

Chapter

A

Acetazolamide

Acetazolamide is a carbonic anhydrase inhibitor normally used to reduce intraocular pressure in glaucoma. Metabolic alkalosis may be partially corrected by the use of acetazolamide. The most common cause of metabolic alkalosis on the ICU is usually the result of furosemide administration.

Uses

Metabolic alkalosis (unlicensed)

Contraindications

Hypokalaemia
Hyponatraemia
Hyperchloraemic acidosis
Severe liver failure
Renal failure
Sulphonamide hypersensitivity

Administration

- IV: 250–500 mg, given over 3–5 minutes every 8 hours
Reconstitute with 5 ml WFI
Monitor: FBC, U&E and acid/base balance

How not to use acetazolamide

IM injection – painful
Not for prolonged use

Adverse effects

- Metabolic acidosis
- Electrolyte disturbances (hypokalaemia and hyponatraemia)
- Blood disorders
- Abnormal LFT

Cautions

- Avoid extravasation at injection site (risk of necrosis)
- Avoid prolonged use (risk of adverse effects)
- Concurrent use with phenytoin (↑ serum level of phenytoin)

Organ failure

Renal: avoid if possible (metabolic acidosis)

CC (ml/min)	Dose (mg)	Interval (h)
20–50	250	Up to 6
10–20	250	Up to 12
<10	250	24

Hepatic: avoid (abnormal LFT)

Acetylcysteine (Parvolex)

Acetylcysteine is an effective antidote to paracetamol if administered within 8 hours after an overdose. Although the protective effect diminishes progressively as the overdose–treatment interval increases, acetylcysteine can still be of benefit up to 24 hours after the overdose. In paracetamol overdose the hepatotoxicity is due to formation of a toxic metabolite. Hepatic reduced glutathione inactivates the toxic metabolite by conjugation, but glutathione stores are depleted with hepatotoxic doses of paracetamol. Acetylcysteine, being a sulphhydryl (SH) group donor, protects the liver, probably by restoring depleted hepatic reduced glutathione or by acting as an alternative substrate for the toxic metabolite.

Acetylcysteine may have significant cytoprotective effects. The cellular damage associated with sepsis, trauma, burns, pancreatitis, hepatic failure and tissue reperfusion following acute MI may be mediated by the formation and release of large quantities of free radicals that overwhelm and deplete endogenous antioxidants (e.g. glutathione). Acetylcysteine is a scavenger of oxygen free radicals. In addition, acetylcysteine is a glutathione precursor, capable of replenishing depleted intracellular glutathione and, in theory, augmenting antioxidant defences (p. 354).

Acetylcysteine can be used to reduce the nephrotoxic effects of IV contrast media. Possible mechanisms include scavenging a variety of oxygen-derived free radicals and the improvement of endothelium-dependent vasodilation.

Nebulized acetylcysteine can be used as a mucolytic agent. It reduces sputum viscosity by disrupting the disulphide bonds in the mucus glycoproteins and enhances mucociliary clearance, thus facilitating easier expectoration.

Uses

- Paracetamol overdose
- Antioxidant (unlicensed)
- Prevent IV contrast-induced nephropathy (unlicensed)
- Reduce sputum viscosity and facilitate easier expectoration (unlicensed)
- As a sulphhydryl group donor to prevent the development of nitrate tolerance (unlicensed)

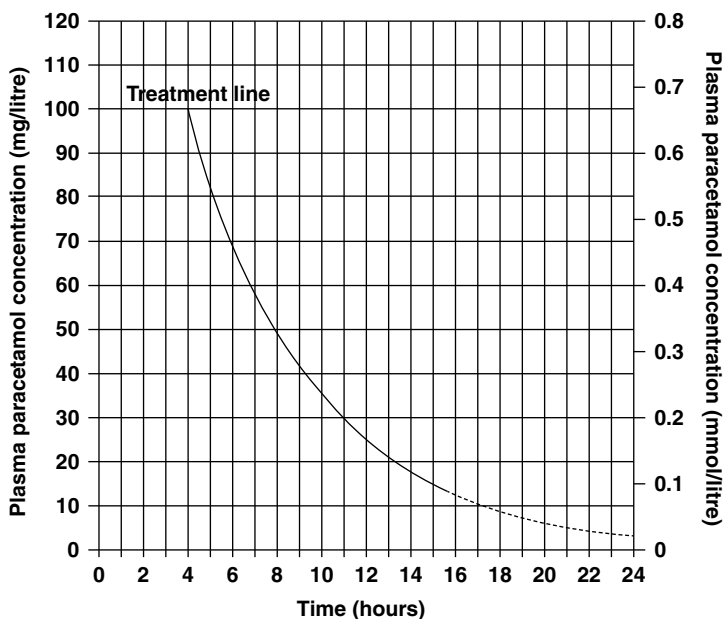
Administration

Paracetamol overdose:

