Clinical toxicology

Objectives

- Explain factors contributing to the action of poison
- Understand the six steps applied in management of poisoned patient

Introduction

- ✓ **Clinical toxicology** involves the detection and treatment of poisonings caused by a wide variety of substances, including household and industrial products, animal poisons and venoms, environmental agents, pharmaceuticals, and illegal drugs.
- ✓ **Poison** is any agent capable of producing deleterious response in a biological system, seriously injuring function or producing death.

Factors contributing to the action of poisons

1. Dose: Drug produces therapeutic effects in small doses but the toxic effect in a large dose. 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 gase s and vapors act more quickly as they are absorbed instantly. Pois ons in the liquid state act faster than solid-state poisons.

3. Method of administration: They are acting rapidly when inhale d in the form of gases or vapors (immediate action). They ar e acting some slowly with Intravenous/Intramuscular or Subcu taneous route as compared to inhalation (fast action) and they are acting very slowly when swallowed or rubbed externally (sl ow action).

4. Condition of the body: (a) Age: old age people and children are more susceptible to poisons than young and adult people. (b) Sl eep: poisons are absorbed slowly during sleep as important f unctions of the body are slowed down

Types of Poisoning

Fulminant: Produced by a massive dose of a poison. Death occur very rapidly, without symptoms i.e. collapse suddenly

Acute: A single large dose or several small doses taken in a short period

Chronic: Produced by small doses taken over a long period

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 hi gh dose or several small dose) and chronic is long term e xposure of poisons in occupationally engaged people at th eir work place.

Mechanism of poisoning

- Poisons produce either local effects or systemic effects. Th ey act by increasing or decreasing body functions or secre tion e.g heart rate, respiration, pupil size, salivation, lacri mation, sweating, urination.Poison also causes biochemical change, a cellular change resulting in physiological change.

Toxicokinetics

- When poison is ingested, the majority of it is lost by vomiting and diarrhea, as the body tends to eliminate inappropriate thi ngs. The remaining poison in the body is biotransformed in the liver. Poisons or its end products are eliminated by urine. Ot her routes of elimination are bile, sweat, saliva, mucus or expire d air

Treatment of acute poisoning

1st Goal - keep concentration of poison as low as possible by preven ting absorption and increasing elimination.

2nd Goal - counteract toxicological effects at effector site, if possibl e.

Management of the poisoned patient

The following general steps represent important components of the initial clinical encounter with a poisoned patient:

1. Stabilization of the patient.
2. Diagnosis of poisoning.
3. Prevention of further toxin absorption.
4. Enhancement of toxin elimination.
5. Administration of antidote.
6. Supportive care and clinical follow-up.

1. Stabilization of the patient

- ''Treat the patient, not the poison''.
- 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 .

1. stabilization of the patient

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 if no convulsion, the water is given and further treatment is provided

Hospital care

- When a patient reaches the hospital, the supportive and sympto matic treatment is essential depending on the clinical status and sig ns of the patient. Attention over vital signs of the body such as pulse, BP, respiration, oxygenation, circulation, blood glucose, ECG and o ther cardiac functions is of utmost importance. In case any of th ese are not proper, then suitable medical treatment must be pro vided e.g orotracheal or nasotracheal intubation, mechanical ventil ation, oxygenation, etc .
- Blood pressure and heart functions are maintained by pressor ag ents, cardiac stimulants, blood sugar level is maintained by infusio n of dextrose solution . Similarly, other supportive treatment for t he management of seizures, acid-base and electrolyte imbalances, and fluid imbalances are also given. IV and urinary catheters are place d to ensure fluid supplement and urine output .

2. Diagnosis of poisoning

- respiratory or CVS depression, impairment of consciousness, d ehydration due to diarrhea/vomiting, convulsions, hypothermia , arrhythmia, convulsions, comas are the commonest symptom s of poisoning. Thus diagnosis is made

  depending on the symptoms produced. Diagnosis is based on: (a) history (b) physical examination (c) toxicological screening(d)laboratory evaluation

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 . This gives an idea about the clinical state of patient, stability and drug clearance.

