Antidotes in Poisoning

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ABSTRACT

Introduction: Antidotes are agents that negate the effect of a poison or toxin. Antidotes mediate its effect either by preventing the absorption of the toxin, by binding and neutralizing the poison, antagonizing its end-organ effect, or by inhibition of conversion of the toxin to more toxic metabolites. Antidote administration may not only result in the reduction of free or active toxin level, but also in the mitigation of end-organ effects of the toxin by mechanisms that include competitive inhibition, receptor blockade or direct antagonism of the toxin.

Mechanism of action of antidotes: Reduction in free toxin level can be achieved by specific and non-specific agents that bind to the toxin. The most commonly used non-specific binding agent is activated charcoal. Specific binders include chelating agents, bioscavenger therapy and immunotherapy. In some situations, enhanced elimination can be achieved by urinary alkalization or hemadsorption. Competitive inhibition of enzymes (e.g. ethanol for methanol poisoning), enhancement of enzyme function (e.g. oximes for organophosphorus poisoning) and competitive receptor blockade (e.g. naloxone, flumazenil) are other mechanisms by which antidotes act. Drugs such as N-acetyl cysteine and sodium thiocyanate reduce the formation of toxic metabolites in paracetamol and cyanide poisoning respectively. Drugs such as atropine and magnesium are used to counteract the end-organ effects in organophosphorus poisoning. Vitamins such as vitamin K, folic acid and pyridoxine are used to antagonise the effects of warfarin, methotrexate and INH respectively in the setting of toxicity or overdose. This review provides an overview of the role of antidotes in poisoning.

Keywords: Antidote, Binding, Poison, Toxin.

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INTRODUCTION

Toxicological emergencies are encountered frequently in intensive care unit (ICU) practice, either as a result of drug overdose (accidental or suicidal) or due to drug toxicity secondary to inappropriate drug dosing or drug interactions. In general, toxic agents can be classified into two groups: those for which specific treatment exists and others for which there is no specific therapy. The latter list by far exceeds the former and hence the most important guiding principle in such emergencies is good supportive care while the patient recovers. "Treat the patient, not the toxin" is hence the guiding dictum in clinical toxicology. In a small proportion (<2%) of toxins,[1] antidotes have been identified. It must be stressed that the expected benefit of the antidote must be determined and weighed against the potential side effects and toxicity of the antidote. In severe poisoning, the antidote is only an adjunct to supportive treatment and its use should not distract the physician from delivering adequate attention to airway, breathing, circulation, and decontamination. When antidotes are administered appropriately, they may limit morbidity and mortality as demonstrated in paracetamol and digitalis overdose.[2] On the other hand, if unavailable or used inappropriately, the patient may suffer adverse effects from the poison or the antidote, respectively.

WHAT IS AN ANTIDOTE?

The International Programme of Chemical Safety broadly defines an antidote as a therapeutic agent that counteracts the toxic actions of a drug/toxin.[3] Broadly, antidotes have been looked at as agents that "modify the kinetics of the toxic substance or interfere with its effect at receptor sites."[4] This may be as a result of prevention of absorption, binding, and neutralizing the poison directly, antagonizing its end-organ effect, or inhibition of conversion to more toxic metabolites.[5] A chemical's safety is defined by its therapeutic index or ratio (TD_{50}/ED_{50}), which is the ratio of the toxic

