REVIEW

Antidotes for childhood toxidromes

Kam Lun Hon1, Wun Fung Hui1, Alexander KC Leung2

1Department of Paediatrics and Adolescent Medicine, The Hong Kong Children’s Hospital, Hong Kong; 2Department of Pediatrics, The University of Calgary and The Alberta Children’s Hospital, Calgary, Alberta, Canada

Abstract

Background: Poisoning causes significant morbidity and sometimes mortality in children worldwide. The clinical skill of toxidrome recognition followed by timely administration of an antidote specific for the poison is essential for the management of children with suspected poisoning. This is a narrative review on antidotes for toxidromes in paediatric practice.

Methods: A literature search was conducted on PubMed with the keywords “antidote”, “poisoning”, “intoxication”, “children” and “pediatric”. The search was customized by applying the appropriate filters (species: humans; age: birth to 18 years) to obtain the most relevant articles for this review article.

Results: Toxidrome recognition may offer a rapid guide to possible toxicology diagnosis such that the specific antidote can be administered in a timely manner. This article summarizes toxidromes and their respective antidotes in paediatric poisoning, with an emphasis on the symptomatology and source of exposure. The antidote and specific management for each toxidrome are discussed. Antidotes are only available for a limited number of poisons responsible for intoxication. Antidotes for common poisonings include N-acetyl cysteine for paracetamol and sodium thiosulphate for poisoning by cyanide.

Conclusion: Poisoning is a common cause of paediatric injury. Physicians should be familiar with the recognition of common toxidromes and promptly use specific antidotes for the management of childhood toxidromes.

Keywords: antidote, extracorporeal treatment, intoxication, paediatric poisoning, toxidrome.

Introduction

Poisoning is a significant cause of childhood injury that may potentially lead to serious morbidity and even mortality.1–3 The World Health Organization reported that children and young adults accounted for approximately 13% of global mortality attributed to accidental poisoning.4 It is estimated that 40% of hospital admissions due to poisoning in children are due to intentional poisoning.5 Young boys have a greater risk of unintentional ingestion whereas adolescent girls are more often found to intentionally use medications for suicidal intent.5,6 It is not always necessarily possible to perform a thorough evaluation of a patient with a drug overdose in the emergency setting as the history obtained may not be complete and there may not be adequate time for a comprehensive physical examination. Additionally, the offending agent(s) is/are often not known during the acute and potentially critical phase of management.7–9 Therefore, the recognition of a toxidrome – a constellation of symptoms and signs caused by an overdose of a specific class of chemicals or drugs – may offer clues to the underlying toxicology diagnosis and help guide the specific management.10

The initial management of patients with a drug overdose involves stabilization of the airway, cardiopulmonary system and gastrointestinal decontamination.11,12 Many specific antidotes for common household poisons can be given in a timely manner if a toxidrome based on the presenting symptomatology can be identified.13,14 However, it should be noted that polydrug overdose may cause confusing symptoms and the toxic effects of poisons may have delayed manifestations due to delayed absorption, volume distribution effects or time-lag for conversion to an active metabolite.14,15

The purpose of this article is to provide an updated narrative review on various toxidromes and their respective antidotes...
available in most emergency departments and critical care units for paediatric poisoning.

A literature search was conducted in November 2020 with the keywords “antidote”, “toxidrome”, “poisoning”, “intoxication”, “children” and “paediatric”. The search was customized by applying the appropriate filters of “age <18 years” and “human” to find the most relevant articles that meet the objective of this review article. Herein, a few commonly used antidotes and their corresponding toxidromes are described.

The antidotes

An antidote is a drug, medicine, chemical or chelating substance given as a remedy that can counteract or neutralize the effects of another drug or a poison. Antidotes for anticoagulants are sometimes referred to as reversal agents such as the box jellyfish venom antidote.  

Table 1 shows various types of antidotes. Some may only counteract a given drug, whereas others (such as charcoal) may help reduce the toxicity of numerous drugs. Most antidotes are not 100% effective and fatalities may still occur even when an antidote has been given.

