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General Principles, Types, Diagnosis and Management of Poisoning

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Abstract **Review Article**

Poisoning is the last consequence of drug action that is harmful to the body. It may be due to overdose or prolonged use of a drug. Any substance that causes deleterious, unwanted and harmful effects on the body is called poison. Poisoning can be acute or chronic. Short time exposure of poison is called acute poisoning whereas repeated, long term or continuous is called chronic poisoning. In chronic poisoning, symptoms may not be seen after each exposure and may be seen after a long period. Poison can cause effects when they are orally taken, injected, swallowed, inhaled or even rubbed on the skin. Commonly observed poisons are pesticides, organophosphates, carbon monoxide, heavy metals, certain plants such as Datura, Cannabis, opium, etc. All of the drugs acting on the nervous system, cardiovascular system, peripheral nervous system, urinary system, and reproductive system can turn to poisons if used in excess quantity. Almost all categories of drugs are involved in one or other forms of toxic effects depending on the dose. Briefly, all drugs in excess can cause poisoning. The effect of poisoning is ranging from short term illness such as rash, diarrhea, seizures, dilated pupils, nausea to long term complications such as organ damage, coma or even death. Poisoning can be accidental, homicidal or suicidal. The diagnosis of poisoning is based on assessing clinical features history, physical examination and toxicological screening. Such toxic effects must be carefully monitored and treated immediately to save the life of a patient. Assessing the symptoms of poisoning, providing life support to maintain vital signs, elimination of poison, preventing further exposure of poison, and use of the antidotes are the basic principles of management of toxicity. With this background, it becomes essential and interesting to elaborate on the detailed study of poisoning and its management. The present review is therefore planned to know the types, nature, principle, diagnosis, effects and general management of poisoning.

Keywords: Poisoning, Datura, Cannabis, Homicidal, Opium.

INTRODUCTION

It has been documented that 1 million illnesses are due to poison. The incidence of poison in India is among the highest in the world. In India, due to toxic exposure, more than 50,000 people die every year. Commonest member in India which causes poisoning are pesticides (chlorinated hydrocarbons, organophosphates, carbamates, aluminium/zinc phosphide) sedatives, alcohol, plant toxins (datura, oleander, strychnos), chemicals (corrosive acids and copper sulfate), venomous animals, and household cleaning agents [1]. A poison is a substance that is harmful to life as it affects one or more vital functions of the body. Poisoning is an adverse effect from a chemical or drug that is taken in excess. A dose is that which distinguishes a drug from poison. The causes of poisoning are civilian, industrial, accidental or planned [2]. In most of the cases, our body tolerates or detoxifies the amount of harmful chemical which we have ingested, but if the peak is reached then the body shows certain toxic symptoms. Poisoning can produce minor to moderate local and systemic effects that can be easily treated in the outpatient clinic but sometimes it may also result in severe reactions that require intensive medical intervention. The highly potent drugs can turn toxic with even small doses [3]. The diagnosis of toxic reaction is based on a wide variety of patient's clinical symptoms. Different drugs display different symptoms [1]. The branch of medicine which deals with the study of detection, clinical features, types, diagnosis of poison and treatment of poisoning is called toxicology and the person trained in this stream is called toxicologist [4]. The poisoning is the major cause of death everywhere although type and morbidity vary among the poisons. Death occurring due to poisoning is regarded as unnatural death and to confirm it medico-legal autopsy (postmortem) is routine practice [5]. The children are more curious about the household things and they accidently ingest them. This causes poisoning [6]. The

huge burden of these poisoning cases needs comprehensive and strategic planning to manage the condition and to reduce morbidity and mortality of the sufferer. Further, pharmacist should be aware of the toxic reaction of a drug and first aid for the management of toxicity. Besides, there are very less number of researches and scientific publications in the field of toxicology. Therefore, this prospective review is planned to study detailed information, clinical features, diagnosis and general management of poisoning.