Diagnosis of poisoning

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. The case is assessed based on the cause of poisoning. The criminal, suicidal, homicidal poisoning is reported to the police and forensic toxicologist . The depressed state or agitated state of the patient is also observed. Drugs such as antipsychotic, antidepressant, adrenergic blockers, sedatives hypnotic cause depressed state whereas caffeine, cocaine, ergot alkaloids, antihistamines, antiparkinsonian drugs cause agitated state
3. Laboratory evaluation: Oxygen level in the blood, arteries, plasma osmolarity, oxygen binding capacity to hemoglobin are recorded by suitable methods

Diagnosis of poisoning

3. 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 absorption of poison and assist in elimination with further management of situation

3. Prevention of further toxin absorption

- ✓ Decontamination from skin surface
- ✓ **Emesis**: indicated after oral ingestion of most chemicals;
  - must consider time since chemical ingested
- ✓ Contraindications:
  - ingestion of corrosives such as strong acid or alkali;
  - if patient is comatose or delirious;
  - if patient has ingested a CNS stimulant or is convulsing;
  - if patient has ingested a petroleum distillate
- ✓ Emesis can be induced with ipecac syrup .
- ✓ Previously popular methods of inducing emesis such as fingerti p stimulation of the pharynx, salt water, and apomorphine are i neffective or dangerous and should not be used.

Gastric lavage

- ✓ Gastric lavage is the process of eliminating the unabsorbed inges ted poisons by administration of fluid through a gastric tube as shown below

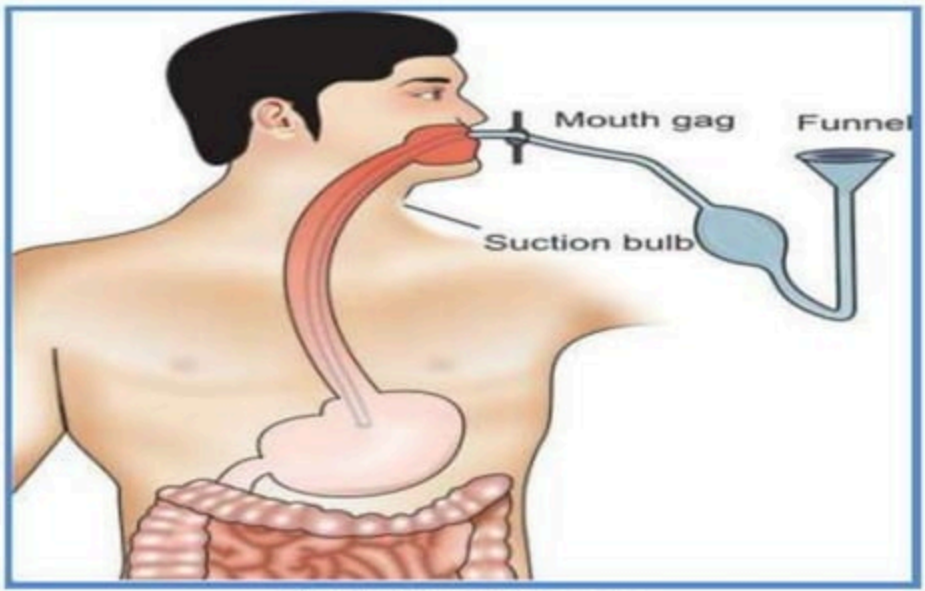

Fig-1: Gastric lavage

Gastric lavage

- ✓ If the patient is awake or if the airway is protected by an endotracheal tube, gastric lavage may be performed using an orogastric or nasogastric tube.
- ✓ This procedure is used when a toxic agent has been ingested . The fluid contains 2-4 liters of warm (37^0C) saline. But there are certain complications of gastric lavage that include laryngospasm, electrolyte and fluid imbalance, aspiration pneumonitis, and mechanical injury

Activated Charcoal

- Toxin absorption can be reduced by activated charcoal administration. It is adsorbent of carbon, black in color as shown in Fig below 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

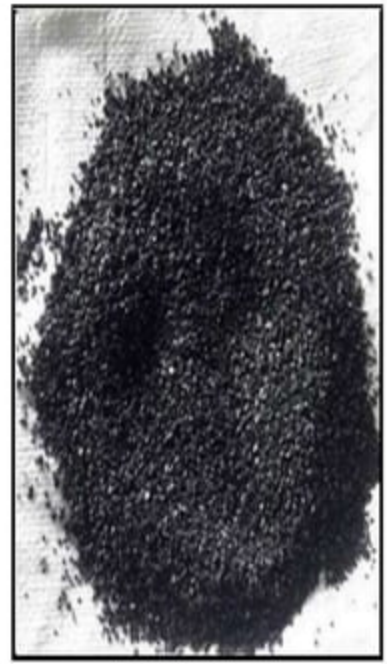

Fig-2: Activated charcoal

Laxatives and purgatives

- Laxative such as sorbitol magnesium citrate and liquid paraffi n are given immediately after charcoal administration to elimina te poison and charcoal poison complex from the gastrointestinal tract.
- They are used only when their effectiveness is confirmed. Whole bowel irritants such as polyethylene glycol electrolyte sol utions, before performing colonoscopy and bowel surgery to remove toxins. They clear the gastrointestinal tract .

