Review Paper

Recent Advances in the Management of Poisoning Cases

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Abstract

Deaths due to poisoning are on the rise over the years, despite advanced knowledge regarding their pharmacokinetics and pathology, and newer and better techniques being developed for the management of poisoning cases. The management of a poisoned patient has changed over the years. Though the general principles of treatment of a poisoned patient remain the same, traditional methods like gastric lavage, for example, have taken a back seat. There has been gaining popularity of newer methods like use of activated charcoal and a variety of newer antidotes. Attention has also shifted to toxidromes, the collection of symptoms and signs that consistently occur after ingestion of a particular toxin or drug. Grouping the various signs and symptoms exhibited by a poisoned patient into different toxidromes helps the physician in rapid identification of the toxidrome and saves time in evaluating and managing a poisoned patient. However, the mainstay of the treatment, according to the experts is stabilization of the patient.

Key Words: Poisoning, Poisoned Patient, Management, Gastric Lavage, Charcoal, Toxidromes

Introduction:

"All substances are poisons; there is none that is not a poison;

The right dose differentiates a poison from a remedy" – Paracelsus [1]

Poisoning and deaths due to poisoning are on the rise over the years, despite advanced knowledge regarding their pharmacokinetics and pathology, and newer and better techniques being developed for the management of poisoning cases. It is estimated that there are more than nine million synthetic and natural chemicals available today.[2] In India, the trends of poisoning have changed over the years, from insecticides in the earlier times to fumigants, at present.[3] The commonest agents in India are the pesticides, followed by sedatives, drugs, chemicals, alcohols, plant toxins and house-hold cleansing agents.[4,5] Of late, aluminum phosphide has emerged as the commonest suicidal agent in Northern India.[6] In UK, around 15-20% of workload of medical units is due to self poisoning,[7] and paracetamol is one of the commonest drugs involved in self-poisoning, accounting for 43% of hospital admissions with history of self-poisoning. [8]

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While in the US, it accounted for 4.1% of deaths from poisoning.[9] The commonest agent causing deaths in poisoning cases in the UK up to 1998 was carbon monoxide.[10] The manner of poisoning differs with the age and poisoning in the paediatric age group generally occurs due to accidental ingestion of commercial and house-hold poisonous products (due generally to curiosity), while in the adolescents and the adults, intentional self poisoning is the common mode.[11]

General Principles:

The general principles of management of poisoning cases, as we know are:

1. Stabilization → which includes assessment and management of
   a) The airway and Breathing
   b) Circulation, and
   c) Depression of the Central Nervous System
2. Evaluation, if the patient is already stable
3. Decontamination → including skin/ eye decontamination, gut evacuation, etc
4. Poison Elimination → diuresis, peritoneal/ haemo dialysis, haemoperfusion, etc
5. Antidote administration → As of now, antidotes are available for < 5% poisons
6. Nursing and Psychiatric care.

Now-a-days, **stabilization** of the patient is being considered as the main stay of management of poisoning emergencies. Gastrointestinal evacuation, in use for centuries, is undergoing critical appraisal. The role of ipecac and gastric lavage are being questioned, while activated charcoal is gaining importance in the management of such cases. [12] Antidotal

therapy is no more the mainstay of the management and the fact that we have antidotes for only about 5% poisons, is mainly responsible for this development.[13] Grouping the signs and symptoms produced by the poisons in to various toxidromes helps in rapid and effective management of the case.

Gastric Decontamination:

Interference with absorption of ingested poison from the gastrointestinal tract is the mainstay of poison management. Because few specific antidotes are available to treat poisonings, absorption prevention, observation, and supportive care are the clinician's greatest assets. The challenge for clinicians managing poisoned patients is to identify those who are most at risk of developing serious complications and who might potentially benefit from gastrointestinal decontamination.[14] American Academy of Clinical Toxicology and European Association of Poison Centers & Clinical Toxicologists gave the position statements in gut decontamination in 1993. **[15, 16]**

Table 1: Summary of recommendations [15, 16]