HISTORICAL BACKGROUND

The history of poisoning is very old. Earlier poisons were derived from only plants and animals. They were used as arrow and dart poisons mainly for hunting e.g. strophanthin, aconitine and extract form Helleborus and snake venom. Dioscorides (AD 40-80) classified poison firstly into animal, vegetable and mineral. Later Nicander (204-135 BC) experimented on animal poison taking criminals as subjects. Theophrastus (370-286 BC) wrote a book De Historia Plantarum on plant poison. RigVeda (12th century BC) also described several poisons. Socrates (470-399 BC) was also executed by the hemlock administration. Murderous use of poisons was performed on Lex Cornelia in 81 BC. Later on, in 1198 Moses Maimonides published his classical work Treatise on Poisons and their Antidotes. Various other scientists were contributed by studying dose-response relationships were namely Ambroise Pare (1510-1590), Paracelsus (1493-1541), and William Piso (1611-1678). Paracelsus also reported that all substances are poisons, only dose is differentiating drug from poison [6]. Pioneering work of toxicology was made by Bonaventure Orfila (1787-1853) who discovered the practice of autopsy using analysis of viscera to confirm poisoning. He published a treatise on Traite des Poisons in 1814 which is the foundation of forensic toxicology. For this work, he was known as the 'Father of Toxicology'. The simplified version of his book was then published by two of his students [1].

Classification of Poisons

The poison is classified depending on use and mode of action as shown in Table-1 [7, 8].

Table-1: Classification of poisons

Classification depending on	Types	Use and examples
Use	Homicidal	They are used for murder. Arsenic, Antimony, Thallium and Aconite.
	Suicidal	They are used for suicides. Organophosphates, barbiturates, potassium cyanide, opium
	Accidental	Belladonna and Datura.
Mechanism of action	Corrosive	They damages tissues by their chemical action. Strong acid and alkalis.
	Irritant	They cause irritation/pain/vomiting Inorganic metals: arsenic, antimony, mercury, and lead, Non metals: phosphorus, chlorine, bromine, iodine. Organic plant: castor oil, animals: scorpions, snake, spiders. Mechanical: glass powder, diamond dust.
	Neurotic	They act on CNS producing drowsiness, delirium, stupor, convulsions, coma and death. (a) Cerebral Poisons: alcohol Opium, sedatives, anaesthetics hypnotics. (b) Spinal Poison: Strychnine. (c) Peripheral: Curare.
	cardiac	Act on heart. Digitalis
	Asphyxiant	Coal gas, war gases, methyl isocynate. CO, CO_2
	miscellaneous	Analgesics, antipyretics, tranquillizers, antidepressants.

Some more examples of poisons are given. However, their detail study is required in order to diagnose, manage and treat their complications.

1. **Corrosive poisons:** Sulfuric acids, nitric acid, hydrochloric acid, hydrofluoric acid, phosphoric acid, chromic acid, boric acid, acetic acid, formic acid, carbolic acid, oxalic acid, iodine, hydrogen peroxide, cetrimide
2. **Chemical poisons:** Phosphorus, phsphine, aluminium phosphide, chlorine, bromine, fluorine and heavy metals such as barium, cadmium, cobalt, lithium, magnesium, thallium,copper.
3. **Organic poisons:** Colocynth, croton, red pepper, eucalyptus, oduvan, rosary pea.
4. **Venomous bites and stings:** Snakes such as cobra, viper, coral snake, sea snake. Ticks and mites, centipedes, millipeds etc.
5. **Asphysixant poisons:** Ammonia, formaldehyde, hydrogen sulfide, smoke and phosgene.
6. **Hydrocarbons and pesticides:** Benzene, naphthalene, pyrethrins and pyrethroids, rodenticides, herbicides, fungicides, nematicides, acaricides, molluscicides
7. **Therapeutic Drugs:** All categories of drugs in their excess amount act as poison and affect one or other functions of body.
8. **Microbial food poisons:** Bacteria, clostridium, viruses, protozoa, parasites and fungi, some forms of mushroom, cyanogenic plants, prickly poppy, some

fishes and chemicals such as monosodium glutamate.

9. **Poisoning due to abuse:** Tobacco, cocaine, cannabis, amphetamines, hallucinogens, volatile inhalants [1].