Paediatric toxidromes and antidotes

Antidote for anticholinergic toxidrome – physostigmine

Anticholinergics inhibit the binding of the neurotransmitter acetylcholine to the muscarinic receptors in the central nervous system (CNS) and the parasympathetic nervous system. Intoxication with an anticholinergic may cause tachycardia, hyperthermia, non-reactive mydriasis, anhidrosis, dry mucous membranes, skin flushing, decreased bowel sounds and urinary retention. The anticholinergic effects in the CNS include delirium, confusion, anxiety, agitation, mumbling speech, visual hallucination and bizarre behaviour. The duration of the toxic effects in the CNS is usually longer than the peripheral effects due to the lipophilic properties of the causative agents. Anhidrosis, mydriasis, skin flushing, hyperthermia and delirium are important features in anticholinergic poisoning. Paediatric patients are at risk of unintentional poisoning by anticholinergics as many medications used for the symptomatic relief of common paediatric viral illnesses contain anticholinergics.  

Physostigmine, a specific antidote for anticholinergic poisoning, inhibits acetylcholinesterase and increases the level of acetylcholine in both the CNS and peripheral nervous system. As most patients with anticholinergic toxicity do well with supportive care alone, physostigmine is usually reserved for those who exhibit both peripheral and moderate central anticholinergic toxicity. It can also be used for diagnostic purposes in suspected anticholinergic poisoning. The onset time is of ~5–10 minutes and the suggested dose is 0.5–2 mg for adults or 0.02 mg/kg for children (maximum 0.5 mg) given by slow intravenous push over 5 minutes. Repeated smaller doses may be required and continuous infusion can be used in severe poisoning. The use of physostigmine has been associated with seizures and arrhythmia in patients with tricyclic antidepressant (TCA) overdose. Therefore, for patients with existing heart block, prolonged QT interval, suspected TCA overdose or underlying epilepsy disorder, a close monitoring for arrhythmia is needed during the administration of physostigmine, or its use should be avoided.

Antidote for carbon monoxide poisoning – oxygen (100%) and hyperbaric oxygen

Carbon monoxide intoxication is common in those with smoke inhalation injury. Carbon monoxide is a colourless, odourless, non-irritating and tasteless gas produced by the incomplete combustion of carbon-containing fuel or charcoal. Carboxyhaemoglobin (COHb) forms readily in red blood cells when haemoglobin comes into contact with carbon monoxide, reducing the availability of haemoglobin to bind and deliver oxygen at tissue level. Carbon monoxide also causes direct cellular toxicity by binding to cytochromes, myoglobin and guanylyl cyclase. The symptoms and signs of carbon monoxide poisoning are non-specific and highly variable depending on the blood level of COHb. Children with chronic exposure to carbon monoxide who have low levels of COHb may develop headache, dizziness, malaise and nausea. COHb levels >20% may cause vomiting, visual disturbance, confusion and transient loss of consciousness. Cherry-red lips, coma and seizure usually occur when the COHb level is >50%. The blood COHb level can be used to confirm the diagnosis. Standard pulse oximetry (SpO2) and arterial partial oxygen pressure (PaO2) cannot differentiate COHb from normal oxygenated haemoglobin and are hence not useful for diagnosing carbon monoxide poisoning. Complications of carbon monoxide poisoning include ventricular arrhythmias, myocardial ischaemia, pulmonary oedema, marked lactic acidosis and delayed neuropsychiatric syndrome. The neurological or psychological sequelae of carbon monoxide poisoning on a developing child may cause significant morbidity for survivors; hence, active follow-ups should be arranged.