Treatment	Indications
Gastric Lavage	Should not be considered unless a patient has ingested a potentially life – threatening amount of a poison and the procedure can be undertaken within 60 minutes of ingestion.
Activated charcoal	May be considered if a patient has ingested a potentially toxic amount of the poison (known to be adsorbed by charcoal) up to 1 hour previously; there are insufficient data to support or to exclude its use after 1 hr of ingestion.
Ipecacuanha	Its routine administration in the emergency department should be abandoned; there are insufficient data to support or to exclude its administration soon after ingestion.
Whole–bowel irrigation	May be considered for potentially toxic ingestion of sustained release or enteric coated drugs; there are insufficient data to support or to exclude its use for potentially toxic ingestion of iron, lead, zinc, or packet of illicit drugs (body – packer)
Cathartics	The administration of a cathartic alone has no role in the treatment of a poisoned patient and is not recommended as a method of gut decontamination

a) Gastric Lavage:

Stomach emptying by gastric aspiration and lavage has been in use in the management of poisoning by ingestion, for almost 200 years. [14] Studies, as early as 1959 [17] have demonstrated that gastric lavage is no more effective than ipecac emesis induced in specific instance. Other investigators, however, have challenged those studies on the basis of improper technique as the studies were carried out with animals and in non-overdose situations. The effectiveness of both gastric lavage and ipecac in removing stomach contents is time dependent and best results are obtained when performed within one hour. [12] Unfortunately, many overdose patients do not arrive to the emergency department within this valuable one hour. Although emptying the stomach in the first hour generally works [12, 18] and may be beneficial for up to a certain period of time thereafter, it is usually not helpful beyond 4 hours of ingestion. Sadly, the same is not applied in our country. Irrespective of the time gap, gastric lavage is performed in most of the hospitals, as the initial part of the treatment. Legal requirement, necessitating the preservation of a sample of the return lavage fluid for toxicological analysis, plays an important role in the continuing use of this technique, despite its efficacy being highly questionable.

Gastric lavage carries potential complications, including aspiration pneumonitis and, rarely, esophageal perforation. It can also promote the rapid passage of tablets into the small bowel rather than removing them. Studies have now shown that gastric lavage did not prove any more beneficial than activated charcoal, alone. [19, 20]

b) Activated Charcoal:

Activated charcoal has been used in the treatment of poisonings since 1830, when its effects were first demonstrated by the French chemist Bertrand.[21] Produced by pyrolysis of carbon containing materials and activated by oxidation with steam at a high temperature, these processed carbon products adsorb many drugs. Most commercially available preparations have a surface area of approximately $1000 m^2/g$. In addition to direct intra-luminal binding, activated charcoal can also decrease the resorption of agents that undergo enterohepatic or enterogastric cycling. [22] It also has a "gastrointestinal dialysis" effect, whereby the charcoal serves as a large "sink" with movement of toxin molecules across semi-permeable membranes from splanchnic circulation. [23]

During the last decade, however, activated charcoal became increasingly popular as a first-line agent for the treatment of poisonings, particularly if more than several hours have passed since ingestion. It is generally considered ineffective against caustics, ethanol, ethylene glycol, methanol, iron lithium, metals, and petroleum distillates. Usually complications of its use are rare, but they include aspiration of activated charcoal and gastric contents, as well as intestinal obstruction, particularly when repeated doses of activated charcoal are given. [24]

The use of multiple-dose activated charcoal (MDC) is now recommended for the

clearance of drugs such as -- carbamazepine, digitoxin, glutethimide, nadolol, phenobarbital, phenylbutazone, theophylline, and others. [25] Multiple dosing appears to decrease both the absorption and blood concentration of many drugs. The multiple-dose regimen consists of an initial dose of 50-100g followed by maintenance doses of 30-50 g every 2-6 h with or without the administration of a cathartic agent. Maintaining a constant amount of activated charcoal in the gut adsorbs the toxin as it is secreted back in to the gut, thereby preventing a delayed peak in the serum concentration. [18]

When activated charcoal is continually present in the gut, it might act as an infinite "sink", keeping the level of the toxin low in the lumen of the gastrointestinal tract. As most of the drugs and toxins are absorbed by simple diffusion, this "sink" may reverse the normal gradient, and actually permit transit of the toxin out of the blood in to the lumen of the tract→ gastrointestinal dialysis. [23] This has been shown to occur with theophylline, carbamazepine, dapsone, quinine and Phenobarbital.