FACTORS CONTRIBUTING TO THE ACTION OF POISONS

1. **Dose**: Drug produces therapeutic effects in small doses but the toxic or adverse effect in a large dose. These effects are allergy, idiosyncrasy, delirium, convulsions and cardiac complications. The severity of these effects varies according to frequency, dose and potency of a drug.
2. **Form of poison**: It is important to know the form of poison gases and vapors act more quickly as they are absorbed instantly. Poisons in the liquid state act faster than solid-state poisons. Certain chemical combinations of chemical substances turn into toxic effects such as lead carbonate and copper sulfide.
3. **Method of administration:** They are acting rapidly when inhaled in the form of gases or vapors (immediate action). They are acting some slowly with Intravenous/Intramuscular or Subcutaneous route as compared to inhalation (fast action) and they are acting very slowly when swallowed or rubbed externally (slow action).
4. **Condition of the body:** (a) Age: old age people and children are more susceptible to poisons than young and adult people. (b) Sleep: poisons are absorbed slowly during sleep as important functions of the body are slowed down [7-9].

SIGNS OF POISONING

The adverse effects produced by poisonous substances are called toxicity. They are ranging from mild effects such as nausea vomiting to severe effects such as convulsion, coma or death. Acute poisoning is short term exposure of poison (single high dose or several small dose) and chronic is long term exposure of poisons in occupationally engaged people at their work place. E.g. mercury, lead, antimony, opium. Some toxic effects are reversible and some are irreversible causing permanent damage to organs or systems [10]. Clinical toxicologist has proposed four grades of acute toxicity in both adult and children.

- None (0): Nil or minimum signs
- Minor (1): Mild, transient or and commonly resolving signs.
- Moderate (2): Prolonged or pronounced symptoms.
- Severe (3): Severe symptoms endangering life.

In mild poisoning, generally symptomatic and supportive treatments are not required, whereas in moderate it is required. In severe poisoning, advanced supportive and symptomatic treatments are essential [1]. Signs of poisoning vary depending on the substance. Signs are also varying if different people poisoned by the same substance. Symptoms typically begin soon after contact or ingestion and sometimes delayed. The delayed symptoms may occur if the metabolite is poisonous rather than the parent drug. E.g ethylene glycol, methanol, Ingestion of hepatotoxic drugs may cause liver damage and failure. E.g acetaminophen. Ingestion of toxic substances causes systemic symptoms. Corrosive or irritant substances damage mucus membrane lining over the gastrointestinal tract causing stomatitis, perforation, etc [11]. General toxicity categories [1] are given in the following Table-2.

Table-2: Signs of toxic effects on various systems

Category	System affected	Signs
Respiratory	Nose, Trachea, Lung	Coughing, irritation, choking, tightness in chest
Gastrointestinal	Stomach, intestine	Nausea, vomiting, diarrhea, perforation, stomatitis.
Renal	kidney	Urine frequency, quantity, color and smell changes.
Nervous	Brain and spinal cord	Confusion, dizziness, convulsions, coma.
Dermatological	skin	Itching, redness, urticaria, dermatitis, burning.
Dematological	blood	Anemia, polycythemia, thrombocytopenia.
Reproductive	Overy, testis	Miscarriage, stillbirth, infertility, birth defects.
Endocrine	Glands	Deficiencies of hormone

MECHANISM OF POISONING

Poisons produce either local effects or systemic effects. They act by increasing or decreasing body functions or secretion e.g heart rate, respiration, pupil size, salivation, lacrimation, sweating, urination. Some cause systemic effects on organs as described in Table-2. Poison also causes biochemical change, a cellular change resulting in physiological change. Certain neurotoxic poison causes damage to neurons e.g lead, ethanol, nitric oxide, botulinum toxin, tetanus toxin, etc [10]. Most of the poisons are involved in changing the oxygen pathway and thereby eventually result in respiratory problems as follows:

- Asphyxiant gases (Carbon dioxide, methane, butane, nitrogen) reduces inspiratory oxygen fraction
- Cyanide, hydrogen sulfide blocks cytochrome enzyme chain reducing tissue oxygen consumption failing oxidative metabolism.
- Some poisons such as a botulinus toxin, organophosphate, and strychnine cause respiratory syndrome by respiratory muscle paralysis or spasm. This results in reduced arterial oxygen tension.

