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ROLE OF ANTIDOTES IN POISONING - A REVIEW

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ABSTRACT

Toxicology is the science that deals with the study of potential harmful effect of chemicals and drugs on living organisms. Toxicology is a branch of pharmacology, and today is developed into a full and independent. Poison is harmful substance which when comes in contact with a living being produces abnormal effects on health. For the treatment of poisoning general and specific treatment are mentioned. In specific treatment antidotes are play an important role for the treatment of specific poisonous substance. Antidotes are substances that act specifically to prevent. Inhibit, inactive, counteract, reverse or relieve the action or poisonous effects of a toxic agent Mechanical, chemical, universal, Pharmacological, chelating agents serological etc antidotes are classified against specific toxic agents. This review article mainly focused on antidotes types, doses and their importance for the treatment of poisoning.

Keywords: Toxicology, Poison, Antidote, Harmful, Specific Poisons.

INTRODUCTION

Toxicology is the science that deals with the study of potential harmful effect of chemicals and drugs on living organisms. The word toxicology is derived from two words – 'toxic' and 'logy'. Toxin is poisonous substance. And logy is the science/study of. Therefore Toxicology is the science/study of poisonous substances**.** The scope of toxicology encompass the qualitative determination of poisons/chemical their deleterious effect on the living organisms, their incidence, mechanism, factors modifying them and reversibility of such adverse effects.[1]

The term Antidote ultimately derives from the Greek "pharmacon antidoton" medicine given as a remedy. Antidote is a chemical especially a drug that limits the effect of poison. There are numbers of medicine available as a antidote for the treatment of poisonous substances but important is correct and early diagnosis there after only suitable antidote can be given.

If any case of poisoning, when poison is completely absorbed or gastric lavage is contraindicated, then antidote are very useful for its treatment, because antidotes are agents which counteract the toxic action of a specified xenobiotic.

DEFINITION

Antidote are substance that act specifically to prevent, inhibit, inactivate, counteract, reverse or relieve the

action or poisonous effect of a toxic agent, i.e. they are remedies used to counteract the action of poison.[2]

COMMON MODE OF ACTION OF ANTIDOTES[3]

1. Inert complex formation, eg. Chelating agent for heavy metals.
2. Accelerated detoxification, e.g. thiosulphate for cyanide.
3. Reduced toxic conversion, e.g ethanol for methanol.
4. Receptor site blockade, e.g. naloxone for opiates,
5. Toxic effect bypasses e.g. 100% oxygen in cyanide poisoning.

ANTIDOTE NEED TO BE USED BECAUSE [4,5]

- The poison may not have been completely removed by emesis or gastric lavage.
- Where these procedures are contra-indicated like corrosives, strychnine, coma, volatile- poisons (petroleum distillates) etc.
- The poison is already absorbed.
- The poison has been administered by route other than ingestion.

Table 1: Classification Of Antidote[6,7]

NON-SPECIFIC	SPECIFIC
1. MECHANICAL ANTIDOTE-	**1.PHARMACOLOGICAL ANTIDOTE**
• Demulcents	• Physostigmine
• Diluents	• Barbiturates
• Bulky food	• Atropine
• Adsorbents	• Naloxen
2. CHEMICAL ANTIDOTE	**2. CHELATING AGENT**
• Weak alkalies for acid	• B.A.L.
• Weak acid for alkalies	• E.D.T.A.
• Comman salt	• Panicillamine
• Egg albumin	• Desferoxamine
• Freshly prepared ferric acid	• Calcium disodium
• Copper sulphate	• Cuprimine
• Lugol's iodine	• Desferal
• Tanic acid	
• $KMNO_4$	

ANTIDOTE CAN BE CLASSIFIED IN ACCORDANCE WITH THEIR MODE OF ACTION

1. MECHANICAL OR PHYSICAL ANTIDOTES[8]

It neutralizes poisons by mechanical action or prevents their absorption.

Multiple-dose activated charcoal (MDAC)- It is defined as at least two sequential doses of activated charcoal.

Fine, black, odorless powder produced by destructive distillation of various organic materials, usually wood pulp and then then high temperature with a variety of activating agents, such as steam or CO_2 , to increase its adsorptive capacity.

Dose- 40-80 (dose 0.5-1 g/kg body wt.) is mixed from a soup like mixture and given orally. Palatability may be increased by adding a sweetener (sorbitol) or a flavoring agent (cherry, chocolate or cola syrup) to the suspension.