- IV infusion: 150 mg/kg in 200 ml glucose 5% over 60 minutes, followed by 50 mg/kg in 500 ml glucose 5% over 4 hours, then 100 mg/kg in 1 l glucose 5% over the next 16 hours

Weight (kg)	Initial	Second	Third
	150 mg/kg in 200 ml glucose 5% over 60 minutes	50 mg/kg in 500 ml glucose 5% over 4 hours	100 mg/kg in 1 l glucose 5% over 16 hours
	Parvolex (ml)	Parvolex (ml)	Parvolex (ml)
50	37.5	12.5	25
60	45.0	15.0	30
70	52.5	17.5	35
80	60.0	20.0	40
90	67.5	22.5	45
x	0.75x	0.25x	0.5x

For children >20 kg: same doses and regimen but in half the quantity of IV fluid
Treatment nomogram:



Patients whose plasma-paracetamol concentrations are on or above the **treatment line** should be treated with acetylcysteine by intravenous infusion.

The prognostic accuracy after 15 hours is uncertain, but a plasma-paracetamol concentration on or above the treatment line should be regarded as carrying a serious risk of liver damage.

Patients whose plasma concentrations fall on or above the treatment line should receive acetylcysteine. The prognostic value after 15 hours is uncertain, although a plasma paracetamol concentration on or above the treatment line is likely to carry a serious risk of liver damage. Use acetylcysteine for paracetamol overdose irrespective of the plasma paracetamol level if the overdose is staggered or there is doubt over the time of paracetamol ingestion, or paracetamol overdose with a timed plasma paracetamol concentration on or above a single treatment line joining points of 100 mg/l at 4 hours and 15 mg/l at 15 hours regardless of risk factors of hepatotoxicity.

Antioxidant:

- IV infusion: 75–100 mg/kg in 1 l glucose 5%, give over 24 hours (rate 40 ml/h)

Prevent IV contrast-induced nephropathy (not required for oral/enterally administered contrast):

- IV bolus 1,200 mg pre-contrast, then after 12 hours 1,200 mg PO/NG (or IV if nil-by-mouth) 12 hourly for 48 hours (there is also evidence for 600 mg as an alternate dose)

Dilution: make up to 20 ml with glucose 5%

If the oral capsules are not available, the IV formulation may be given orally
 To mask the bitter taste, dilute the injection to a concentration of 50 mg/ml with an acidic drink (e.g. orange juice, blackcurrant juice or cola)

To be given in conjunction with IV sodium bicarbonate 1.26% at 3 ml/kg/h over 1 hour prior to IV contrast; continue at reduced rate of 1 ml/kg/h for 6 hours following contrast

Reduce sputum viscosity:

- Nebulized: 4 ml (800 mg) undiluted Parvolex (20%) driven by air, 8 hourly
 Administer before chest physiotherapy

How not to use acetylcysteine

Do not drive nebuliser with oxygen (oxygen inactivates acetylcysteine)

Adverse effects

Anaphylactoid reactions (nausea, vomiting, flushing, itching, rashes, bronchospasm, hypotension)

Fluid overload

Cautions

There are no contraindications to treatment of paracetamol overdose with acetylcysteine

Asthmatics (risk of bronchospasm)

Pulmonary oedema (worsens)

Each 10 ml ampoule contains Na⁺ 12.8 mmol (↑ total body sodium)

Aciclovir

Aciclovir interferes with herpes virus DNA polymerase, inhibiting viral DNA replication. Aciclovir is renally excreted and has a prolonged half-life in renal impairment.