- Opioid, sedative-hypnotic and barbiturate cause respiratory depression by reducing alveolar oxygen tension and failure of ventilation.
- Carbon monoxide, nitrites, arsine, stibine causes hemolysis. So, the hemoglobin function reduces.
- Beta-blockers and tricyclic antidepressant reduces oxygen delivery to heart producing myocardial depression [7, 12, 13]

TOXICOKINETICS

When poison is ingested, the majority of it is lost by vomiting and diarrhea, as the body tends to eliminate inappropriate things. The remaining poison in the body is biotransformed in the liver. Poisons or its end products are eliminated by urine. Other routes of elimination are bile, sweat, saliva, mucus or expired air. The substances like Arsenic are retained by the epidermis, nails and hairs similarly bone may retain lead or radioactive metal. During the period in the body, poisons show clinical signs as described above [7-9, 14].

DIAGNOSIS OF POISONING

As discussed above, respiratory or CVS depression, impairment of consciousness, dehydration due to diarrhea/vomiting, convulsions, hypothermia, arrhythmia, convulsions, comas are the commonest symptoms of poisoning. Thus diagnosis is made depending on the symptoms produced. Diagnosis is based on (a) history (b) physical examination (c) laboratory evaluation and (d) toxicological screening.

1. **History:** The information regarding name, type of drug, time of drug ingestion, co-administration of other drugs such as alcohol, route of ingestion, amount of drug is obtained by patient or witness and is recorded [10, 15]. This gives an idea about the clinical state of patient, stability and drug clearance.
2. **Physical examination:** In this, first of all, respiration, airway patency, circulation, mental status, pupil size, temperature, blood pressure, blood glucose, pulse, ECG, muscle tone, and reflexes are monitored. This is followed by recording circumstantial evidence in the form of a suicide note or container of toxins. The case is assessed based on the cause of poisoning. The criminal, suicidal, homicidal poisoning is reported to the police and forensic toxicologist [1]. The depressed state or agitated state of the patient is also observed. Drugs such as antipsychotic, antidepressant, antiarrhythmic, adrenergic blockers, carbamates, narcotic, sedatives hypnotic cause depressed state whereas caffeine, cocaine, ergot alkaloids, antihistamines, antiparkinsonian drugs cause agitated state [16].
3. **Laboratory evaluation:** In this oxygen level in the blood, arteries, plasma osmolarity, oxygen bindin capacity to hemoglobin are recorded by suitable methods [9].
4. **Toxicological screening:** It provides direct evidence of poison in the body. Before conducting such screening, initial and primary supportive measures must be instituted to the patient. This screening process helps to decide suitable antidote, reduce of absorption of poison and assist in elimination with further management of situation [17, 18].

MANAGEMENT OF POISONING

Management of poisoning is based on stabilization & evaluation of patient, decontamination and elimination of poison and with antidote administration. In stabilization of patient, assessment of patient and vital signs are carefully monitored and maintained. In evaluation of patient, hyperthermia, hypothermia, acid base disorders, convulsions, electrolyte disturbances, movement disorders are noted. In decontamination, the impact of poison is reduced by various methods described as under. In elimination, poison is eliminated by forced dieresis, hemodialysis, hemoperfusion, hemofiltration, and in antidote administration, suitable agent is administered to patient which counteract the effect of poison. These all parameters are briefly discussed in following way.