Table 2: Charcoal & M D A

Substances not readily adsorbed to activated charcoal[18]	
Ferrous salts	Acids
Lithium preparations	Alkalies
Potassium salts	Fluorides
Ethanol	Organic solvents
Methanol	Mercury and its salts
Ethylene glycol	Lead and its salts

Indications for multiple dose activated charcoal[18]
Slow release preparations such as theophylline (but not lithium)
Carbamazepine
Dapsone
Digoxin
Paraquat
Phenobarbitone
Quinine
Amanita phalloides

The Coordination Committee in Accident and Emergency (A&E) Services of Hong Kong Protocol advocates activated charcoal as the treatment of choice for most poisons, except metals, alcohol, cyanide, acids and alkalies, which are not adsorbed by it.

c) Cathartics:

Catharsis actually means purification and this is achieved in the poisoning cases by purging the gastrointestinal tract of all the poisonous material. This is the premise that promotes their use for the rectal evacuation of gastric contents - both the drug and the drug-charcoal complex. Despite their widespread use, however, little evidence exists that cathartics alter the outcome of poisoned patients. The most commonly used cathartics are magnesium sulfate, magnesium citrate, and sorbitol. Sorbitol works the most quickly; causing bowel movements within one hour.[12] Contraindications to cathartics include caustic ingestions and signs of intestinal obstruction. If being considered, one dose is generally sufficient.

d) Whole - Bowel Irrigation:

Polyethylene glycol-electrolyte solutions, which once were used for bowel cleansing before surgical procedures, are now being applied for gastrointestinal decontamination. These iso-osmotically balanced, non-absorbable solutions are safe, causing no fluid retention or electrolyte disturbances.[26] The procedure has been advocated for overdoses of agents such as iron, lithium, arsenic, lead-oxide and enteric-coated or sustained-release medications. In practice, hemodynamically stable and cooperative patients are best suited for this intensive cathartic treatment. [24, 27] Adults should be given the solution at a rate of 2 L/h, children at 500 ml/h, either orally or through a naso-gastric tube. The endpoint of treatment is a clear effluent, which may take 4-6 hours to appear. Contraindications include ileus or bowel obstruction, hemodynamic instability or where airway cannot be protected. [28]

e) Emesis:

Ipecac syrup has long been used as a first-line agent for prevention of toxicity from ingested poisons, especially in children. However, this is not freely available in our country [13] and its effectiveness in recovering ingested substances is poor, and its ability to reduce the severity of poisoning has never been demonstrated. Moreover, the emesis induced by ipecac may preclude the use of other oral treatment options. [29] It is contraindicated in ingestion of caustic substances and volatile hydrocarbons, in patients who have decreased gag reflex or altered mental status, and in patients at risk for rapid alteration in consciousness. Complications of ipecac include aspiration pneumonia, lethargy, diaphragmatic rupture, Mallory-Weiss esophageal tears and cerebral hemorrhages.[30] Ipecac is also still recommended by poison control centers for use in the home, where early administration can be assured.

Laboratory Tests:

Although laboratory analysis of various body fluids of overdose patients frequently identifies substances that are clinically unsuspected, these additional findings rarely alter the patient's clinical course, largely because the presence of a substance does not necessarily correlate with acute toxicity;

moreover, analysis can be time-consuming and in most clinical settings falls short of being comprehensive.[12] Most poisoned or overdose patients do well with supportive care alone. Again, no rapidly available universal screening tool exists and many patients require little, if any, laboratory investigation.

Rational use of Antidotes:

Antidotes are chemical or physiological antagonists that prevent the toxicological effect of specific poisons. In most toxicological emergencies, effective antidotes are not available. Symptomatic treatment and supportive care are still the primary approach to treatment; antidotal therapy often plays a relatively minor role. When appropriately used in specific situations, however, antidotes can substantially reduce morbidity and mortality in the poisoned patient.

Some Newer Antidotes:

a) **Hydroxycobalamin:** [31] It is the synthetic form of vitamin B_{12} and is given in cases of cyanide poisoning presenting with hypotension, where the conventional antidote sodium nitrite is contraindicated. It works by sequestering cyanide from the plasma-cyanide to give non-toxic cyanocobalamin. The only adverse effects are brown discoloration of the body fluids, nausea and vomiting. The recommended dose is 5g) of the reconstituted solution over 30 minutes.

b) **Digoxin specific antibodies (Fab antibodies):** [32] Digoxin specific antigen binding fragments are indicated in life threatening arrhythmia/hyperkalaemia caused by intoxication with cardiac glycosides. As the antibodies are produced in sheep, monitoring for anaphylaxis and serum sickness is necessary.