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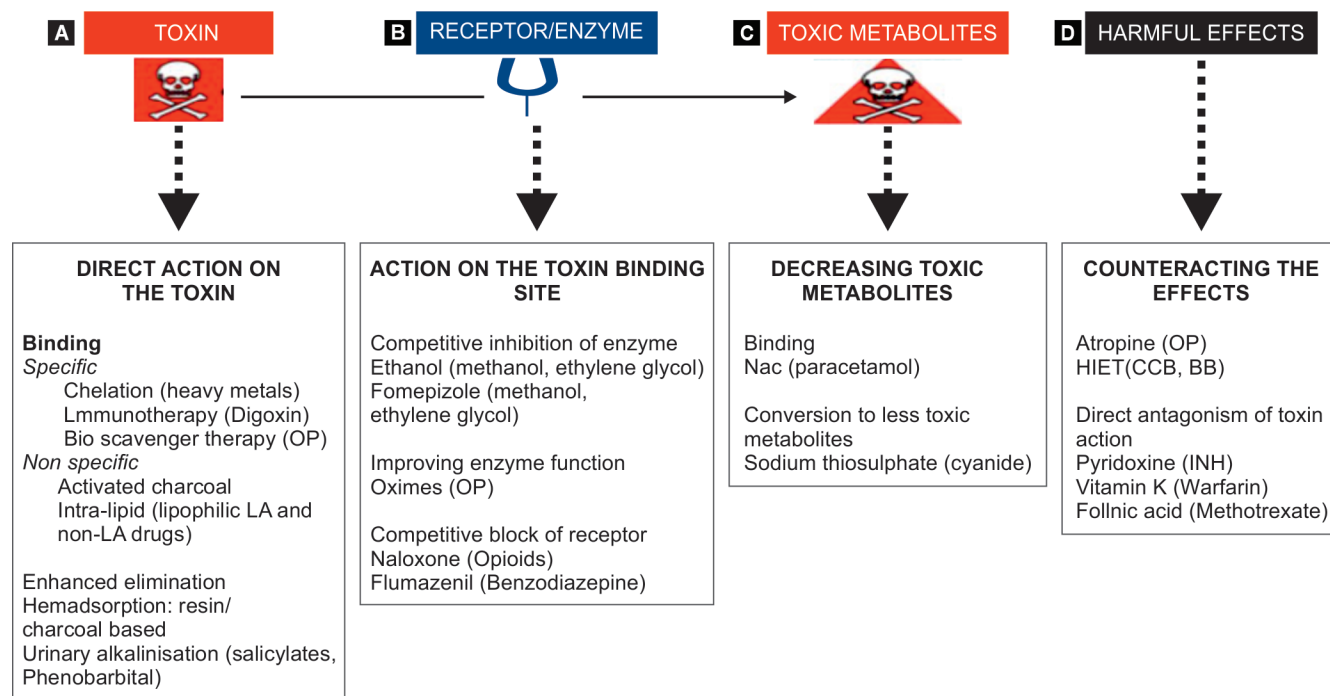
dose (TD) or lethal dose (LD) to the effective dose (ED). Based on this, an antidote has also been defined as an agent that "increases the mean lethal dose of a toxin."[1]

HOW DOES AN ANTIDOTE WORK?

When one thinks of antidotes, one generally considers those that operate through a distinct logical mechanism such as naloxone and flumazenil that function as competitive receptor antagonists or vitamin K for warfarin overdose to overcome enzyme inhibition. Antidotes, however, have a broader meaning in terms of altering the effect of a toxin. Two main variables impact the harmful effect of a toxin on the body, namely the dose and the duration of exposure to the toxin.[1] These in turn depend on the type of toxin, the dose, the route of administration, lag time to presentation to a hospital, and pharmacokinetics (absorption, distribution, and elimination).

Thus, four basic mechanisms (Fig. 1) guide antidotal therapy in toxicology that result in the alteration of the toxin load and the duration of exposure and elevate the victim's threshold for toxicity. This includes (a) decreasing the active toxin level, (b) blocking the site of action of the toxin, (c) decreasing the toxic metabolites, and (d) counteracting the effects of the toxin.

A TOXIN	**B** RECEPTOR/ENZYME	**C** TOXIC METABOLITES	**D** HARMFUL EFFECTS
DIRECT ACTION ON THE TOXIN **Binding** *Specific* Chelation (heavy metals) Lmmunotherapy (Digoxin) Bio scavenger therapy (OP) *Non specific* Activated charcoal Intra-lipid (lipophilic LA and non-LA drugs) Enhanced elimination Hemadsorption: resin/charcoal based Urinary alkalinisation (salicylates, Phenobarbital)	**ACTION ON THE TOXIN BINDING SITE** Competitive inhibition of enzyme Ethanol (methanol, ethylene glycol) Fomepizole (methanol, ethylene glycol) Improving enzyme function Oximes (OP) Competitive block of receptor Naloxone (Opioids) Flumazenil (Benzodiazepine)	**DECREASING TOXIC METABOLITES** Binding Nac (paracetamol) Conversion to less toxic metabolites Sodium thiosulphate (cyanide)	**COUNTERACTING THE EFFECTS** Atropine (OP) HIET(CCB, BB) Direct antagonism of toxin action Pyridoxine (INH) Vitamin K (Warfarin) Follnic acid (Methotrexate)