Pre-Hospital Care

First Aid

The breathing, airway, circulation is monitored and manual cardiopulmonary resuscitation is started immediately if needed. This restores blood circulation, preserves brain function and reverses cardiac arrest if any. To prevent further progression of serious intoxication, early decomposition of poison is very important. The emergency department of the hospital is consulted immediately and the patient is placed on the left side for easy clearance of airway and slower absorption of poison till arrival in hospital [19]. Following measures are exercised as first aid

- For inhaled poison: the patient should be taken to fresh air, windows and doors are opened, if the patient is not breathing then artificial respiration must be provided.
- For the local effects on skin: contaminated clothing is removed and fresh water is poured over the affected area. The contaminated area is washed with soap and rinsed with water.
- For poisoning in the eye: the open eyes are washed with cold fresh water and repeat for 15 minutes. Contact lenses should be removed.
- For swallowed poison: unless unconsciousness, or convulsion, the water is given and further treatment is provided [3].

Hospital care

When a patient reaches the hospital, the supportive and symptomatic treatment is essential depending on the clinical status and signs of the patient. Attention over vital signs of the body such as pulse, BP, respiration, oxygenation, circulation, blood glucose,

ECG and other cardiac functions is of utmost importance. In case any of these are not proper, then suitable medical treatment must be provided e.g orotracheal or nasotracheal intubation, mechanical ventilation, oxygenation, etc [20]. Blood pressure and heart functions are maintained by pressor agents, cardiac stimulants, defibrillation, pacing and blood sugar level is maintained by infusion of dextrose solution [2]. Similarly, other supportive treatment for the management of seizures, acid-base and electrolyte imbalances, and fluid imbalances are also given. IV and urinary catheters are placed to ensure fluid supplement and urine output [21].

Emesis & gastric lavage

Syrup ipecac, a non-prescription has been used traditionally to induce vomiting. But now its use is not recommended due to lack of outcome of poisoning, and difficulty in diagnosis. If fruitful emesis has occurred spontaneously then there is no need for inducing. Emesis is induced by a toxicologist if he feels better by the suitable method [2]. Gastric lavage is the process of eliminating the ingested poisons by administration and aspiration of fluid through a gastric tube as shown in Fig-1. This procedure is used when a toxic agent has been ingested. The fluid contains 2-4 liters of warm (37^0 C) saline. But there are certain complications of gastric lavage that include laryngospasm, hypothermia, electrolyte and fluid imbalance, aspiration pneumonitis, and mechanical injury [22].

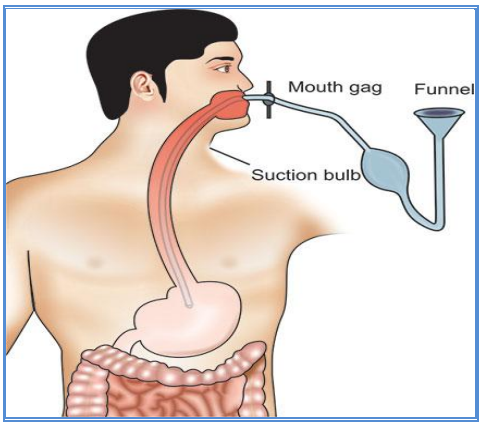

Fig-1: Gastric lavage

Activated charcoal

Toxin absorption can be reduced by activated charcoal administration. It is adsorbent of carbon, black in color as shown in Fig-2 and prevents the absorption of poison by binding it with the poison. It is generally less effective for iron, lead, alcohol, lithuium and corrosives and not indicated for aliphatic hydrocarbons because of emesis and aspiration. It is given in the first hour of the ingestion of poison. The recommended dose of activated charcoal is 25-50 gm for children upto 2 years and 25-100 g for adults. It is mixed with water to make slurry and administered through a nasogastric tube. This therapy is used if a patient has ingested a life-threatening amount of Phenobarbital, carbamazepine, dapsone, theophylline or quinine. This is also used for cimetidine, digitalis, NSAIDs, Opiates, phenothiazines, strychnine, tetracycline, andidiabetic drugs, kerosene, paracetamol, phenol, alcohol, carbamates, heavy metals, hydrocarbons, cyanide, etc [23].