4. Enhancement of toxin elimination

Diuresis

- 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, el ectrolyte balance and acid base balance is carefully monitored.
- Furosemide, mannitol are commonly used drugs for this purpose.

Hemodialysis and hemoperfusion

- Hemodialysis and hemoperfusion are treatments to filter water and wastes from your blood, in addition to creatinine and urea, this technique also removes poison.
- Hemodialysis and hemoperfusion are used only when there are s evere cases of poisoning and symptoms are continuing to progress.

Hemodialysis and hemoperfusion

- Also used when the normal pathway of elimination of poison is compromised.

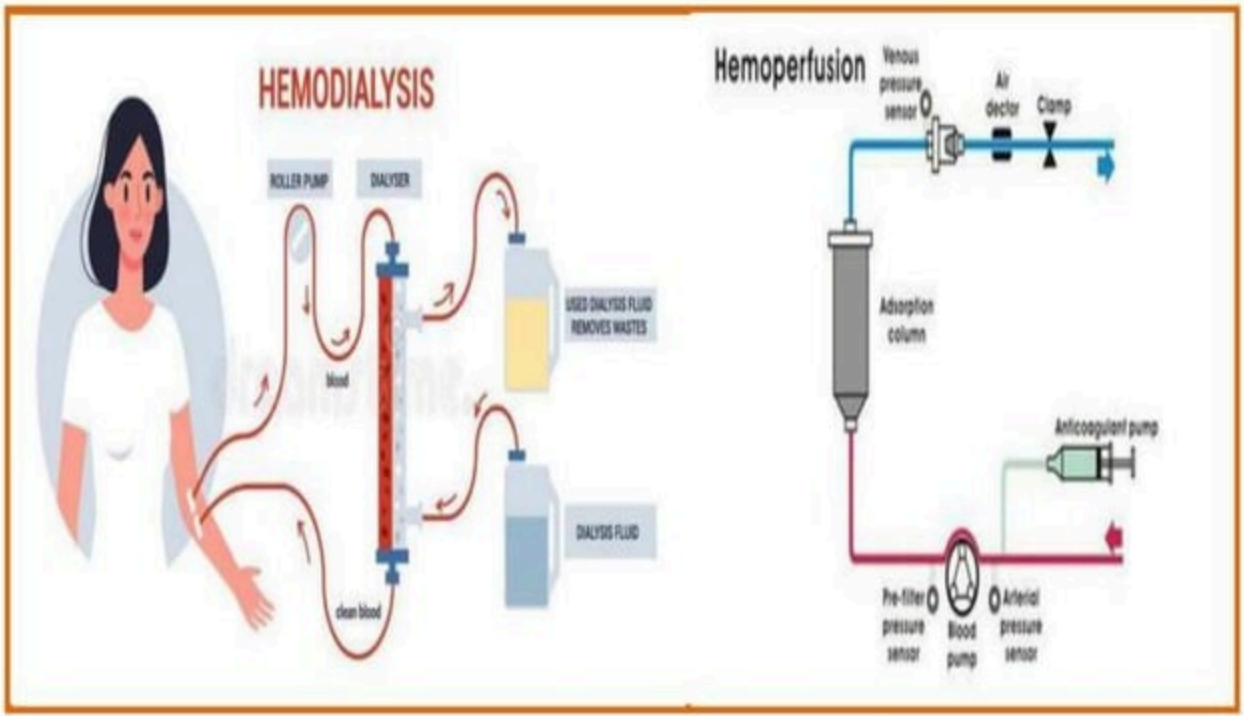

Fig-3: Hemodialysis and hemoperfusion

Hemodialysis

- An instrument called dialyzer is needed and drugs to be e liminated must have low molecular weight and not tightl y protein -bound and less distributed among tissues.
- This method is effective if ethylene glycol, ethanol, the ophylline, salicylate poisoning is noted.
- Like other methods, this is also having disadvantages that they are having the risk of thrombosis, loss of blo od elements, fluid and electrolyte disturbances, air emb olism, infection.