Figs 1A to D: Antidotes act by four predominant mechanisms; (A) Direct action on the toxin involves specific and nonspecific binding and enhanced elimination. Specific binding can be achieved by chelation (e.g., heavy metals), immunotherapy (e.g., digoxin), and bioscavenger therapy (e.g., organophosphorus (OP) compounds). Nonspecific binding occurs with the use of activated charcoal and intralipid therapy (e.g., lipophilic local anesthetics (LA) and non-LA drugs). Enhanced elimination of toxin can be facilitated through urinary alkalization (e.g., salicylates, phenobarbital) and hemadsorption with the use of resin or charcoal; (B) Action on the toxin binding site can be achieved by competitive inhibition of the enzyme (e.g., ethanol or fomepizole for methanol and ethylene glycol poisoning) or by competitive blockade of the receptor (e.g., naloxone for opioid overdose and flumazenil for benzodiazepine overdose; (C) Decreasing toxic metabolites can be done by binding (e.g., N-acetyl cysteine (NAC) as for paracetamol overdose) and conversion to less toxic metabolites (e.g., sodium thiosulphate for cyanide poisoning); (D) Counteracting the effects: drugs such as atropine counteract the muscarinic effects of OP poisoning. High-dose insulin euglycemic therapy (HIET) is used for calcium channel blocker (CCB) and β-blocker (BB) overdose. Direct antagonism of toxin action is the mechanism for reversing the toxicity of INH (pyridoxine), warfarin (vitamin K), and methotrexate (folinic acid)

Decreasing the Free or Active Toxin Level

A reduction in the free or active toxin level can be achieved by agents that "bind" to the toxin (Table 1). This binding can be either specific or nonspecific. Specific binding occurs in the form of chelating agents for heavy metal poisoning, Digi-Fab for digoxin overdose, hydroxycobalamin for cyanide poisoning, or bioscavenger therapy (human butyryl cholinesterase) for organophosphorus poisoning,[6,7] where the antidote enables the formation of inert complexes[8] that are then eliminated from the body (Table 1).

Activated charcoal has been included in the list of nonspecific antidotes because it can decrease the toxin levels by its high adsorption capacity and by interrupting the enterohepatic recirculation of the toxin. A higher charcoal to drug ratio will more effectively inhibit systemic absorption; while 10:1 is ideal, some reports suggest that a 40:1 charcoal to drug ratio might be superior. Activated charcoal has been in use for over a century and while it has been reported to be the most common form of gastrointestinal decontamination in the poisoned patient, its use has declined from 7.7% to 5.9%.[9] The reason for this is twofold; first, the evidence[10,11] from randomized controlled trials (RCTs) has failed to show any added benefit of activated charcoal. Second, the complications from its administration, such as charcoal aspiration with pneumonitis[12] and constipation and bowel obstruction,[13] preclude widespread use. The position paper on charcoal recommends that "single-dose activated charcoal should not be administered routinely in the management of poisoned patients."[9] This can however be considered in a patient who has ingested a toxin within an hour of presentation.[9] Multidose activated charcoal is recommended in life-threatening ingestions of carbamazepine, dapsone, phenobarbital, quinine, or theophylline.[14]

Lipid sink therapy has also been considered under nonspecific binders since its recognition of benefit in local anesthetic toxicity in rats in 1998.[15] Intravenous lipid therapy has been in use in humans for both lipophilic local anesthetics and nonlocal anesthetic agents (β-blockers, calcium channel blockers, psychotropic drug overdose). This works on the lipid sink principle where lipophilic drugs, with an octanol to water partitioning coefficient of $\log p > 2$,[16] are trapped in the plasma lipid compartment. Lipid emulsion therapy has also been proposed to have a direct inotropic effect through increase in calcium levels in cardiac myocytes.[17]