Action- It acts mechanically by adsorbing and retaining within its pores, especially alkaloid poisons, allowing the charcoal-toxin complex to be evacuated with stool. The network of pores adsorbs 100-1000mg of drug/g of charcoal.

Uses- It is used in cases of poisoning with strychnine, morphine, atropine, nicotine, phenobarbital, amanita, phalloides, alcohol, salicylates, KCN and phenol. Charged chemicals, such as mineral acids, alkalis and highly dissociated salts of cyanide, fluoride, iron, and

lithium are not well adsorbed by charcoal. Activated charcoal does not bind metal and thus is of limited usefulness in cases of acute metal ingestion.

Contraindications- Ingestion of caustic acid /alkali or aliphatic hydrocarbons like kerosene/gasoline, unprotected airway, depressed level of consciousness, and functional or mechanical bowel obstruction (absent bowel sounds/ileus).

Side effect- Nausea, vomiting and diarrhea or constipation. Charcoal may also prevent the absorption of orally administered therapeutic agents.

Complication- Include mechanical obstruction of the airway aspiration, bowel obstruction and infarction caused by inspissated charcoal.

ii).DEMULCENT- Are the substances which from protective coating on the gastric mucous membrane, e.g. milk, starch, egg-white, mineral oil, aluminum hydroxide and milk of magnesia.

Contraindication- Fats and oils should not be used for oil-soluble poisons, such as kerosene, phosphorous, OPC, DDT, phenol, turpentine, aniline and CCI_4.

iii).BULKY FOODS- Acts as mechanical antidote to glass powder by imprisoning its particles within its meshes.

2. CHEMICAL ANTIDOTES[9]

Chemical antidote neutralizes the poison chemically within the GIT. Example are-

1. ACIDS- Neutralize alkalis. Weak solutions should be given e.g. Canned fruit juice, lemon juice, and vinegar. Neutralization of acids with strong alkalis and vice versa must be avoided, because the antidote may itself be injurious and strong exothermic reactions cause further injury. Sodium carbonate and bicarbonate to neutralize acids are avoided because of excessive release of Co_2 which may cause perforation of the weakened stomach walls.
2. ALBUMIN- Found in egg white. Can be given in mercury chloride poisoning (from insoluble mercury albuminate) and Cu poisoning (forms insoluble copper albuminate)
3. ALKALIS- Neutralize acids. Weak solutions should be given. Ex: Alkaline hydroxides, e.g. (i) magnesium hydroxide (ii) calcium hydroxide [$Ca(OH)_2$; slaked lime] is a white powder obtained when calcium oxide [CaO; lime or quicklime] is mixed, or "slaked" with water. Also called hydrated lime, builders lime, slack lime, cal, or pickling lime. For medicinal use slaked lime is sweetened [saccharated lime] for ease of ingestion. It may be given against many acids.
4. COMMON SALT – May be given for silver nitrate poisoning. Forms insoluble silver chloride.
5. COPPER SULFATE – Was once given for phosphorus poisoning. Forms insoluble cupric phosphide. Not used now.
6. DIALYSED IRON – was once given for arsenic poisoning because it forms insoluble ferric arsenite with arsenic salts. Not used now.
7. DICOBALT EDETATE – chemically combines with cyanides.
8. FRESHLY PREPARED HYDRATED FERRIC OXIDE [Fe_2O_3] – was once given in arsenic poisoning because it forms insoluble ferric arsenite with arsenic salts.
9. IODINE – A solution of tincture iodine or Lugol's iodine 15 drops added to half a glass of warm water precipitates most alkaloids [e.g. quinine, strychnine, etc] lead, mercury and silver.
10. POTASSIUM PERMANGANATE – has oxidizing properties, 1:5000 solution is used. The wash must be continued till the solution coming out of stomach is pink in color. It is effective against most of the alkaloids (opium, strychnine or atropine), barbiturates, phosphorus and cyanide.
11. TANNIC ACID – 4% solution or tannin [strong tea] precipitates aconite, apomorphine, cinchona, cocaine, metals [aluminum, cobalt, copper, lead, mercury, nickel, silver, zinc] nicotine, pilocarpine and strychnine.