Oxygen (100%) is indicated for carbon monoxide poisoning toxidrome. During initial management, patients with carbon monoxide poisoning should be put on 100% oxygen. Intubation with ventilatory support should be considered early. Whether hyperbaric oxygen is useful remains controversial. A Cochrane review on this topic did not demonstrate a significant benefit amongst those who were given hyperbaric oxygen therapy. Nevertheless, hyperbaric oxygen therapy has been found to be effective in reducing the neurological sequelae amongst moderate to high-risk patients with carbon monoxide intoxication. Whether hyperbaric oxygen is useful remains controversial. A Cochrane review on this topic did not demonstrate a significant benefit amongst those who were given hyperbaric oxygen therapy. Nevertheless, hyperbaric oxygen therapy has been found to be effective in reducing the neurological sequelae amongst moderate to high-risk patients with carbon monoxide poisoning.
| Antidote                                      | Type of poisoning                                                                 |
|----------------------------------------------|-----------------------------------------------------------------------------------|
| Activated charcoal with sorbitol             | Many oral toxins                                                                  |
| Antimuscarinic drugs (e.g. atropine)         | Cholinergic toxidrome Organophosphate and carbamate insecticides, nerve agents, some poisonous mushrooms (see Pralidoxime) |
| Benzodiazepam ± antipsychotics               | Amphetamine/cocaine                                                              |
| Benzodiazepam for seizures + potassium chloride | Theophylline                                                                      |
| Beta blocker                                 | Theophylline                                                                      |
| Calcium gluconate                            | Calcium channel blocker, hydrofluoric acid burns                                   |
| Chelators (e.g. EDTA, dimercaprol, penicillamine and 2,3-dimercaptosuccinic acid (succimer)) | Heavy metal                                                                       |
| Cyanide antidotes (hydroxocobalamin, amyl nitrite, sodium nitrite or thiosulfate) | Cyanide                                                                          |
| Cyproheptadine                               | Serotonin syndrome                                                               |
| Deferoxamine mesylate                        | Iron                                                                             |
| Digoxin immune fab antibody (Digibind and DigiFab) | Digoxin, Oleander ingestion                                                      |
| Dimercaprol                                  | Arsenic, gold or inorganic mercury                                               |
| Diphenhydramine hydrochloride and benztrpine mesylate | Extrapyramidal reactions associated with antipsychotics                           |
| Ethanol (100%) or fomepizole                 | Ethylene glycol, methanol                                                        |
| Flumazenil                                   | Beware of precipitating seizure in those with proconvulsant overdose Benzodiazepine |
| Oxygen (100%) or hyperbaric oxygen therapy   | Carbon monoxide, cyanide                                                         |
| Idarucizumab                                 | Dabigatran etexilate                                                             |
| Insulin + glucagon                           | Beta blocker, calcium channel blocker                                            |
| Intralipid                                   | Local anaesthetic                                                                |
| Leucovorin                                   | Methotrexate, trimethoprim, pyrimethamine                                       |
| Methylene blue ± ascorbic acid               | Contraindicated for children with glucose-6-phosphate dehydrogenase deficiency Acquired methaemoglobinemia |
| Naloxone hydrochloride                       | Opioid                                                                          |
| N-acetylcysteine                             | Paracetamol (acetaminophen)                                                      |
| Nitrites + thiosulphate + hydroxocobalamin   | Cyanide                                                                          |
| Octreotide                                   | Oral hypoglycaemic agents                                                        |
| Physostigmine sulfate                        | Anticholinergic toxidrome                                                        |
| Pralidoxime chloride + atropine              | Organophosphate insecticides, anticholinesterase nerve agents, some poison mushrooms |
| Protamine sulfate                            | Heparin                                                                          |
| Prussian blue                                | Thallium                                                                         |
| Pyridoxine                                   | Hydrazine (e.g. from Gyromitra mushrooms), ethylene glycol, isoniazid            |
| Sodium bicarbonate                           | Aspirin, tricyclic antidepressants with a wide QRS                               |
| Silibinin (intravenous)                      | Amatoxin                                                                         |
| Succimer (i.e. dimercaptosuccinic acid)       | Lead, mercury and arsenic                                                        |
| Vitamin K (phytomenadione)                   | Warfarin, some (but not all) rodenticides                                        |
Atropine can also be given to nicotinic activation such as muscle fasciculation or urinary. The symptoms caused by muscarinic receptor activation can be summarized by SLUDGE/BBB (salivation, lacrimation, urination, defecation, gastrointestinal cramping, emesis/bradycardia, bronchorrhea, bronchospasm). Activation of the nicotinic receptor may result in muscle fasciculation and flaccid paralysis, bradycardia, delirium, seizure and coma. However, reports on carbamate and organophosphate poisoning in young children revealed a high proportion of CNS manifestation, including hypotonia, stupor and coma. Therefore, paediatricians should have a high index of suspicion for cholinergic poisoning in children with possible history of exposure. Atropine is the antidote used for cholinergic poisoning. It acts as a competitive antagonist of acetylcholine at the muscarinic receptors. However, atropine does not have direct action towards the nicotinic receptors. The recommended dose is 1–5 mg given intravenously for adults. For paediatric patients, the usual dosage is 0.01–0.03 mg/kg every 3–5 minutes titrated according to clinical response. The maximum cumulative intravenous dose is 1 mg in children and 2 mg in adolescents. Atropine can also be given as a continuous infusion. It has been shown that using rapidly incremental doses of atropine followed by infusion results in a lower mortality, lower requirement of respiratory support and a shorter duration to achieve atropinization compared to conventional bolus doses. Atropine can also be used in combination with a benzodiazepine for seizure control in children with cholinergic overdose. As atropine has no nicotinic effect, it is not helpful for symptoms related to nicotinic activation such as muscle fasciculation or paralysis.

