

National Essential Anaesthesia Drugs List (NEADL)

February 2015

Corrections made on 11/05/2015; see end of document for details



THE ASSOCIATION OF ANAESTHETISTS

of Great Britain & Ireland

The National Essential Anaesthesia Drug List (NEADL) 2015

The Association of Anaesthetists of Great Britain and Ireland (AAGBI) is pleased to present NEADL 2015. An important purpose of NEADL is to advise suppliers and managers of a minimum set of drugs that must be available wherever anaesthesia is to be conducted safely. Efforts can then be focussed on ensuring the sustainability of their supply. The list is in no way prescriptive, and anaesthetists may well find they prefer other drugs in their own practice; this is to be encouraged because it takes pressure off the supply of the NEADL drugs, making shortages less likely. Moreover, it spreads familiarity with the use of alternatives when an essential drug is in shortage. Shortages principally affect generic injectables. When a shortage occurs, we look first to find a direct alternative, e.g. lorazepam for midazolam or vecuronium for rocuronium. The NEADL is an obvious resource in that situation. Sometimes it will be necessary to look beyond injectables and to develop protocols that make use of non-injectable formulations. For example, if injectable opioids were in shortage, a protocol for anaesthesia for orthopaedic surgery might include premedication with simple, oral analgesics and long-acting opioids. Additional steps will help during shortages. They include:

- Decrease waste: only draw up what you will use, and consider alternatives to patient-controlled analgesia.
- Decrease use: develop alternative techniques such as regional analgesia during opioid shortage and vice versa.
- Decrease supplies: provide clinicians with the best alternatives, with advice on their safe use.
- Decrease activity: triage to protect emergency and live-saving surgical procedures.

It may be a helpful exercise for teams to consider how reliant their service is on certain generic injectables, and to make contingency plans for shortages. The AAGBI would be pleased to see such exercises submitted as abstracts at WSM London meetings and at its Annual Congresses so that experiences might be shared.

In 2014, the AAGBI joined the American Society of Anesthesiologists (ASA) and other National Societies in considering the global aspects of anaesthetic drug shortages. Under the Chairmanship of Dr Adrian Gelb, this group hopes to develop an International Essential Anaesthetic Drug List similar to NEADL. Currently a professor of anesthesiology in San Francisco, Adrian has also worked in Canada and the United Kingdom; he is well placed to lead this international initiative.

We are grateful to all those AAGBI members and others who have contributed to the creation of NEADL 2015. We also thank the following contributors from the AAGBI's Group of Anaesthetists in Training (GAT), in no particular order: Surrah Leifer, Anna Costello, Emma Plunkett, Lyndsey Forbes, Caroline Wilson, Liam P Scott, Phil Bewley, Annemarie Docherty, Sally El-Ghazali, Mohamed Eid, Benjamin Fox, Jonny Price, Sarah Gibb, Rowena Clark, Siân Barford-Turner and Kate O'Connor.

Kathleen Ferguson
Honorary Treasurer, AAGBI

Tom Woodcock
Chair, Safety Committee, AAGBI

Contents

The British National Formulary (BNF) classification for drugs used in anaesthesia is given in parentheses in this contents list.

Medical gases	3
Intravenous anaesthetic: propofol (1.1).....	4
Inhalational anaesthetic: sevoflurane (1.2).....	5
Anti-muscarinic drugs: atropine (1.3)	6
Anti-muscarinic drugs: glycopyrronium (1.3)	7
Benzodiazepine (1.4.1)	8
Non-opioid analgesic; paracetamol (1.4.2).....	9
Opioid analgesics: fentanyl (1.4.3).....	10
Opioid analgesics: morphine (1.4.3).....	11
Neuromuscular blocking drugs: suxamethonium (1.5)	12
Neuromuscular blocking drugs: rocuronium (1.5)	13
Neuromuscular blocking drugs: atracurium (1.5)	14
Drugs for reversal of neuromuscular blockade: neostigmine (1.6)	15
Drugs for reversal of neuromuscular blockade: sugammadex (1.6).....	16
Antagonists of central and respiratory depression: flumazenil (1.7).....	17
Antagonists of central and respiratory depression: naloxone (1.7)	18
Drug for the treatment of malignant hyperthermia: dantrolene (1.8)	19
Local anaesthetics: lidocaine (2)	20
Local anaesthetics: levobupivacaine (2)	21
Local anaesthetics: hyperbaric bupivacaine (2)	22
Drug used for local anaesthetic overdose	23
Anti-emetics: dexamethasone	24
Anti-emetics: ondansetron.....	25
Pressors given by bolus: phenylephrine.....	26
Pressors by bolus: metaraminol	27
Pressors by bolus: ephedrine.....	28
Pressors by infusion: noradrenaline (norepinephrine).....	29
Pressors by infusion: adrenaline (epinephrine)	30
Magnesium sulphate	31
Appendix - Summary.....	32