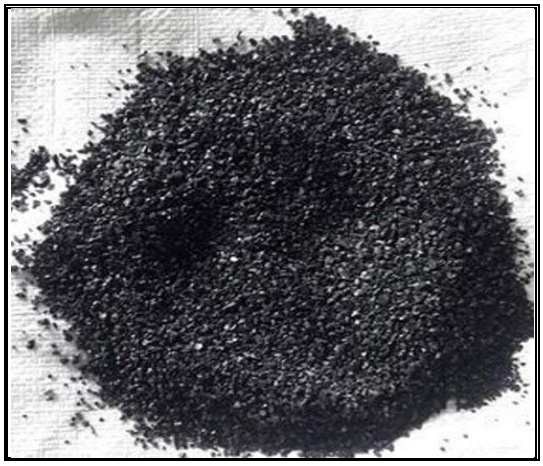

Fig-2: Activated charcoal

Laxatives and purgatives

Laxative such as sorbitol magnesium citrate and liquid paraffin are given immediately after charcoal administration to eliminate poison and charcoal poison complex from the gastrointestinal tract. But their use is not always advocated and value is unproven. They are used only when their effectiveness is confirmed. Whole bowel irritants such as polyethylene glycol electrolyte solutions, before performing colonoscopy and bowel surgery to remove toxins. They clear the gastrointestinal tract [24].

Diuresis

The elimination of poison is further enhanced by using diuretics. The poison whose route of elimination is urine is predominantly forcefully eliminated by urine using diuretics. During the use of diuretics, the fluid balance, blood pressure, electrolyte balance and acid base balance is carefully monitored. Furosemide, mannitol are commonly used drugs for this purpose. This technique is also not always beneficial due to certain adverse effects [2].

Hemodialysis and hemoperfusion

Hemodialysis is a treatment to filter water and wastes from your blood, in addition to creatinine and urea, this technique also removes poison. *Hemoperfusion* a method of filtering the blood outside the body to remove a toxic product. Hemodialysis and hemoperfusion are used only when there are severe cases of poisoning and symptoms are continuing to progress. Both the processes are shown in Fig-3. It is also used when the normal pathway of elimination of poison is compromised. For it suitable instrument called dialyzer is needed and drugs to be eliminated must have low molecular weight and not tightly protein-bound and less distributed among tissues. This method is effective if ethylene glycol, ethanol, theophylline, salicylate

poisoning is noted. Like other methods, this is also having disadvantages that they are having the risk of thrombosis, loss of blood elements, fluid and electrolyte disturbances, air embolism, infection. In addition, hemodynamically unstable patient cannot tolerate such a technique [1, 2, 25, 26].

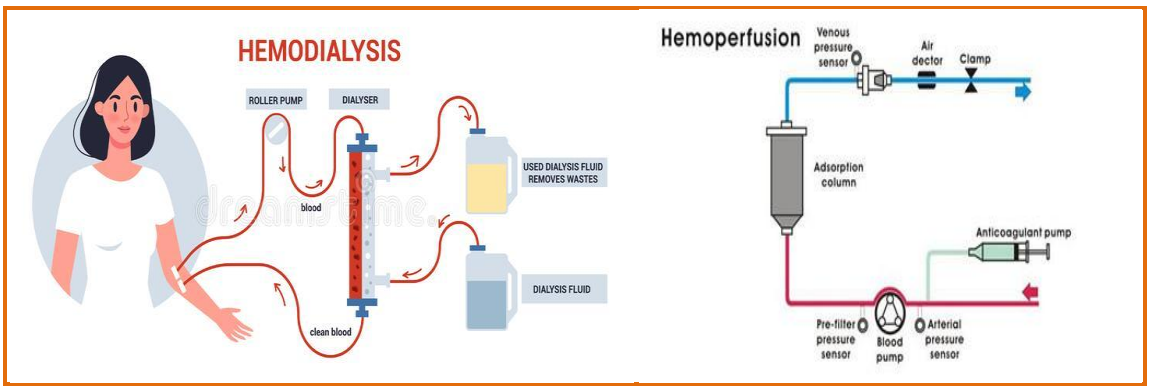

Fig-3: Hemodialysis and hemoperfusion

Antidotes

Antidotes are those which counteract the poison. This drugs or substances reverse the action of poison and symptoms. They are produced when a small dose of toxin is injected into animals and antibodies are extracted from animal blood. E.g. antivenom is produced from antibodies and used to counteract venous secreted from certain snakes, spiders. Antidotes work by following mechanisms