Enhancing the elimination of toxins with the use of antidotes can be done either through hemoperfusion techniques (charcoal or resin based)[18] or urinary alkalinization (targeting a pH > 7.5) with intravenous sodium bicarbonate therapy.[19] Hemoperfusion is useful for protein-bound toxins, high lipid solubility, or toxins with a high volume of distribution. Urinary alkalinization is useful for acidic toxins such as salicylates and phenobarbital and acts by increasing ionization of the toxin, thereby limiting their tubular reabsorption.[19]

Action on the Toxin-binding Site

This can be either at the enzyme level or the receptor level (Table 2). At the enzyme level, the action could be twofold: competitive

Table 1: Antidotes acting by decreasing the toxin level

	Mechanism	Example	Where and when	Mechanism of action	Dose	Other salient points and evidence
Decrease toxin level	Decrease absorption	Activated charcoal (AC)	Multidose can be considered for: carbamazepine, dapsone, quinine, phenobarbitone, theophylline	Adsorbs chemicals within minutes of contact	Single-dose activated charcoal (SDAC): <1–12 years: 0.5–1.0 g/kg (max 50 g) adults: 25–100 g	SDAC should not be administered routinely to poisoned patients; MDAC may be of benefit in antiepileptic overdose. Not useful in organophosphorus poisoning
			Recent ingestion within 1 hour;[9] may be considered at a later interval if modified-release product; may be beneficial if administered up to 4 hours after large ingestions and for ingestion of substances with anticholinergic or opioid properties that decrease intestinal motility	Higher stoichiometric ratio of charcoal to drug will more effectively inhibit systemic absorption (10:1 is ideal but reports suggest that 40:1 might be superior)	Multidose activated charcoal (MDAC): 50 g Q4H	Not useful for: acids, alkalis, and alcohols; metals: iron, lithium, potassium, lead, silver
	Bind to the toxin chelation	Dimercaprol (British anti-Lewisite)	FDA-approved treatment for arsenic, gold, and mercury poisoning. Also approved for lead poisoning in combination with ethylene diamine tetraacetic acid (EDTA)	Sulfhydryl group combines with heavy metals to form relatively stable, nontoxic, soluble chelates that are excreted in urine	Administered as deep IM injection	In lead poisoning, dimercaprol must be given before calcium disodium edetate to prevent redistribution of lead to the brain
			More effective if given soon after exposure in gold-induced thrombocytopenia, symptomatic or asymptomatic mercury poisoning with mercury whole blood or 24-hour urine levels ≥100 µg/dL, lead poisoning with whole blood levels ≥100 µg/dL		Severe arsenic or gold poisoning: 3.5–5 mg/kg Q4H for six doses, then Q6H for four doses, Q8H for three doses, followed Q12H for two doses and then OD for 10 days	Dimercaprol not complexed with metal is metabolized in the liver
					Mercury: 5 mg/kg initially Q4H for 1–2 days, followed by 2.5 mg/kg 1–2 times/day for 10 days	Short half-life and is excreted in urine
					Lead: 4 mg/kg Q4H for 3 days, begin chelation with EDTA with second dose, followed by 2.5 mg/kg for 1–4 days	Dissociation of the metal from the sulfydryl group can occur in acidic urine—it is therefore important to maintain alkaline urine pH
						Evidence mainly from animal experiments and human reports and series[40]
	Immuno-therapy	Digi-Fab (digoxin-specific antibody fragments)	Acute severe or chronic digoxin toxicity with life-threatening tachy or bradyarrhythmias, hyperkalemia (>6 mmol/L) or renal failure or hemodynamic instability with digoxin concentration >2 µg/L; some recommend in acute ingestions >10 mg (adult) and >4 mg (children)	Fab portion of IgG anti-digoxin antibodies bind free digoxin, forming digoxin-immune fragment complexes. Fall in free digoxin facilitates dissociation of digoxin from sodium-potassium ATPase. Digoxin-Fab fragment complexes renally excreted	1 vial binds 0.5 mg of digoxin. If unknown ingestion, administer 10 vials for adults and 5 vials for children	Not indicated for asymptomatic patients with elevated serum digoxin levels. Digoxin load based on concentration will be overestimated when concentration measured before distribution is complete (around 6 hours).[41] Do not measure digoxin levels after administration of digibind for at least 3 weeks as it may be falsely high since most assays measure both free and Digi-Fab-bound digoxin. Evidence mainly from case series[41]