Essential, necessary and critical drugs

In this document, we will use the following definitions:

- Essential medicines:** **E** Those that satisfy the priority healthcare needs of the population, as defined by the World Health Organization¹.
- Necessary drugs:** **N** Those used to treat or prevent a serious disease or medical condition for which there is no alternative medicine available in adequate supply, as defined by the US Food and Drugs Administration².
- Critical drugs:** **C** Those that are both necessary and vulnerable to shortage, as defined by the US Drug Shortage Prevention Act 2012³.
- Priority indications:** **P** In times of shortage, these are the priority indications for which the drug should be reserved until further supplies are guaranteed.

¹ http://www.who.int/topics/essential_medicines/en/

² <http://www.fda.gov/Drugs/DrugSafety/default.htm>

³ <http://thomas.loc.gov/cgi-bin/query/z?c112:H.R.3839:>

Medical gases

Drug name and formulation

Air and oxygen are necessary for the safe administration of anaesthesia.

Clinical indications

- Carrier gases for anaesthetic agents. **P**
- Air is used to drive medical equipment including ventilators and surgical tools.

Alternative drugs or techniques

- Nitrous oxide (as a carrier gas).
- A self-inflating bag-valve-mask or draw-over system can be used to ventilate the lungs with air from the atmosphere.

General comments

- Use of oxygen 100% during shortage of air risks oxygen toxicity and collapse of the lung (atelectasis).
- Nitrous oxide has been shown to be a safe carrier gas with weak anaesthetic and analgesic properties. Its tendency to provoke nausea and vomiting can be offset with anti-emetic therapy.

Essential? Necessary? Critical?

- **E**
- **N**

Intravenous anaesthetic: propofol (1.1)

Drug name and formulation

Propofol 10 mg.ml⁻¹ (1%) in a 20 ml ampoule or 50 ml bottle.

Clinical indications

Induction of general anaesthesia. **P**

Maintenance of general anaesthesia, often in conjunction with neuraxial anaesthesia or with intravenous opioids.

In sub-hypnotic doses for short procedures, e.g. reduction of dislocated joints.

Sedation for critically ill patients being mechanically ventilated. **P**

Alternative drugs or techniques

- Thiopental sodium.
- Etomidate.

General comments

- Patients may be sensitive to the drug or its diluents, in which case an alternative must be used.
- Propofol infusion syndrome may occur in children or adults after prolonged infusion of larger doses in the ICU. It is often fatal.
- Thiopental is not more widely used because supply is limited.
- CAUTIONS for thiopental when used as an alternative to propofol:
- Thiopental is not an anti-emetic.
- Thiopental does not suppress laryngeal and airway reflexes as effectively as propofol.
- Thiopental causes severe tissue necrosis if extravasated. On intra-arterial injection crystals form causing distal ischaemia.
- Thiopental has a longer elimination half time than propofol; it is unsuitable for rapid recovery after infusion or repeated boluses.
- Thiopental is CONTRA-INDICATED in patients with porphyria or barbiturate allergy.
- Etomidate is not more widely used because it inhibits 11-beta-hydroxylase in the synthesis of cortisol.
- CAUTIONS for Etomidate when used as an alternative to propofol:
 - A glucocorticoid should be given to cover adrenal suppression that lasts up to 24 hours after a single dose of etomidate.
 - Etomidate is not an anti-emetic.
 - Involuntary movements, rigidity, coughing, hiccoughing and laryngospasm are much more common with etomidate than with propofol (50% vs. 10%).
 - Pain on injection, venous thrombosis and thrombophlebitis are particularly problematic with etomidate.
 - Etomidate can be lethal as a sedative infusion when used for critically ill patients.

Essential? Necessary? Critical?