3. PHYSIOLOGICAL OR PHARMACOLOGICAL ANTIDOTE[10]

These agents act on the tissue of the body. These substances work either one of the following ways:

1. Reduces the toxic conversion of poison- e.g., ethanol is used as antidote in methyl alcohol poisoning because ethanol inhibits the metabolism of methanol to toxic metabolites by competing for the same enzyme (alcohol dehydrogenase)

2. Competition at receptor site- some antidotes are capable to compete with the poison and displace the poison from the specific receptor site there by antagonizing the poisonous effects completely. For e.g., in opiate poisoning naloxone is used. Naloxone antagonizes the effect of opiate by acting at opiate receptors.
3. Blocking the receptor site – some antidotes are capable of blocking the receptor site acted by poisonous substance thereby blocking the poisonous effect of substance. For e.g., in organophosphorus poisoning atropine is used. Organophosphorus acts at muscarinic receptors producing toxic effects. Administration of atropine will block the effects of organophosphate.

3. UNIVERSAL ANTIDOTE[11]

It is an antidote that is used in those cases where the nature of the ingested poisons is unknown or where it is suspected that a combination of two or more poisons has been taken. It consists of a mixture of readily available substances, as follows:

TABLE 2: Universal Antidote

CONSTITUENTS	QUANTITY	PURPOSE
1.Powdered charcoal (burnt toast)	2 parts	Adsorbs alkaloids
2.Magnesium oxide (milk of magnesia)	1 parts	Neutralizes acids
3.Tannic acid (strong tea)	1 parts	Precipitates alkaloids, certain glucosides and many metals

The mixture is administered in a dose of a tablespoonful stirred up in a tumblerful (200 ml) of water, and may be repeated once or twice. Even when given soon after the ingestion of poison, it is not very effective. Though it is called universal antidote, it is not a Panacea in all cases. Infact, in many institutions, this is replaced by activated charcoal administration. However, its immediate household or hospital use cannot be written off.

5. CHELATING AGENT[12]

Chelating agents (metal complexing agents) are used in the treatment of poisoning by heavy metals. They have a greater affinity for the metals as compared to the endogenous enzymes. The complex of the agent and metal is more water-soluble than the metal itself, resulting in higher renal excretion of the complex. They can form stable, soluble complexes with calcium and certain heavy metals.

1. **B.A.L. (British anti-lewisite; dimercaprol; dimercaptopropanol):** It is used as a physiological antidote in arsenic, lead, bismuth, copper, mercury, gold, thallium and antimony. Many heavy metals have great affinity for suphydryl (SH) radicles and combine with them in tissues and deprive the body of the use of respiratory enzymes of tissue cells. Dimercaprol has two unsaturated sulphydryl groups which combine with the metal, and thus prevent union of arsenic with the SH group of the respiratory enzyme system. The compound formed by the heavy metal and dimercaprol is relatively stable, which is carried into the tissue fluids, particularly plasma, and is excreted in the urine. In severe poisoning a dose of 3 to 4mg/kg is given. Each ml. contains 50 mg. Three ml of 10% BAL and 20% benzyl benzoate in arachis oil is injected deep i.m. fourth hourly for the first two days, and then twice daily for ten days or till recovery. It should not be used when liver is damaged. BAL may induce haemolysis in the 6-PGD deficient individuals.
2. **E.D.T.A. (ethylenediaminetetraacetic acid; calcium disodium versenate; edathemil; edetic acid; versene):** It is a chelating agent and is effective in lead, mercury, copper, cobalt, cadmium, iron and nickel poisoning. The usual dose is 25 to 35mg/kg body weight in 250 to 500 ml. of 5% glucose or normal saline i.v. over one to 2 hour period twice daily for five days, and may be repeated after two to three days. It forms chelates with lead which are water-soluble, non-toxic, non-ionised, non-metabolized and excreted intact in the urine. It is superior to B.A.L. for the treatment

of poisoning by arsenic and mercury. It is the treatment of choice in lead poisoning.

3. **Penicillamine (cuprimine; dimethyl cysteine):** It is a hydrolysis product of penicillin. It has a stable SH group. It is given in a dose of 30mg/kg. body weight up to a total of 2g. per day in 4 divided doses orally for about 7 days. One to 3g. can be given in slow normal saline drip daily for 2 to 4 days. It is the chelating agent of maximum efficiency for copper, lead and mercury.
4. **DMSA, succimer (Meso-2, 3-dimercaptosuccinic acid):** it is used in lead, mercury and arsenic poisoning. It is superior to EDTA in the treatment of lead poisoning, as it does not lead to redistribution of lead to the brain. It is less toxic to the kidneys. It can be given in patients with 6 PGD (6-phosphogluconate dehydrogenase) deficiencies. It is given in a dose of 10mg/kg orally every 8 hours for 5 days, followed by the same dose every 12 hours for 14 days. A combination of succimer and EDTA is said to be more effective.