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Mechanism	Example	Where and when	Mechanism of action	Dose	Other salient points and evidence
Lipid sink	Intralipid	Treatment of poisoning by lipid-soluble drugs such as bupivacaine, propranolol, and verapamil	Expanding lipid compartment within intravascular space, sequestering lipid-soluble drugs from tissues. Efficacy related to metabolic effects in the myocardium, specifically its ability to enhance fatty acid intracellular transport in myocardial cells	1.5 mL/kg of 20% intralipid as an initial bolus followed by 0.25 mL/kg/minute for 30–60 minutes; depending upon response, bolus could be repeated one to two times and infusion rate increased	Case series and animal studies[16]
Enhance elimination	Urinary alkalinization (for "acid" overdose)	Tricyclic antidepressant with ECG abnormalities (QRS >100 ms predictive of seizures; QRS >160 ms predictive of ventricular arrhythmias) and salicylate overdose >300 mg/kg	Urinary alkalinization increases the ionized form of the toxin and hence less is reabsorbed from the renal tubules	Bolus 1–2 mEq/kg followed by infusion diluted in 5% dextrose	Small randomized cross-over studies[19]
	Hemoperfusion (charcoal or resin based)	Useful for protein-bound toxins and high lipid solubility.[42] Charcoal hemoperfusion: may have a role in early Paraquat poisoning. While there were reports of benefit with theophylline, aluminium, phenobarbital, and aspirin overdose, dialysis is now preferred with the advent of high-flux filters	Blood is passed through a column made of either AC or synthetic anion exchange resin. Protein-bound substances bind to the adsorptive material in the column and are removed from circulation. This will decrease the blood concentration of the poison, then decrease the severity of toxicity		Hemoperfusion will not be helpful if[42] • Toxin has large VD > 1 L/kg as the toxin will be multicompartmental and unlikely to be removed • Toxin has high endogenous or systemic clearance • If molecular size >5,000 Da, clearance is reduced Evidence from animal studies and case reports

Table 2: Antidotes acting on the toxin-binding site

	Mechanism	Example	When and where	Mechanism of action	Dose	Salient features and evidence
Action on the toxin-binding site	Competitive receptor block	Naloxone	Opioid overdose characterized by life-threatening respiratory depression—either hypopnea (respiratory rate <12/minute) or apnea associated with either miosis or stupor	Competitive antagonist at μ opioid receptors	IV (preferred); can also be administered IM, S/C, or IN 0.4–2 mg	Onset of action <2 minutes if given IV with duration of action of 20–90 minutes. Dosing is empirical and is guided by clinical response[28]
					Repeat doses every 2–3 minutes, if no response after 10 mg, consider alternate diagnosis	
					Smaller doses of 0.04 mg to be given if opioid dependence suspected	
					May need an IV infusion of naloxone	
		Flumazenil	Treatment of and preventing recurrence of benzodiazepine-induced coma	Nonspecific competitive antagonist of the GABA-benzodiazepine receptor by decreasing the inward chloride current	0.1–0.2 mg IV and repeat every minute until there is reversal (max dose not exceeding 2 mg)	Onset of action in about 1–2 minutes; 80% response seen within the first 3 minutes
					Children: 0.01–0.02 mg/kg, repeat every minute	Peak effect 6–10 minutes after administration
					May need infusion if resedation occurs since duration of action of flumazenil (0.7–1 hour) is shorter than most benzodiazepines	Contraindication in seizure disorder and mixed overdose
						Evidence from retrospective case series and cohort studies[25]
	Competitive enzyme block	Fomepazole	Methyl alcohol and ethylene glycol toxicity	Competitive inhibition of alcohol dehydrogenase that catalyzes the metabolism of ethanol, ethylene glycol, and methanol to their toxic metabolites	Loading dose of 15 mg/kg should be administered, followed by doses of 10 mg/kg every 12 hours for 4 doses, then 15 mg/kg every 12 hours, thereafter until alcohol concentrations <20 mg/dL	Case reports and prospective case series[20,21]
			Must be done early since alcohol dehydrogenase (ADH) inhibition does not prevent toxicity if toxic metabolites already formed			
	Reactivation of enzyme activity	Oximes	Potential for benefit in very early presentation of organo-phosphorus (OP) poisoning (<2 hours)	Nucleophilic agents that reactivate OP-bound acetyl cholinesterase	Suggested dosing regimen: pralidoxime loading dose 2 g over 20 minutes followed by 0.5 g/hour for a maximum of 7 days or till no atropine required[22]	Largest trial of oxime in OP poisoning showed no beneficial effect.[11] One trial[38] showed benefit of high-dose oximes in those who presented very early (<2 hours). Systematic reviews null effect or harm[23]