- Propofol is the most widely used intravenous anaesthetic. **E**
- Strong clinical familiarity and a long established safety record.
- Shortages of propofol have occurred in North America. **C**

Inhalational anaesthetic: sevoflurane (1.2)

Drug name and formulation

Sevoflurane

Clinical Indications

- For the maintenance of general anaesthesia. **P**
- Induction of anaesthesia as an alternative to intravenous induction.

Alternative drugs or techniques

- Isoflurane.
- Desflurane.

General comments

- Sevoflurane is a polyfluorinated isopropyl methyl ether with a low blood : gas partition coefficient and a low minimum alveolar concentration (MAC) of 1.8%. It is regarded as non-irritant to the airways. As with all volatile agents, it can be a trigger for malignant hyperthermia.
- Isoflurane is a halogenated methyl ether with a slightly lower blood : gas partition coefficient and a slightly higher MAC. It is not as rapid in onset or washout as the more modern agents.
- Desflurane is a fluorinated methylethyl ether (blood: gas partition coefficient of 0.45) that demonstrates a rapid onset and a fast wash out time. MAC is significantly higher than sevoflurane at around 6%.

Essential? Necessary? Critical?

- Sevoflurane is a widely used inhalation anaesthetic agent in the UK. **E**
- It is the preferred agent for gaseous inductions in children.
- It has an excellent safety profile.

Anti-muscarinic drugs: atropine (1.3)

Drug name and formulation

Atropine 0.6 mg in a 1 ml ampoule or 1 mg in a 10 ml prefilled syringe.

Clinical indications

- For resuscitation from cardiac arrest or peri-arrest arrhythmia. **P**
- Treatment and prevention of intra-operative bradycardia.
- As an antisialogogue.
- Control of the muscarinic side effects of neostigmine.

Alternative drugs or techniques

- Glycopyrronium.

General comments

- Atropine is a competitive muscarinic receptor antagonist that increases heart rate by blockade of the vagus nerve.
- Glycopyrronium has a similar onset and duration of action to neostigmine and is preferred to atropine for this indication.

Essential? Necessary? Critical?

- Essential for the management of life threatening bradyarrhythmias. **E**
- Long safety record.

Anti-muscarinic drugs: glycopyrronium (1.3)

Drug name and formulation

Glycopyrronium bromide (glycopyrrolate) 200 µg in 1 ml or 600 µg in 3 ml. Also comes premixed 0.5 mg with neostigmine 2.5 mg in 1 ml for reversal of non-depolarising neuromuscular block.

Clinical indications

- Treatment or prevention of intra-operative bradycardia.
- Treatment of acute bradyarrhythmias.
- As a premedication to dry bronchial and salivary secretions.
- For prevention of muscarinic side effects of neostigmine, which is given to reverse neuromuscular blockade. **P**

Alternative drugs or techniques

- Atropine sulphate.
- Hyoscine hydrobromide.

General comments

- Glycopyrronium does not cross the blood-brain barrier and has no effect on the sensorium.
- Atropine as an alternative has a faster speed of onset and a shorter duration of action (20 – 30 min) than glycopyrronium and so a late, unopposed bradycardia may occur when used with neostigmine.
- Hyoscine is an effective anti-sialagogue alternative but crosses the blood-brain barrier to cause sedation; it is an effective anti-emetic.

Essential? Necessary? Critical?

- Glycopyrronium is superior to atropine (in terms of both pharmacokinetics and pharmacodynamics) in combination with neostigmine for reversal of neuromuscular blockade. Established safety record and clinician familiarity. **E**

Benzodiazepine (1.4.1)

Drug name and formulation

Midazolam 1 mg.ml⁻¹, 2 mg.ml⁻¹ and 5 mg.ml⁻¹.

Clinical indications

- Premedication.
- Intra-operative sedation.
- Sedation in intensive care. **P**
- Co-agent for induction of anaesthesia.
- Emergency treatment of status epilepticus. **P**

Alternative drugs or techniques

- Lorazepam 4 mg in 1 ml.
- Diazepam 10 mg in 2 ml.
- DiazemulsTM 10 mg in 2 ml.