Antidotes for cholinergic toxidrome

Atropine

Acetylcholine is a neurotransmitter acting on the muscarinic and nicotinic receptors in the CNS, autonomic nervous system and neuromuscular junction and is regulated by acetylcholinesterase. Cholinergic toxidromes can be caused by exposure to or ingestion of pesticides containing organophosphates or carbamate, nerve gas, medications such as echothiophate, pyridostigmine, donepezil and tacrine, or mushroom species (e.g. Inocybe rimosa, Clitocybe species may also cause cholinergic poisoning). Stimulation of the muscarinic receptors may cause bradycardia, bronchospasm, bronchorrhea, lacrimation, miosis, diaphoresis, profuse watery salivation, gastrointestinal hyperactivity with vomiting, abdominal cramps, diarrhoea and involuntary urination. The symptoms caused by muscarinic receptor activation can be categorized as SLUDGE/BBB (salivation, lacrimation, urination, defecation, gastrointestinal cramping, emesis/bradycardia, bronchorrhea, bronchospasm). Activation of the nicotinic receptor may result in muscle fasciculation and flaccid paralysis, bradycardia, delirium, seizure and coma. However, reports on carbamate and organophosphate poisoning in young children revealed a high proportion of CNS manifestation, including hypotonia, stupor and coma. Therefore, paediatricians should have a high index of suspicion for cholinergic poisoning in children with possible history of exposure.

Pralidoxime

Pralidoxime is the antidote used for organophosphate poisoning as it cleaves the organophosphate–acetylcholinesterase complex and releases the enzyme to degrade acetylcholine. It is effective for both muscarinic and nicotinic symptoms. However, pralidoxime should only be used as an adjunctive therapy to atropine as monotherapy with pralidoxime may aggravate symptoms due to transient oxime-induced acetylcholinesterase inhibition. The suggested intravenous dose of pralidoxime is 1–2 g for adults and 25–50 mg/kg for children (maximum 2 g/dose) to be given over 30 minutes. Continuous infusion can also be used and may be associated with better clinical response than bolus doses. The adverse events associated with pralidoxime use are not commonly observed in children and include hypertension, headache, blurred vision, nausea and vomiting. Laryngospasm and muscle rigidity have also been reported in those that were given rapid administration of pralidoxime.

Antidotes for cyanide overdose – sodium nitrite, sodium thiosulfate and hydroxocobalamin

Cyanide poisoning can occur through inhalation of the colourless hydrogen cyanide or ingestion of cyanide salts such as sodium cyanide or potassium cyanide. Smoke inhalation is an important source of cyanide toxicity as hydrogen cyanide may be produced through the combustion of substances containing carbon and nitrogen. Other sources of cyanide include natural substances and foods such as cassava or apricot kernels, accidental consumption of chemicals used in the electroplating or mining industry, and prolonged use of sodium nitroprusside in the intensive care unit for the control of hypertension as one molecule of sodium nitroprusside would produce five molecules of cyanides. Cyanide toxicity comes from its binding to the ferric ion of cytochrome oxidase a3, which interferes with oxidative phosphorylation. Cyanide poisoning leads to cellular hypoxia, causing the activation of anaerobic metabolism and the subsequent development of lactic acidosis.