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Mechanism	Example	When and where	Dose	Mechanism of action	Salient features and evidence
		No effect or potential harm as per evidence in systematic reviews			
		Best supportive care in those who present late (>2 hours); in early presenters, risk vs. benefit to be evaluated for use of oximes			

inhibition or reactivation of enzyme activity. The classical example of competitive enzyme inhibition is the use of ethyl alcohol or fomepizole in methyl alcohol or ethylene glycol poisoning. These agents act by competing with methyl alcohol[20] and ethylene glycol[21] for alcohol dehydrogenase (ADH), thereby decreasing the formation of toxic metabolites. This must be done early since ADH inhibition does not prevent toxicity if the toxic metabolites are already formed.

Reactivation of enzyme activity in the setting of organophosphorus poisoning is achieved with the use of nucleophilic agents such as oximes that reactivate organophosphorus-bound acetyl cholinesterase. Meta-analysis of studies on oxime therapy in acute organophosphorus poisoning has shown a null effect or potential harm.[7] While the largest randomized trial of oximes showed clear reactivation of red cell acetylcholinesterase, there was no evidence of improved survival with oxime therapy.[22] There are several reasons for the failure of oximes in acute organophosphorus poisoning.[23] More research on this aspect may throw light on possible options of dosing and timing of antidotal therapy in organophosphorus poisoning.

At the receptor level, flumazenil and naloxone are the classical antidotes. Flumazenil is a competitive antagonist at the benzodiazepine site on the GABA-A receptor complex.[24] This decreases the inward chloride current and thereby reverses CNS and respiratory depression. Flumazenil has been shown to be effective in the treatment of and preventing recurrence of benzodiazepine-induced coma.[25–27]

Flumazenil is contraindicated in patients with unknown or mixed overdose, benzodiazepine tolerance, seizure disorders, or a prolonged QRS interval. Naloxone is a pure opioid antagonist that competes and displaces opioids at opioid receptor sites and has been shown in uncontrolled studies to be useful in opioid reversal.[28] Given the risk of opioid withdrawal that can happen not only in regular opioid abusers but also with acute opioid toxicity, the recent American Heart Association recommends using the "lowest effective dose"[29] of naloxone.

Decreasing Toxic Metabolites

Once toxic metabolites are formed, antidotes may be used to either mop up the toxic metabolite or convert the metabolites into a less toxic form (Table 3). *N*-Acetyl cysteine (NAC) has been used for paracetamol poisoning for the past 50 years.[30] *N*-Acetyl cysteine restores hepatic glutathione stores, which in turn is responsible for conjugating the toxic metabolite, *N*-acetyl P-benzoquinone imine (NAPQI). This is believed to be the mechanism of prevention of paracetamol-induced hepatic injury. While there are no randomized controlled trials to assess the efficacy of NAC for liver injury prevention, there are several studies[31,32] that have reported benefit and hence it is considered unethical to perform a RCT.

In cyanide poisoning, sodium thiosulphate[33] has been found to catalyze the formation of thiocyanate from cyanide by being a sulfhydryl donor to rhodonase enzyme. This is an example of conversion of toxic metabolites to less toxic compounds.