Uses

Herpes simplex virus (HSV) infections:

- HSV encephalitis
- HSV genital, labial, peri-anal and rectal infections

Varicella zoster virus infections:

- Beneficial in the immunocompromised patients when given IV within 72 hours; prevents complications of pneumonitis, hepatitis or thrombocytopenia
- In patients with normal immunity, may be considered if the ophthalmic branch of the trigeminal nerve is involved

Contraindications

Not suitable for CMV or EBV infections

Administration

- IV: 5–10 mg/kg 8 hourly (*i.e. 5 mg/kg for herpes simplex, herpes zoster; 10 mg/kg for herpes zoster in immunocompromised, HSV encephalitis)
- In obesity, use ideal body weight for dosing

Available in 250 mg/10 ml and 500 mg/20 ml ready-diluted or in 250 mg and 500 mg vials for reconstitution

Reconstitute 250 mg vial with 10 ml WFI or sodium chloride 0.9% (25 mg/ml)

Reconstitute 500 mg vial with 20 ml WFI or sodium chloride 0.9% (25 mg/ml)

Take the reconstituted solution (25 mg/ml) and make up to 50 ml (for 250 mg vial) or 100 ml (for 500 mg vial) with sodium chloride 0.9% or glucose 5%, and give over 1 hour

Ensure patient is well hydrated before treatment is administered

If fluid-restricted, can give centrally via syringe pump undiluted (unlicensed)

In renal impairment:

CC (ml/min)	Dose (mg/kg)*	Interval (h)
>50 or CWH rate >3 l/h	5–10	8
25–50 or CWH rate 1.5–3 l/h	5–10	12
10–25 or CWH rate <1.5 l/h	5–10	24
<10	2.5–5	24

How not to use aciclovir

Rapid IV infusion (precipitation of drug in renal tubules leading to renal impairment)

Adverse effects

- Phlebitis
- Reversible renal failure
- Elevated LFTs
- CNS toxicity (tremors, confusion and fits)
- Neuropsychiatric side effects – in renal failure may be due to accumulation of aciclovir metabolite, 9-carboxymethoxymethylguanine (CMMG)

Cautions

- Concurrent use of methotrexate
- Renal impairment (reduce dose)
- Dehydration/hypovolaemia (renal impairment due to precipitation in renal tubules)

Adenosine (Adenocor)

This endogenous nucleoside is safe and effective in ending >90% of re-entrant paroxysmal SVT. However, this is not the most common type of SVT in the critically ill patient. After an IV bolus effects are immediate (10–30 seconds), dose-related and transient (half-life <10 seconds; entirely eliminated from plasma in <1 minute, being degraded by vascular endothelium and erythrocytes). Its elimination is not affected by renal/hepatic disease. Adenosine works faster and is superior to verapamil. It may be used in cardiac failure, in hypotension and with beta-blockers, in all of which verapamil is contraindicated.

Uses

It has both therapeutic and diagnostic uses:

- Alternative to DC cardioversion in terminating paroxysmal SVT, including those associated with WPW syndrome
- Determining the origin of broad complex tachycardia; SVT responds, VT does not (predictive accuracy 92%; partly because VT may occasionally respond). Though adenosine does no harm in VT, verapamil may produce hypotension or cardiac arrest

Contraindications

Second- or third-degree heart block (unless pacemaker fitted)

Sick sinus syndrome (unless pacemaker fitted)

Asthma – may cause bronchospasm

Patients on dipyridamole (drastically prolongs the half-life and enhances the effects of adenosine – may lead to dangerously prolonged high-degree AV block)

Administration

- Rapid IV bolus: 3 mg over 1–2 seconds into a large vein, followed by rapid flushing with sodium chloride 0.9%
- If no effect within 2 minutes, give 6 mg
- If no effect within 2 minutes, give 12 mg
- If no effect, abandon adenosine
- Need continuous ECG monitoring
- More effective given via a central vein or into right atrium

How not to use adenosine

Without continuous ECG monitor

Adverse effects

Flushing (18%), dyspnoea (12%) and chest discomfort are the commonest side effects but are well tolerated and invariably last <1 minute

If given to an asthmatic and bronchospasm occurs, this may last up to 30 minutes

Use aminophylline to reverse

Cautions

AF or atrial flutter with accessory pathway (↑ conduction down anomalous pathway may increase)

Early relapse of paroxysmal SVT is more common than with verapamil but usually responds to further doses

Adenosine's effect is enhanced and extended by dipyridamole – if essential to give with dipyridamole, reduce initial dose to 0.5–1 mg