The symptoms and signs of cyanide toxicity are often non-specific and clinical manifestations include anxiety, headache, vomiting, abdominal pain, chest pain, confusion, bitter almond odour, cherry-red skin, mydriasis, tachypnoea, tachycardia, arrhythmia, blurred vision, loss of consciousness and seizures. A three-phase change of initial tachycardia and hypertension, followed by tachycardia and hypotension, and eventually hypotension with cardiac arrest has been described. Complications of cyanide poisoning include pulmonary oedema, cardiopulmonary collapse, rhabdomyolysis, acute kidney injury, hepatic necrosis and even death. Neurological deficits and Parkinsonism may be observed amongst the survivors.
Making the diagnosis requires a high index of suspicion as blood cyanide level is usually not readily available in the acute setting to aid diagnosis. Alternatively, a plasma lactate level of ≥10 mmol/L with a suggestive history and presentation may alert the physician to the possibility of cyanide intoxication. Sodium nitrite, sodium thiosulfate and hydroxocobalamin are antidotes used for cyanide toxicity. These antidotes can be given simultaneously. Intravenous sodium nitrite 300 mg for adults or 6 mg/kg for children (maximum dose 300 mg) displaces the cyanide from binding cytochrome oxidase in the form of cyanomethaemoglobin, which can further combine with the thiosulfate (250 mg/kg, maximum dose 12.5 g given as slow intravenous infusion following sodium nitrite) to become thiocyanate, which can be excreted by the kidneys. Furthermore, hydroxocobalamin is an alternative antidote, which has a higher affinity for cyanide than cytochrome oxidase and the bound non-toxic complex cyanocobalamin can be excreted through urine. The recommended dose of hydroxocobalamin is 5 g for adults and 70 mg/kg for children (maximum 5 g) to be given intravenously.

**Antidote for hypnotic/sedative toxidrome – flumazenil**

The manifestation of sedative and hypnotic toxidrome includes slurred speech, ataxia, incoordination and disorientation. In those with severe toxicity, stupor and coma may also be seen. Hypoventilation is rare amongst those who have sedation/hypnotic overdose by the oral form of benzodiazepine. The absence of hypoventilation and miosis can be an indicator to help distinguish sedation/hypnotic overdose from opioid poisoning. The common description of ‘coma with normal vitals’ is a good illustration of this toxidrome. However, mild bradycardia, hypotension and respiratory depression can still occur in those with intravenous benzodiazepine overdose.

Specifically, children with benzodiazepine overdose usually present with ataxia and drowsiness; respiratory depression is less commonly encountered. As the continuous infusion of benzodiazepines is a common practice in intensive care units for sedative purposes, the recognition of such a toxidrome is essential, and all medical and nursing staff working in the intensive care units should be familiar with its presentation. Cardiac toxicity leading to dysrhythmia may also be seen in chloral hydrate overdose.

Flumazenil is a competitive benzodiazepine antagonist used for the overdose of benzodiazepine or non-benzodiazepines (e.g. zolpidem), which share the agonistic action at the benzodiazepine receptors. The usual starting dose is 0.2 mg for adults and 0.01 mg/kg for children (maximum 0.2 mg) to be given intravenously. Repeated doses with an increment of dose can be given to titrate against clinical response. The maximum dose is usually 1 mg, though higher doses ranging from 2.5 mg to 10 mg have been reported. It should be noted that, for those with chronic benzodiazepine abuse, flumazenil may precipitate withdrawal symptoms.

**Antidote for methaemoglobinaemia – methylene blue**

Methaemoglobinaemia can be broadly classified into congenital or acquired. Congenital methaemoglobinaemia can be due to the deficiency of cytochrome b5- methaemoglobin (MetHb) reductase or due to a mutant globin that facilitates the spontaneous oxidation of the iron moiety from the ferrous (Fe²⁺) to the ferric (Fe³⁺) state (haemoglobin M disease). Acquired causes include exposure to chemicals (e.g. nitrates, nitrites, aniline, phenylhydroxylamine, aminophenol, acetonilide), foods (e.g. nitrite-containing vegetables or fava beans), herbicides, pesticides, medications (e.g. chloroquine, dapsone), topical anaesthetic agents (e.g. benzocaine, lidocaine) and inhaled nitric oxide.