Counteracting the Harmful Effects of the Toxin

Counteracting the harmful effect of the toxin could be effected in two ways, either by mitigating the effect of the toxin or by direct antagonism of drug action. Atropine, used in organophosphorus poisoning, is an example of an antidote that is used to counter and mitigate the several muscarinic effect of the poison. Several vitamins are used to directly antagonize the effect of a drug or toxin.

Table 3: Antidotes decreasing toxic metabolites

Mechanism	Example	When and where	Mechanism of action	Dose	Evidence
Decrease toxic metabolites	Mopping up toxic metabolites	N-Acetyl cysteine (NAC)	Serum acetaminophen concentration taken 4 hours or more after acute ingestion above the treatment line of the nomogram	NAC restores hepatic glu-tathione stores, which in turn conjugate the toxic metabolite N-acetyl P-benzoquinone imine (NAPQI) that is responsi-ble for liver injury	IV or oral	While there are no randomized controlled trials (RCTs) to assess the efficacy of NAC for liver in-jury prevention, there are several studies[31] that have reported benefit and hence it is consid-ered unethical to perform a RCT
			Single ingestion of >150 mg/kg in a patient where levels may not be available for >8 hours from time of ingestion		IV: 150 mg/kg over 60 minutes followed by 50 mg/kg over 4 hours and 100 mg/kg over 16 hours	
			Unknown time of ingestion with concentration >10 µg/mL with evidence of liver injury		Oral: 140 mg/kg PO, fol-lowed by 70 mg/kg PO every 4 hours for a total of 17 doses	
			Can consider in patients with delayed presentation >24 hours after ingestion if evidence of liver injury		If evidence of continued liver injury, can consider a longer infusion of NAC	
	Formation of less toxic metabolites	Sodium thiosul-phate	Cyanide poisoning	Sodium thiosulphate catalyzes the formation of thiocyanate from cyanide by being a sulfhydryl donor to rhodonase enzyme	1 ampule or 12.5 g in 50 mL, given IV for 30 min-utes in adults	This has poor intracellular penetration, slow onset of effect, a short half-life, and limited distribution volume. Usually con-sidered when features of tissue hypoxia despite maximum dose of hydroxycobalamin Animal studies and case re-ports[43]

Examples include vitamin K for warfarin overdose, pyridoxine[34] for isoniazid (INH) overdose, and folinic acid for methotrexate toxicity.[35] Pyridoxine binds to INH, replaces stores of pyridoxine, and facilitates the production of γ-amino butyric acid (GABA) that helps in controlling seizures.

When Should the Antidote be Administered?

The "benefit from antidotes is generally time-dependent and uncertain."[36] It is difficult to give a prescribed approach to guide the decision to administer an antidote in a toxicological emergency as this depends on the lag time to presentation, toxicokinetics properties, and the mechanism of action of the antidote.

Antidotes that decrease the toxin level by reducing absorption or by adsorption (binding agents) at the receptor/enzyme level are generally beneficial if administered early. On the other hand, antidotes that modify the toxic metabolites or modulate the effects (either symptomatic or direct antagonism of the effect of the toxin) could be given at variable times. Tables 1 to 3 provide an overview of the various mechanisms of action of antidotes, the clinical setting where it could be used, and the dosing of common antidotes.

How Long Should the Antidote be Administered for?

The duration of antidotal therapy depends on the type of toxin consumed, the estimated dose that the individual has been exposed to, route of exposure, clinical features of toxicity, half-life, and pharmacokinetics as well as the risk vs benefit for the use of the antidote. In case the antidote has a short half-life, an infusion may need to be started particularly if symptoms of toxicity resurface.

What is the Evidence of Efficacy of Antidotes?

Results from animal studies, human case reports, pharmacokinetic data, expert opinion, and logic have generally guided the timing, indications, and dosing of antidotes. Although there are some RCTs that have explored the role of activated charcoal in poisoning,[37] there is a paucity of RCTs on specific antidotes in poisoning other than organophosphorus poisoning.[38,39] The lack of high-level evidence should not deter the clinician from considering a particular antidote as long as the benefits outweigh the risks.

Conclusion

Successful outcomes in a toxicological emergency not only require appropriate management of airway, breathing, and circulation but also the knowledge and application of appropriate antidotal therapy. The latter may result in reducing the intensity of the poisoning and improving outcomes.

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