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Acute poisoning: best practice in antidote stock and supply management

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Keypoints

Appropriate supply of antidote stocks in a peripheral hospital is essential to meet time-critical administration windows.

Abstract

The clinical impact and outcomes of poisoning can vary markedly according to the substance involved.
Identifying the causative toxic agent(s) in a patient is fundamental to optimal clinical management.
Clinical presentation may differ with the agent, dose, duration of exposure, and pre-existing comorbidities.
In a peripheral hospital, adequate planning and organisation of care pathways, together with appropriate procurement and stockholdings of antidotes, are essential for effective clinical management.

Keywords

Antidotes; acute poisoning; antidote classification, drug storage

Introduction[1-5]

The epidemiology of acute poisoning is under-represented in both the Italian and international medical literature, and is largely confined to publications within paediatric injury literature. In 2019, the Global Burden of Disease (GBD) study reported that unintentional poison ing accounted for 0.14% of all global deaths, whereas self-harm contributed 1.34%. The World Health Organization (WHO) estimates that approximately 800,000 people die each year due to suicide and self-poisoning. According to the most recent report from the Italian Istituto Superiore di Sanità, in 2021 more than 29,000 cases of chemical exposure were recorded, the majority (92%) occurring in the home. Among patients, 44% were under six years of age, with a marked peak at one and two years. The products most frequently implicated include detergents, cosmetics, biocides, and medicines, while the predominant route of exposure is ingestion. In nearly half of cases, patients developed symptoms; treatment was initiated in 75% of cases. The Italian regions with the highest number of calls to Poison Control Centres are Lombardy, Emilia-Romagna, Tuscany, and Piedmont. Antidotes are therapeutic agents which, through specific or non-specific mechanisms, can improve the prognosis quoad vitam (survival) or quoad functionem (function) in poi

soning. Some antidotes are commonly used in clinical practice and their therapeutic and adverse effects are well known; others are rarely used and remain unfamiliar.

Analysis and discussion[1-11]

Acute poisonings account for a variable proportion between 1–5% of Emergency Department (ED) attendances. Toxicological emergencies are frequently encountered in both Intensive Care Units (ICUs) and Emergency Departments (EDs), arising from accidental or intentional ingestion (with suicidal intent) as well as from drug toxicity secondary to inappropriate dosing or drug–drug interactions.

Broadly, toxic agents can be divided into two categories: those for which a specific therapy exists, and those for which no specific therapy is available. The latter group far outnumbers the former; therefore, the central guiding principle in such emergencies is high-quality supportive care of the patient's vital functions. "Treat the patient, not the poison" remains the guiding principle in clinical toxicology.

In severe poisoning, antidotal therapy serves as an adjunct to supportive treatment and continuous monitoring of vital functions. When administered appropriately, antidotes can reduce morbidity and mortality. *Timely availability within Emergency and Urgent Care Services is an essential component of antidotal treatment.*

As reported by Locatelli (2006), antidotes act by:

1. Reducing the toxicant's bioavailability through decreased absorption;
2. Slowing or inhibiting the formation of toxic metabolites;
3. Acting on toxicodynamic mechanisms: displacing the toxicant from the receptor when target binding is reversible; counteracting the toxicant's effect at the receptor level; reactivating the modified target; bypassing the toxicant's action;
4. Supplying physiological components depleted by the toxicant;
5. Modifying the distribution of the toxicant in the body: binding the toxicant and rendering it inactive; altering its binding to plasma proteins;
6. Promoting the formation of less harmful or inert compounds;
7. Accelerating the formation of non-toxic metabolites;
8. Enhancing clearance of the toxicant in unchanged form.

Antidotes are therapeutic agents that, through specific or non-specific mechanisms, improve the prognosis of acute poisoning. Some are truly life-saving medicines; others play a decisive role in patient management even when used as part of multimodal regimens alongside advanced supportive care, decontamination, and enhanced elimination techniques. In the management of acute poisoning, medicines licensed for other indications are often prescribed off-label for antidotal purposes, sometimes at atypical doses; their pharmacology and adverse-effect profiles may be less well characterised, with differing pharmacokinetics and potential metabolic interactions. For optimal clinical use, the timely availability of antidotes within the ICUs and EDs of the national health service is essential. However, studies from several countries (the United States, Canada, the UK, France, Spain, and Italy) indicate that key antidotes are frequently unavailable—or available only in insufficient quantities—even in national or regional referral hospitals; the problem is often more pronounced in peripheral hospitals.

Antidotes are categorised into priority classes according to the maximum permissible time to availability:

A (Priority 1): Available within 30 minutes; accordingly, these agents should be stocked in all Emergency Departments and urgent care services. (Tab 1)

B (Priority 2): Available within 2 hours; these agents may be held by hospital pharmacies (24-hour service or on-call arrangements) or within urgent clinical services of referral hospitals. (Tab 2)

C (Priority 3): Available within 6 hours; typically held

at regional or supra-regional referral hospitals and Poison Control Centres. (Tab 3)

D (Priority 4): Some antidotes are placed in a separate class because their availability may exceed 6 hours; (an over-regional stockpile or single national centre may be sufficient) (Tab 4).

The criteria used to define required antidote stocks integrate guidance from the European Economic Community (EEC) Resolution of 3 December 1990 (Official Journal of the European Communities, C 329/6, 31 December 1990) and the WHO–IPCS Guidelines for Poison Control Centres (1997; updated 2021).