Methaemoglobinaemia causes cyanosis when the level of MetHb is >1.5 g/dL, that is, equivalent to 8–12% MetHb at normal haemoglobin concentrations. The clinical manifestations of acquired methaemoglobinaemia depend on the level of MetHb. Infants consuming an excessive amount of nitrite causing methaemoglobinaemia may present with marked cyanosis (‘blue baby syndrome’). Anxiety, headache and dizziness can occur at MetHb levels of >20%. Fatigue, confusion and tachyypnoea can occur at MetHb levels of 30–50%. Arrhythmia, seizure and coma can occur at MetHb levels of >50%.

The diagnosis of methaemoglobinaemia is usually made based on clinical observation. A patient with sudden onset of cyanosis with suggestive symptoms after suspicious exposure that is not responsive to increased oxygen delivery may require the evaluation of methaemoglobinaemia. There is a saturation gap between the reading from the pulse oximeter and the measured value obtained from blood gas analysis. A normal PaO₂ level is usually shown by blood gas analysis. To confirm the diagnosis, a direct measurement of MetHb is required. Methylene blue is used in the treatment of acquired methaemoglobinaemia. Methylene blue accelerates the NADPH-MetHb reductase pathway to clear MetHb.

The standard dose of methylene blue is 1–2 mg/kg to be given intravenously over 5 minutes and a repeated dose may be needed if symptoms/signs are persistent. The recommended dosage should not be exceeded. Alternative interventions may be required if methaemoglobinaemia does not resolve after two doses. The colour of urine is bluish green after the administration of methylene blue. The monitoring of
MetHb concentration is advised as there may be a rebound phenomenon. Methylene blue is contraindicated in those with glucose-6-phosphate dehydrogenase (G6PD) deficiency as G6PD is required for the NADPH-MetHb reductase pathway. In children with G6PD deficiency, methylene blue may increase the risk of haemolysis. For those children in whom methylene blue is contraindicated, ascorbic acid may be used instead.

**Antidote for opioid toxidrome – naloxone**

Opioid poisoning may occur in young children who obtain access to pain medications or illicit drugs at home. It has been reported that children who were exposed to >1 mg/kg of codeine may develop toxicity within 1 hour of ingestion. Miosis is a consistent finding in pure opioid overdose; however, it is not a specific sign and the diagnosis of opioid overdose should not be made solely based on this finding. Other clinical manifestations include respiratory depression, CNS depression, hyporeflexia, muscle rigidity, bradycardia, hypotension, flushing, pruritus and decreased or absent bowel sounds. Hypoventilation is the most important complication and may lead to mortality. Other complications include amenorrhea, impaired fertility, non-cardiogenic pulmonary oedema, acute rhabdomyolysis and acute kidney injury. Likewise, seizures can also occur after intravenous sufentanil or fentanyl, prolonged use of meperidine, or ingestion of large amounts of tramadol or propoxyphene. It should be noted that children with opioid overdose may show a delayed onset of toxicity and the clinical effects may be more severe and prolonged than adults.

Naloxone is a synthetic opioid receptor antagonist that is used for both the diagnosis and treatment of opioid poisoning. It has a rapid onset of action and can be given either through intravenous, intramuscular, intranasal or endotracheal route, though the intravenous route is usually preferred. The intranasal route is as effective as intravenous naloxone in reversing the respiratory and CNS depression. The requirement of a rescue dose is higher for intranasal naloxone. The use of naloxone is indicated in those with respiratory depression or a respiratory rate of <12 breaths/minute. The initial intravenous dose is 0.4–2 mg for adolescents and adults and it can be repeated every 3–5 minutes until the desirable clinical response (restoration of respiratory effort) is achieved. The maximum total dose is 10 mg. The recommended initial dose for children is 0.01 mg/kg to be given intravenously. Similarly, the dose can be increased to up to 0.1 mg/kg (maximum 2 mg per dose) until the desired response is obtained. Naloxone may precipitate acute withdrawal, leading to lacrimation, piloerection, diaphoresis, vomiting, diarrhea and yawning in those with chronic opioid abuse. A longer observation period of at least 24 hours may be required for opioid poisoning in the paediatric populations due to their delayed onset and the prolonged effect of toxicity.