DMSA and DMPS possess the same dithiol (sulphydryl) chelating grouping as dimercaprol and the molecules are more hydrophilic. They have a better therapeutic index.

5. **DMPS: (2, 3-dimercaptopropane 1-sulfonate)** is effective in the treatment of mercury, lead and arsenic poisoning. It is given in a dose of 5mg/kg i.v. in 6 divided doses, followed by 100 mg. orally twice a day for 24 days.
6. **Desferrioxamine:** It contains trivalent iron as a chelate and is very useful in acute iron poisoning. 8 to 12g. is given orally daily to absorb iron in the stomach. Two g. in five percent of laevulose solution is given i.v. to bind absorbed iron, repeated twelve hourly if necessary. It is also used to promote removal of radioactive heavy metals.

6. SEROLOGICAL ANTIDOTE[13]

Anti Snake Venom Serum- Each 1 ml contain- cobra venom 0.6 mg + krait venom 0.45 mg+ russel venom 0.6 mg+ saw scale venom 0.45 mg

It is used for the treatment of big 4 bite (i.e.-Cobra, krait, russel viper and saw scale viper). Dose of 10 vials (100 ml) with RL/ IV drip are used till the signs symptoms will be reverse.

Anti Rabies Serum- It is used in high risk Rabid bite (having wound with bleeding) firstly clean the bite area, then use of ERIG 40 IU/Kg of body wt. (3000 IU). It contains globulin which neutralizes the rabies virus.

TABLE 3: COMMONLY EMPLOYED SPECIFIC ANTIDOTES[14]

ANTIDOTE	FREQUENCY(n=11)	POISONING INDICATION(s)	PRESANTATION	DOSE (70kgpatient)
N-acetylcystine	2	Acetaminophen	200mg/mi, 10ml ampoule	19.6g
Snake antivenin	1	Snake bites	10 ml/vial	10 vials
Calcium gluconate	11	Hydrogen fluoride (HF) or calcium channel blocker	10%, 10 ml ampoule	100mEq
Sodium bi - carbonate	11	1)Tricyclic antidepressant 2)cocaine 3)salicylates	8.4%, 50ml vial	500 mEq
Deferoxamine	4	Iron	500 mg/vial	8.4g
Digoxin specific fab	NA	Digoxin, digitoxin, or natural products (plants, toads)	38 mg/vial	15 vials
Dimercaprol	1	Acute arsenic, inorganic mercury, lead	50 mg/ml, 2 ml ampoule	280mg
Atropine	11	Carbamate or organophosphate insecticide	600 mcg/ml, 1 ml ampoule	75mg
Cyanide ant	1	Cyanide	30 mg/ml, 10 ml am-	1kit

idote			poule	
Ethanol	NA	1)Methanol, 2)ethylene glycol	5 ml/ampoule	90.7ml
Fomepizole	NA	1)Methanol, 2)ethylene glycol	5mg/ml, 20ml ampoule	1.05g
Glucogon	NA	1)ß-adrenergic antagonist, 2)calcium channel blocker	1 mg/vial	50mg
Methelene blue	3	Methemoglobinemia	10mg/ml, 10 ml ampoule	140mg
Naloxone	11	Acute opioid poisoning	10mg/ml, 10 ml ampoule	15mg
Obidoxime	4	Organophosphate insecticide	400 mcg/ml, 1ml ampoule	1g
Pyridoxine	1	Isoniazid (INH)	100 mg/1ml, 10 ml ampoule	10g

CONCLUSION

Poisons are fatal for human being's and antidotes are most important life saving measure in poisoning support to the vital system and removal of unabsorbed poison is the 1st line of treatment, then we use antidote according to the type of poison. Antidote is important measure in emergency and severe condition of poisoning. The mode of action of antidote can be better understood by their individual properties, mode of action for e.g.- potassium permanganate (1:1000) is best chemical antidote. This antidote should have affinity for that very specific system or organ in the body and also it will act vigorously like that of poison so as to nullify it and save the life of patients. Antidote is playing an important role in the treatment of poisoning. While good supportive care and elimination techniques may in many cases restore a poisoned patient to good health and stabilize his or her body function, the appropriate use of antidotes and other agent may greatly enhance elimination and reduce the toxic action of the poison.

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