- Inert complex formation-e.g chelating agent for heavy metal, dicoblalt edentate for cyanide, Prussian blue for thallium
- Accelerated detoxification: e.g thiousulfate accelerated the conversion of cyanide to non toxic thiocyanate, acetylcysteine detoxifies paracetamol metabolites reducing hepatotoxicity.
- Receptor site competition: e.g naloxone acts at the opioid receptor site and antagonizes the effect of opiates.
- Receptor site blockade: e.g. atropine blocks organophosphates at muscarinic site.
- Reduced toxic conversion: ethanol inhibits methanol metabolism ot toxic metabolites by competing same enzyme (alcohol dehydrogenase)
- Toxic effect bypass: e.g. oxygen in cyanide poisoning [1].

Most commonly used antidote for their respective indications are shown in Table-3.

Table-3: Antidotes with their indications

Antidote	Main indication for	Antidote	Main indication for
Acetylcystein	Paracetamol	Flumazenil	Benzodiazepines
Amyl nitrate	Cyanide	Glucose	Insulin
Atropin	Cholinergic drugs	Guanidin	Bolulism
Isoprenaline	Beta blockers	Ascorbic acid	Organic peroxides
Aurintricarboxylic acid	Beryllium	Calcium salts	Oxalate, Fluorides
Desferrioxamine	Iron, Aluminium	Diazepam	Chloroquine
Dimercaprol	Arsenic	Ethanol	Methanol, ethylene glycol
Methionine	Paracetamol	N-acetlpenicillamine	Mercury
Naloxone	Opiates	Oximes	Organophosphates
Oxygen (hyperbaric)	Carbon monoxides, cyanide	Penicillamine	Copper
Phentolamine	Alpha adrenergics	Prussioan blue	Thallium
Propranolol	Beta adrenergics	Protamine sulphate	Heparine
Pyridoxine	Isoniazid	Sodium nitroprusside	Ergotism
Succimer	Lead mercury	Tocopherol	Carbon monoxide
Triethylene tetramine	Copper	Activated charcoal	Given above
Calcium chloride	Calcium channel blocker, spider bites	Cyproheptadine	Serotonin syndrome
Diphenhydramine HCl & Benztropin mesylate	Antipsychotics (extrapyramidal reactions)	Calcium gluconate	Calcium channel blocker toxicity, hydrofluoric acid burns

CONCLUSION

Poisoning is the last complication of the ingestion of excess drugs. Modes of poisoning are varying i.e it may result from attempts of accident, homicide or suicide. Accidental poisoning is most commonly observed in children because of their inability to read warning labels and due to their curiosity to eat. Further, food poisoning, insect bites are other forms of accidental poisoning to both children and adults. Criminal poisoning occurs when individuals are intentionally committing suicides or attempts. Homicidal poisoning involved destruction of another person's life with poison Forensic toxicology is an important branch of medical science to identify the presence of any drug or chemical in the body. Food poisoning is also common problem affecting the people around the world. Various food-borned illnesses are observed due to food poisoning. Oral rehydration therapy, antidiarrheal drugs, antimicrobial drugs are treatment options for food poisoning. But overall hygiene is most important preventive measures to avoid food poisoning. The diagnosis of poisoning is very important in uncooperative or unconscious patients for its management. Apart from their life-threatening complications, there is dramatic advancement for the treatment of the poisoning. Recently clinical pharmacists are involved in the identification and the treatment protocol of poisoning. The community pharmacist is promoting the prevention of poisoning by encouraging the patient to take the dose as prescribed by the physician. Pharmacist is also involved in patient care by identifying a patient at risk of drug addiction, abuse or misuse. The present review is, therefore, an attempt to provide the basic information about health hazards, diagnosis and the management of poisoning.

CONFLICT OF INTEREST

The author declares that there is no conflict of interest in the publication of this paper.

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