treated (e.g., by the use of epinephrine).

Some other toxins have no known antidote. For example, the poison Aconitine a highly poisonous alkaloid derived from various aconite species has no antidote and as a result is often fatal if it enters the human body in sufficient quantities. The use of antidotes may reduce the use of other medical resources needed for the treatment of poisoning, shorten hospital stay and even save of life. However, these drugs are not without side effects and in some cases, their economic cost is high. It is therefore necessary to evaluate the benefit and risk involved in the administration of antidotes.

Table 1.1 List of antidotes

S. NO	NAME	ANTIDOTE
1	Acetaminophen	N-Acetylcystein
2	Anticholinergics agent	Physostigma
3	Benzodiazepine	Flumazenil
4	Carbom monoxide	Oxygen, hyperbaric oxygen
5	Cyanamide	Amyl Nitrate, Sodium Nitrate, SodiumThiosulfate, Hydroxycobalamin.
6	Digitalis	Digoxin immune feb
7	Methanol Ethylene glycol	Femepizol
8	Heparin	Protamin sulfate
9	Lead	Dimercapto-succinic acid
10	Mercury arsenic gold	Dimercaprol
11	Methemoglobinemia	Methylene blue
12	Opiates	Naloxone, nalmefene or naltrexone
13	Organophosphomates, carbamates, cholinergics	Atropine, pralidoxime
14	Toxic Alcohols	Ethanol Drip, Dialysis Experimental trials underway on Enzyme Inhibitors.
15	Tricyclic Antidepressants	Sodium Bicarbonate
16	Barbiturates	Activated charcoal
17	Phenothaizine	Benztropine, procyclidine
18	Kerosene	Oxygen, antibiotics, steroids
19	Oleander seeds	Atropine,dopamine,epinephrine,isoprenaline
20	Isoniazid	Pyridoxine (vitamin B6)
21	Radioactive iodine	Potassium iodide
22	Snake, coral	Micrurusfulvius antivenin
23	Snakes (rattlesnakes, cotton-mouth, copperhead)	Crotalidae polyvalent antivenin Crotalidae polyvalent immune fab
24	Thallium	Prussian blue

- Antidotes are typically given after the patient has been stabilized and the diagnosis has been made. In certain cases, prompt administration of antidote is imperative.
- Glucose must be given immediately in hypoglycemia.
- Prompt administration of naloxone may avoid the need for endotracheal intubation in opiate overdose.
- Pyridoxine should be given as soon as possible for seizures associated with isoniazid overdose (Guideline of Investigation of the poisoned patient, 2006).

An antidote is a chemical that will counteract the effects of a poison. If administered soon enough and in sufficient quantities, an antidote can save the life of a human or animal that has been poisoned. Antivenom or antivenin is a kind of antidote for the venom resulting from the bite or sting of a poisonous creature. While many poisons have a known antidote, some are expensive and difficult to produce. If someone is known or suspected to have been poisoned, a poison control center will be able to determine the best course of action.

Most poisons and venoms are spread rapidly through the body by the bloodstream, so prompt medical attention is essential for the effectiveness of an antidote. Activated charcoal is used as the antidote for a wide range of poisoning cases. Ingested by the patient, it absorbs some poisons and prevents them from passing into the blood stream. Ethanol, insulin and sodium bicarbonate or baking soda is other well-known substances that serve as antidotes for some poisons.

Table 1.2 Newer Antidotes

Sr. No.	POISON	ANTIDOTES
1	Cardiac glycoside	Fab antibodies
2	Sympathomimetic drugs	Esmolol hydrochloride
3	Hypoglycemic agent (sulphonylurea)	Octreotide
4	Arcenic, lead, mercury	Succimer
5	Methanol, ethylene glycol	Fomepizole (4-methylpyrazole)
6	Cyanide	Hydroxycobalamine

Unfortunately, antivenoms are costly to produce and demand is low. The economics of the Pharmaceutical industry mean they are often not available in impoverished countries. Scientists have had some success in creating universal antivenoms by studying the DNA of venomous creatures. It is also possible to build up immunity to venoms and other poisons by regularly ingesting small quantities of the poison. This process is called mithridatism. (Raquel Aguilar Salmeron et al. 2009).

Conclusion

Acute poisoning is a common and urgent medical problem in our country. The mortality and morbidity due to poison can be reduced by the conducting educational programs, and various audio-visual presentations like how to prevent the poisoning in rural areas and providing counselling services and poison information service to the people. People involved in health care professional must be aware of pattern of the common poisoning agents as well as their emergency household management. Young adults should be educated about the hazards of chemical use, establishing a counselling center in each hospital. Tertiary care hospitals should establish a poison information center (PIC), which should be networked with other poison information center in India and to developed countries which can help in identifying the poison and managing the cases and providing information to the public regarding poison prevention.

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AUTHORS' CONTRIBUTIONS

Authors contributed equally to all aspects of the study.

PEER REVIEW

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CONFLICTS OF INTEREST

The authors declare that they have no competing interests.