General comments

- Benzodiazepines act via sites on the neuronal GABA receptor.
- Midazolam is available in a variety of concentrations and so has the potential for drug error.
- Overdose with high concentration midazolam during conscious sedation, outside the environment of anaesthesia and intensive care, is one of the 2013/14 NHS England Patient Safety Never Events⁴.
- The alternative drugs lorazepam and diazepam have longer onset times after administration and longer durations of action. DiazemulsTM is the preferred formulation of diazepam for intravenous injection. All can be antagonised with flumazenil.

Essential? Necessary? Critical?

- Most commonly used benzodiazepine in anaesthesia and critical care. **E**

⁴ www.england.nhs.uk/wp-content/.../2013/12/nev-ev-list-1314-clar.pdf

Non-opioid analgesic; paracetamol (1.4.2)

Drug name and formulation

Paracetamol 1 g in 100 ml for intravenous injection, and various enteral preparations.

Clinical indications

- Analgesia. **P**
- Antipyrexial. **P**

Alternative drugs or techniques

- Ketorolac.
- Diclofenac.
- Parecoxib.

General comments

- In shortage of the injectable, plan to use other routes of administration.
- Intravenous paracetamol was first licensed in the UK in 2000, since when it has formed an important part of peri-operative analgesic regimens. Following a Fatal Accident Inquiry in Scotland in 2011, the Safe Anaesthesia Liaison Group (SALG) issued guidance on its administration⁵. This includes careful prescribing of paracetamol according to weight, age and comorbidities. It is also recommended that for patients weighing <33 kg, 50 ml vials should be used. Intravenous paracetamol remains under close monitoring from the MHRA and yellow card reporting should follow any adverse events.
- Injectable cyclo-oxygenase inhibitors as an alternative simple analgesic are either cyclo-oxygenase (COX)2 specific (parecoxib) or non-specific (ketorolac, diclofenac). The evidence for preferring one over another is slim.
- There is no good substitute for paracetamol as an anti-pyretic.

Essential? Necessary? Critical?

- Paracetamol is the most commonly used simple analgesic and has an established place in a multimodal approach to analgesia. **E**

⁵ <http://www.rcoa.ac.uk/node/12854>

Opioid analgesics: fentanyl (1.4.3)

Drug name and formulation

Fentanyl 100 µg in 2 ml, 500 µg in 10ml.

Clinical indications

- Intra-operative analgesia as part of a balanced technique. **P**
- Treatment of severe acute and chronic pain by various routes and under patient control.
- Analgesia/sedation in intensive care.

Alternative drugs or techniques

- Alfentanil.
- Remifentanil.

General comments

- Fentanyl is 100 times more potent than morphine and produces respiratory depression in a dose-dependent manner. As a result of its haemodynamic stability, fentanyl can be used in very high doses while ventilation is controlled. Muscle rigidity (including the chest wall) can occur but is prevented by muscle relaxants. When used in small doses ($1-2 \mu\text{g}\cdot\text{kg}^{-1}$) fentanyl's duration of action is 30 - 60 min, and this short duration of action is due to redistribution. However, when given in higher doses or after prolonged administration as an infusion, the effects last until the drug is eliminated from the body (terminal half life: 3.5 h).
- Alfentanil has a shorter duration of action than fentanyl. It is not recommended for postoperative analgesia.
- Remifentanil is used as a continuous infusion for intraoperative analgesia. It is not suitable for routine postoperative analgesia.

Essential? Necessary? Critical?

- Widely used opioid to treat intra-operative and postoperative pain, and important role in providing analgesia for day case surgery. **E**
- Shortages have been reported. **C**

Opioid analgesics: morphine (1.4.3)

Drug name and formulation

Morphine 10 mg in 1 ml, and many enteral formulations.

Clinical indications

- Analgesia for postoperative, acute and chronic pain by intravenous, subcutaneous or oral administration. **P**
- Sedation as an infusion in critical care, especially neonatal and paediatric units. **P**

Alternative drugs or techniques

- Oxycodone.
- Diamorphine.

General comments

- Morphine causes histamine release that may lead to hypotension, rash, itching and bronchospasm.
- Caution in renal failure due to the accumulation of metabolites morphine-3-glucuronide and morphine-6-glucuronide.
- Oliguric patients are sometimes switched to fentanyl to avoid accumulation of morphine glucuronides.
- Morphine can cause psychological and physical dependence, as well as tolerance, with long-term use.
- Some patients experiencing unwanted side effects benefit from switching, typically to fentanyl or oxycodone.
- Diamorphine is a suitable alternative when morphine is in shortage, but it is traditionally associated with palliative care.
- While injectables are in shortage, consider enteral administration of opioid analgesics.