Ethanol 95% (v/v), solution for injection	Digoxin-specific antibody fragments (Fab), lyophilised powder
Andexanet alfa (recombinant factor Xa reversal agent)*	Glucagon (as hydrochloride), lyophilised powder
Atropine sulfate	Idarucizumab*
Sodium bicarbonate 8.4%, solution for infusion	Hydroxocobalamin, lyophilised powder
Methylene blue (methylthioninium chloride) 1%, solution for injection	Magnesium sulfate ($MgSO_4$), powder
Calcium chloride 10%, solution for injection	Naloxone hydrochloride
Calcium gluconate 10%, solution for injection	Liquid paraffin (mineral oil)
Activated charcoal (powder/granules) for oral suspension	Polyethylene glycol (PEG) 400
Dantrolene sodium**	Polyethylene glycol (PEG) 3350/4000
Diazepam 10 mg injection ampoules	Protamine sulfate, solution for injection
20% intravenous lipid emulsion	Simeticone oral drops
Physostigmine salicylate 1 mg/mL, solution for injection	Sodium thiosulfate, solution for injection (sodium hyposulfite)
Flumazenil	Vitamin B6 (pyridoxine hydrochloride)
Fomepizole (4-methylpyrazole sulfate)	Vitamin K, solution for injection (phytomenadione)

Table 1. Priority 1 Antidotes

** Andexanet alfa (a specific reversal agent for apixaban or rivaroxaban) and idarucizumab (a specific reversal agent for dabigatran) are available at Poison Control Centres in Lombardy. Specific guidance on routine availability under standard administration depends on the Regional Medicines Commission.*

***Priority 1 for malignant hyperthermia; Priority 2 for neuroleptic malignant syndrome*

Antidotes assigned to Priority 2 (available within 2 hours; Table 2), Priority 3 (within 6 hours; Table 3) and Priority 4 (beyond 6 hours; Table 4) require predefined pathways, developed with the hospital pharmacy and hospital management, to guarantee availability within the specified time limits.

Folic acid	N-acetylcysteine (solution for infusion; oral formulations)
Folinic acid - Calcium folinate/ levofolinate	C1-esterase inhibitor concentrates and bradykinin B2-receptor antagonists
Bromocriptine	Levocarnitine (L-carnitine), injection
Calcium gluconate 2.5% gel	Neostigmine methylsulfate
Cyproheptadine hydrochloride	Octreotide
Chlorpromazine	Pralidoxime powder for reconstitution
Dantrolene sodium	Silymarin/Silibinin
Fomepizole concentrate for infusion	Vitamin B1 (thiamine), solution for injection
European viper antivenom	Vitamin C (ascorbic acid), injection ampoules
Mannitol	

Table 2. Priority 2 Antidotes

** Symptomatic therapy for acute hereditary angioedema and ACE-inhibitor–related angioedema*

Deferoxamine mesilate	Penicillamine
Edetate calcium disodium injection ampoules	Propylthiouracil
DMPS (2,3-Dimercapto-1-propanesulfonic acid)	Succimer (DMSA)
Phentolamine	

Table 3. Priority 3 Antidotes

Amyl nitrite	Dimercaprol (BAL)
Botulism antitoxin	Glucarpidase
Argatroban	Potassium iodide
Prussian blue	Uridine triacetate
Pentetate calcium trisodium / pentetate zinc trisodium (DTPA)	

Table 4. Priority 4 Antidotes

The organisation of peripheral hospitals frequently conflicts with the optimal management of acute poisoning. Many centres lack a hospital pharmacy operating 24/7, or providing out-of-hours on-call support; this can delay timely access to antidotes, particularly overnight and at weekends.

Effective arrangements involving the EDs and urgent care services, the hospital pharmacy, the Medical Directorate(s), and the designated Poison Control Centre are therefore essential. Given that rapid availability of antidotes (in some cases within minutes or 1–2 hours of the patient's arrival at urgent care services) is critical to the appropriate treatment of poisoned patients, Emergency and urgent care services should maintain adequate in-house stocks of antidotes, both in terms of the agents required and the quantities held. Procurement should anticipate poisoning outbreaks (e.g., contaminated or adulterated foods), prolonged treatment courses over several days, simultaneous multiple cases (e.g., mushroom ingestion), chemical incidents, and other mass-casualty scenarios. Decisions on antidote stockholding should be informed by international, national, and local epidemiological data, where available.

Every ED should maintain a dedicated trolley for acute poisoning, stocked with priority 1 antidotes (to be administered within 30 minutes) and, where appropriate, priority 2 antidotes (to be administered within 2 hours). Local logistics, the hospital's geographical location, the availability of a 24/7 out-of-hours on-call pharmacy service, and the activation of specific pathways for antidote provision should be taken into account. In hospitals without a 24/7 pharmacy and/or where pathways do not guarantee access to priority-2 antidotes within 2 hours, priority-2 medicines should also be held on the dedicated poisoning trolley. The provision of priority-3 antidotes should remain governed by internal protocols.

Conclusion

Timely administration of antidotes is critical to the optimal clinical management of acute poisoning.

Particularly in peripheral centres, the establishment of dedicated pathways and robust organisational arrangements is essential to optimise the therapeutic pathway.

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