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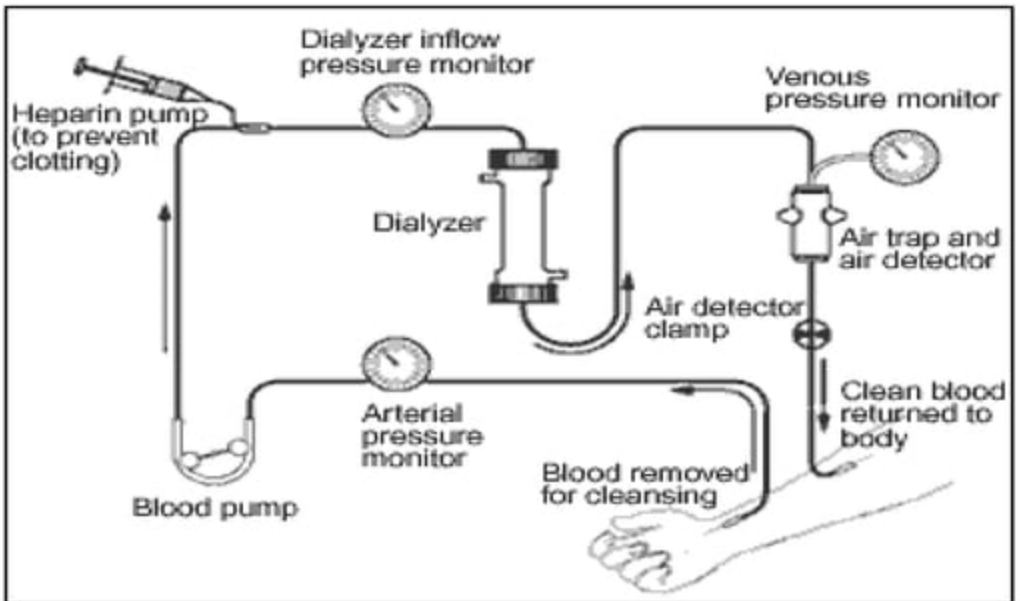

Hemodialysis.

Hemoperfusion

- ✓ is a treatment technique in which large volumes of the patient's blood are passed over an adsorbent substanc e in order to remove toxic substances from the blood.
- ✓ Adsorption is a process in which molecules or particles of one substance are attracted to the surface of a solid material and held there.
- ✓ These solid materials are called sorbents.
- ✓ Hemoperfusion is sometimes described as an extracorp oreal form of treatment because the blood is pumped t hrough a device outside the patient's body.

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Hemoperfusion and hemodialysis have three major uses:

- ✓ to remove nephrotoxic drugs, poisons or wastes from t he blood in emergency situations (A nephrotoxic subst ance is one that is harmful to the kidneys.)
- ✓ to remove poisons or overdose administered drugs fro m the blood in poisoned patients
- ✓ to provide supportive treatment before and after trans plantation for patients in liver failure

Hemofiltration

- ✓ is a therapy similar to hemodialysis, used to replace th e function of the kidneys in the case of renal failure.
- ✓ Unlike hemodialysis, hemofiltration is nearly always u sed in intensive care settings in cases of acute renal fai lure.
- ✓ The therapy works by passing the patient's blood thro ugh a machine that filters out waste products and wat er, and then adds replacement fluid before returning t he blood to the body.
- ✓ The replacement fluid maintains fluid volume in the bl ood and provides electrolytes

5. Administration of antidote

- ✓ Antidotes are those which counteract the poison. This drugs or substances reverse the action of poison and symptoms.
- ✓ There is a popular misconception that there is an antidote for every poison. Actually, selective antidotes are available for only a few classes of toxins.

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

5. Administration of antidote

- ✓ 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 to toxic metabolites by competing same enzyme (alcohol dehydrogenase)

Poison	Antidote	Poison	Antidote
Paracetamol	Acetylcystein	Organic peroxides	Ascorbic acid
Cyanide	Amyl nitrate	Chloroquine	Diazepam
Cholinergic drugs	Atropine	Methanol, ethylene glycol	Ethanol
Beta blockers	Isoprenaline	Organophosphates	Oximes
Insulin	Glucose	Heparine	Protamine sulphate
Iron, Aluminium	Desferrioxamine	Oxalate, Fluorides	Calcium salts
Arsenic	Dimercaprol	Beta adrenergics	Propranolol
Opiates	Naloxone	Mercury	N-acetlpenicillamine
Carbon monoxides, cyanide	Oxygen (hyperbaric)	Calcium channel blocker, spider bites	Calcium chloride
Alpha adrenergics	Phentolamine	Benzodiazepines	Flumazenil

6. Supportive care and clinical follow-up

- ✓ Once the initial treatment phase in the clinical manage ment of the poisoned patient has been completed, thos e patients who require admission are generally shifted t o an inpatient hospital setting.
- ✓ This supportive care phase of poison treatment is very i mportant.
- ✓ Poisoned patients who are unstable or at risk for signific ant clinical instability are generally admitted to a medica l intensive care unit (ICU) for close monitoring.
- ✓ In addition, patients who are excessively sedated from t heir poisoning or who require mechanical ventilation or invasive hemodynamic monitoring are usually candidate s for an ICU stay.