Essential? Necessary? Critical?

- Morphine is the most widely used opioid analgesic with a long safety record. **E**
- Shortages have been reported. **C**

Neuromuscular blocking drugs: suxamethonium (1.5)

Drug name and formulation

Suxamethonium 100 mg in 2 ml.

Clinical indications

- Used as part of the 'traditional' rapid sequence induction (RSI) to produce rapid onset, short-acting neuromuscular blockade. **P**
- At lower doses, to relieve laryngospasm and to modify the seizure activity associated with electroconvulsive therapy.

Alternative drugs or techniques

- Rocuronium.

General comments

- Suxamethonium is the only depolarising neuromuscular blocking drug in clinical use in the UK. It is structurally related to acetylcholine, and causes a persisting membrane depolarisation by binding to nicotinic receptors at the neuromuscular junction. It is then rapidly hydrolysed by plasma cholinesterase to inactive compounds.
- Suxamethonium is associated with many significant side-effects:
 - Painful muscle fasciculations during the initial depolarisation.
 - Postoperative myalgia.
 - Bradycardia and ventricular arrhythmias.
 - Transient hyperkalaemia that can provoke life-threatening arrhythmias in susceptible patients, e.g. renal failure, burns, spinal cord injuries or chronic neuropathies.
 - Increased intraocular pressure.
 - Anaphylaxis.
 - Prolonged paralysis in patients with congenital or acquired deficiencies of plasma cholinesterase.
 - Malignant hyperthermia.
- Rocuronium is also used for rapid sequence induction. With sugammadex immediately available, a short duration of action can be achieved.

Essential? Necessary? Critical?

- The only rapid-onset, short-acting neuromuscular blocking agent used in the UK. It provides superior intubating conditions in the fastest time. **E**
- Shortages have been reported. **C**

Neuromuscular blocking drugs: rocuronium (1.5)

Drug name and formulation

Rocuronium 50 mg in 5 ml or 100 mg in 10 ml

Clinical indications

- Non-depolarising neuromuscular blockade for anaesthesia and to assist controlled lung ventilation.
- Used as part of the 'modified' Rapid Sequence Induction [RSI] to produce a rapid onset neuromuscular blockade that is rapidly reversible in airway emergencies. **P**

Alternative drugs or techniques

- Vecuronium.
- Atracurium.
- Cisatracurium.

General comments

- Rocuronium is an aminosteroid non-depolarising neuromuscular blocker that can provide good tracheal intubating conditions after 60 s. It is secreted unchanged mainly in bile and urine. Its elimination and duration of action are prolonged in hepatic dysfunction, but not by renal failure.
- Rocuronium is comparatively free from side effects. It causes mild tachycardia at higher doses, but causes no significant histamine release or bronchospasm, and does not accumulate after repeated administration. It has the added benefit of being completely and rapidly reversed by sugammadex. Its major disadvantage is that is associated with the highest incidence of IgE-mediated anaphylaxis amongst all the neuromuscular blockers.
- Vecuronium is considered a 'clean' neuromuscular blocker, with minimal cardiovascular side effects or histamine release and a lower incidence of anaphylaxis. It can be given as a continuous infusion and is not thought to accumulate. Its onset is not rapid, but the block reversible with sugammadex.
- Atracurium is a benzyloisoquinolinium non-depolarising neuromuscular blocker. Onset is not rapid, and refrigeration is recommended. It can be used as a continuous infusion. It is metabolised by Hoffman degradation and ester hydrolysis via non-specific esterases. Its major side effect is histamine release when higher doses are used, although atopic or asthmatic patients may be susceptible at lower doses. This can cause cutaneous flushing, bronchospasm and hypotension. Slow injection minimises these effects. The block not reversed by sugammadex.
- Cisatracurium's principle benefit compared to atracurium is that the potential for histamine release is extremely low, with good haemodynamic stability. Lowest incidence of anaphylaxis of all the neuromuscular blockers.

Essential? Necessary? Critical?

- Rapid onset, long acting neuromuscular blocker with minimal side effects; suitable for use as part of a modified RSI; rapidly reversible in the event of airway emergencies. **E**
- Shortages have occurred. **C**

Neuromuscular blocking drugs: atracurium (1.5)

Drug name and formulation

Atracurium 50 mg in 5 ml.