c) **Esmolol hydrochloride:** [32] It is a short acting cardioselective beta- adrenoceptor blocking drug that has no sympathomimetic activity. It is used to control hypertension and tachyarrythmia due to poisoning by sympathomimetic drugs.

d) **Octreotide:** [32] A synthetic polypeptide that antagonizes pancreatic insulin release, it is indicated in overdose of insulin or oral hypoglycemic agents, mainly sulphonylurea.

e) **Succimer (2,3dimercaptosuccinicacid):** [33] it is a chelating agent used for the treatment of lead, mercury and arsenic poisoning. It is the water soluble analogue of dimercaprol and can be taken orally.

f) **Fomepizole (4-methypyrazol):** [33] It is a potent competitive inhibitor of alcohol dehydrogenase and prevents the formation of toxic metabolites following methanol and ethylene glycol poisoning. It is now preferred to ethanol as the antidote as it does not cause sedation.

g) **Nalmefene and Naltrexone:** [33] they are long acting opioid antagonists and are used to manage opioid dependence. They are more potent than Nalaxone but are much more expensive.

Toxidromes:

The term was first coined by Mofenson and Greensher. [34] They are a collection of symptoms and signs that consistently occur after ingestion of a particular toxin or drug and can often be identified with a basic history & physical examination. Many physicians now group the various signs and symptoms of the poisons into different toxidromes as the rapid identification of the toxidrome saves time in evaluating and managing a poisoned patient. The various toxidromes are anticholinergic, cholinergic, sympathomimetic (adrenergic), opiod and sedatve-hypnotic. Each of these toxidromes has specific signs and symptoms and requires a set pattern of management. Hence even if the poison cannot be identified, it can be classified into one of the above syndromes based on the signs and symptoms exhibited and appropriate treatment can be initiated.

Conclusion:

There has been a major change in the treatment of poisoned patients, particularly in the area of gastric decontamination. The trend is away from the use of ipecac, except in limited situations such as accidental ingestions in pediatric patients. For that reason, activated charcoal has attained a prominent role, not only as an adjunct for gastric emptying with either ipecac or gastric lavage but also for use as the sole decontamination agent. Gastric lavage still plays an important role, especially if it can be performed early, or if drugs are involved that may delay gastric emptying. Whole–bowel irrigation is safe and effective in limited situations such as iron, lithium, or sustained-release medications, and for body packers. Antidotes play an important role in specific situations. Oxygen is extremely useful for the treatment of CO. Naloxone is useful for the treatment of opiate intoxication. Fab fragment antibodies are safe and effective for the treatment of digitalis intoxication. Despite the advances in gastric decontamination and the development of new antidotes, the mainstay of treatment for the poisoning victim remains

supportive care and frequent re-evaluation for a change in clinical status.

Table 3: Common Toxidromes: Signs and Symptoms [35]

Physical findings	Adregenic Toxidrome (decongest., amphetamine, cocaine)	Anticholinergic Toxidrome (antihist., phenothiazine)	Cholinergic Toxidrome (Insecticides)	Opiod Toxidrome	Sedative-hypnotic Toxidrome (tranquilizer, barbiturates, ethanol)
Vital Signs					
Resp. Rate	Increased	No change	Increased/ no change	Decreased	Normal/ decreased
Heart rate	Increased	Increased	Decreased	Normal/ decreased	Normal
Temperature	Increased	Increased	No change	Normal/ decreased	Normal
Blood P	Increased	Increased/ no change	No change	Normal/ decreased	Normal
Physical Examination					
Mental status	Alert/ agitated	Depressed/ confused/ hallucinating	Depressed/ confused	Depressed	Depressed
Pupils	Dilated	Dilated	Constricted	Constricted	Normal
Mucous membranes	Wet	Dry	Wet	Normal	Normal
Skin	Diaphoretic	Dry	Diaphoretic	Normal	Normal
Reflexes	Increased	Normal	Normal/ decreased	Normal/ decreased	Normal/ decreased
Bowel sounds	Increased	Decreased	Increased	Decreased	Normal
Urination	Increased	Decreased	Increased	Decreased	Normal
Other	Possible seizures	Possible seizures	Musclefasciculations /possibe seizures	--	--

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