**Antidote for paracetamol overdose – N-acetyl cysteine**

Paracetamol poisoning in the paediatric population can be caused by both intentional overdose, unintentional consumption or medication error. It has been reported that a single dose of 200 mg/kg may produce acute toxicity and the consumption of more than 75 mg/kg/day in children under 6 years old may also develop toxicity. Children may be relatively asymptomatic at initial presentation and the most concerned toxicity is hepatotoxicity and liver failure. The timing of initiating treatment varies between different international and local guidelines but in general it requires the plotting of paracetamol concentration to the Rumack–Matthew nomogram.

N-acetylcysteine is a medication that is used to treat paracetamol (acetaminophen) overdose. In the treatment of acetaminophen overdose, acetylcysteine acts to maintain or replenish depleted glutathione reserves in the liver and enhance the non-toxic metabolism of acetaminophen. As such, acetylcysteine protects liver cells from N-acetyl-p-benzoquinone imine toxicity. This antidote is most effective in preventing or lessening hepatic injury when administered within 8–10 hours after paracetamol overdose.

**Sodium bicarbonate as an antidote for miscellaneous toxidromes**

Sodium bicarbonate infusion is indicated for poisoning with TCA, aspirin or cocaine that presents with a wide QRS. The dose for TCA and cocaine-associated cardiac toxicity is usually 1–2 mmol/kg infused intravenously using 8.4% sodium bicarbonate. Sodium bicarbonate should be titrated up until a urine pH between 7.5 and 8.0 is achieved.

In small children, a small amount of ingestion can be fatal for TCA poisoning. An electrocardiogram should be performed when there is a concern of TCA overdose. If in TCA overdose, activated charcoal is often recommended. In those who have a wide QRS complex (>100 ms), sodium bicarbonate is recommended in addition to activated charcoal. If seizures occur, benzodiazepines should be given. In those with hypotension, intravenous fluids, norepinephrine and intravenous lipid emulsion may be tried.

There is no specific antidote for salicylate poisoning and the initial treatment of salicylate overdose involves maintaining an adequate airway and adequate circulation followed by gastric decontamination by administering activated charcoal, which adsorbs the salicylate in the gastrointestinal tract. The alkalinization of the urine and plasma, by giving an intravenous bolus of sodium bicarbonate then adding sodium bicarbonate to maintenance fluids, is an effective method to increase the clearance of salicylates from the body. The alkalinization of urine causes salicylates to be trapped in renal tubules in their ionized form and then readily excreted in the urine. Alkalinization of the plasma decreases the lipid soluble form...
of salicylates facilitating movement out of the CNS. Oral sodium bicarbonate is contraindicated in salicylate toxicity as it can cause the dissociation of salicylate tablets in the gastrointestinal tract and subsequent increased absorption. Intravenous fluid containing dextrose, such as dextrose 5% in water with addition of sodium bicarbonate is recommended to keep a urinary output between 1 and 1.5 ml/kg/hour.

Sodium bicarbonate should be given to those with significant aspirin overdose (salicylate level greater than 35 mg/dL 6 hours after ingestion) regardless of the serum pH, as it enhances the elimination of aspirin in the urine. Sodium bicarbonate should be given until a urine pH between 7.5 and 8.0 is achieved.

Cocaine is a stimulant and its overdose may result in a sympathomimetic toxidrome. The clinical manifestations of sympathomimetic toxidromes include mydriasis, hyperthermia, piloerectio, diaphoresis, agitation, anxiety, delusion and paranoia. Cardiac toxicity includes hypertension, tachycardia, arrhythmias and myocardial infarction. Rarely, cocaine overdose may induce seizures, cerebral vascular accident, bowel infarction and pulmonary oedema.

Arrhythmia, especially ventricular tachycardia, ventricular fibrillation or torsade de pointes, can occur with cocaine overdose due to sodium channel blockade, potassium channel blockade, catecholamine excess or myocardial infarction. Apart from the initial stabilization and correction of electrolyte abnormalities, sodium bicarbonate infusion and lidocaine are effective medications to be administered. However, there is a lack of data from clinical trials.

**Conclusion**

The diagnosis and management of childhood poisoning remain challenging and the recognition of toxidromes guided by history and physical findings as well as the results of selected investigations is indispensable. Antidotes can be used for both diagnostic and therapeutic purposes. Physicians should be familiar with some of the specific antidotes as timely administration is crucial to reverse the damage caused by the toxic substances.
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