Clinical indications

- Medium duration, non-depolarising neuromuscular blockade for anaesthesia, and to assist controlled lung ventilation when lower risk of anaphylaxis is important and Hoffman degradation is a perceived advantage.

Alternative drugs or techniques

- Cisatracurium.
- Vecuronium.

General comments

- Atracurium is mixture of 10 stereoisomers resulting from the presence of four chiral centres. It is stored at 4° C to prevent hydrolysis. In high doses in animal models, the metabolic product laudanosine has been shown to cause seizures, but this is at levels far higher than those encountered in normal clinical practice.
- Cisatracurium's principle benefit compared to atracurium is that the potential for histamine release is extremely low, with good haemodynamic stability. It has the lowest incidence of anaphylaxis of all the neuromuscular blockers.
- Vecuronium is considered a 'clean' neuromuscular blocker, with minimal cardiovascular side effects or histamine release and a lower incidence of anaphylaxis. It can be given as a continuous infusion and is not thought to accumulate. Its onset is not rapid, and the block is reversible with sugammadex.

Essential? Necessary? Critical?

- A medium duration blocking agent that is safe in renal and hepatic dysfunction with minimal cardiovascular instability; established clinician familiarity. **E**

Drugs for reversal of neuromuscular blockade: neostigmine (1.6)

Drug name and formulation

Neostigmine 2.5 mg in 1ml. Also in premixed preparation: 2.5 mg with glycopyrronium 0.5 mg in 1 ml for reversal of non-depolarising neuromuscular block.

Clinical indications

- Competitive reversal of non-depolarising neuromuscular blockade, primarily at the end of anaesthesia. **P**

Alternative drugs or techniques

- Edrophonium chloride
- Sugammadex
- Extended respiratory support

General comments

- Neostigmine forms a carbamylated enzyme complex with acetylcholinesterase so that breakdown of acetylcholine at the neuromuscular junction is inhibited. Unwanted muscarinic effects such as bradycardia, bronchospasm and salivation are countered by concurrent glycopyrronium or atropine.
- Edrophonium is a shorter-acting anti-cholinesterase. When used as an alternative to neostigmine, there is a risk of recurarisation.
- Sugammadex is only effective against neuromuscular block established with rocuronium and vecuronium.

Essential? Necessary? Critical?

- Established safety record and clinician familiarity. **E**

Drugs for reversal of neuromuscular blockade: sugammadex (1.6)

Drug name and formulation

Sugammadex 100 mg.ml⁻¹ in 2 ml or 5 ml.

Clinical indications

- Sugammadex enables the use of rocuronium for high-risk induction of anaesthesia, particularly when suxamethonium is contraindicated. **P**

Alternative drugs or techniques

- Neostigmine

General comments

- Sugammadex is a modified gamma cyclodextrin used for the reversal of rocuronium and, to a lesser extent, vecuronium. Sugammadex can be used at any point after administration of rocuronium, resulting in full reversal of neuromuscular blockade. It therefore provides the option of using rocuronium instead of suxamethonium in the high-risk patient, e.g. the obese or those with a difficult airway.
- Exercise caution in patients with severe renal impairment due to uncertainty about excretion of the sugammadex-rocuronium complex.
- Hypersensitivity reactions, including anaphylaxis, have been reported with its use.

Essential? Necessary? Critical?

- Sugammadex enables the safe use of rocuronium in high-risk induction of anaesthesia in situations where suxamethonium is contraindicated. **E**

Antagonists of central and respiratory depression: flumazenil (1.7)

Drug name and formulation

Flumazenil 100 $\mu\text{g}\cdot\text{ml}^{-1}$ in 5 ml.

Clinical indications

- To reverse benzodiazepine-induced sedation

Alternative drugs or techniques

- None

General comments

- Flumazenil is a GABA-A receptor antagonist. The onset of action is rapid and effects are usually seen within 1 – 2 min.
- Patients show marked variation in their sensitivity to benzodiazepines and the ability to reverse enables safer use of the sedative.

Essential? Necessary? Critical?

- Rapid reversal of benzodiazepine overdose. E

Antagonists of central and respiratory depression: naloxone (1.7)

Drug name and formulation

Naloxone 0.4 mg in 1 ml.

Clinical indications

- Complete or partial reversal of opioid sedation, including respiratory depression.

Alternative drugs or techniques

- Naltrexone.
- Buprenorphine.

General comments

- Naloxone has an extremely high affinity for μ -opioid receptors and can produce rapid onset of withdrawal symptoms if not carefully titrated to effect.
- Naltrexone is structurally similar but has a slightly increased affinity for κ -opioid receptors over naloxone, but can only be administered enterally.
- Buprenorphine is a partial agonist and could be used to decrease but not reverse μ receptor stimulation.

Essential? Necessary? Critical?

- It is on the World Health Organization's List of Essential Medicines for the complete or partial reversal of opioid overdose. **E**

Drug for the treatment of malignant hyperthermia: dantrolene (1.8)

Drug name and formulation

Dantrolene sodium 20 mg to be reconstituted with water.

Clinical indications

- Malignant hyperthermia. **P**

Alternative drugs or techniques

- None.

General comments

- An AAGBI Safety Guideline⁶ recommends that 12 vials are immediately available to provide an initial dose of 2.5 mg.kg^{-1} . The total recommended maximum dose is 10 mg.kg^{-1} , so a treatment may require up to 48 vials.
- The treatment of acute malignant hyperthermia will also require rapid access to ice-cold normal saline 2 l, calcium chloride 10%, sodium bicarbonate 8.4%, glucose 20%, amiodarone 300 mg and a beta-blocker.
- Each vial contains mannitol 3 g.

Essential? Necessary? Critical?

- E N C

⁶ <http://www.aagbi.org/sites/default/files/MH%20recommended%20contents%20for%20web.pdf>

Local anaesthetics: lidocaine (2)

Drug name and formulation

Lidocaine 5 mg.ml⁻¹, (0.5%), 10 mg.ml⁻¹ (1%) and 20 mg.ml⁻¹ (2%).

Clinical indications

- Rapid onset local anaesthetic agent. **P**
- Vaughan Williams Class 1b anti-arrhythmic.
- Intravenous analgesic.
- Modifies the pressor response to laryngoscopy

Alternative drugs or techniques

- Prilocaine.

General comments

- Lidocaine is an amide local anaesthetic.
- Prilocaine is also an amide but with a shorter duration of action. One of its metabolites may precipitate methaemoglobinemia.

Essential? Necessary? Critical?

- The World Health Organization lists lidocaine as an Essential Medicine for basic health care needs. **E**
- It boasts a good safety record, has multiple applications and is very familiar to a whole range of clinicians.
- Lidocaine is the most commonly used local anaesthetic for infiltration.
- Awake fiberoptic intubation (and other similar procedures) relies heavily on this agent.

Local anaesthetics: levobupivacaine (2)

Drug name and formulation

Levobupivacaine 2.5 mg.ml⁻¹ (0.25%), 5 mg.ml⁻¹ (0.5%) and 7.5 mg.ml⁻¹ 0.75%) in 10 ml. Infusions: 0.625 mg.ml⁻¹ (0.0625%), 1.25 mg.ml⁻¹ (0.125%) in 100 ml and 200 ml bags.

Clinical indications

- Slow onset, long-acting local anaesthetic agent.

Alternative drugs or techniques

- Racemic bupivacaine.
- Ropivacaine.

General comments

- Levobupivacaine is an amide local anaesthetic and the levorotatory enantiomer of bupivacaine, which is on the World Health Organization List of Essential Medicines. The levorotatory form binds less avidly to cardiac sodium channels and is less likely to cause cardiac toxicity.
- To dilute solutions, add sodium chloride 0.9%.
- Ropivacaine is a long-acting agent with a shorter onset time than levobupivacaine and has an arguably safer profile. It can be used like levobupivacaine for infiltration, peripheral nerve block and epidural anaesthesia. Compared to levobupivacaine, ropivacaine is slightly less potent (ropivacaine 6 mg.ml⁻¹ is equipotent to bupivacaine 5 mg.ml⁻¹), and has a shorter duration of action.

Essential? Necessary? Critical?

- A popular agent for long acting peripheral nerve block and epidural analgesia. **E**
- Levobupivacaine is used commonly for epidural anaesthesia for emergency caesarean sections. **N**

Local anaesthetics: hyperbaric bupivacaine (2)

Drug name and formulation

Bupivacaine with glucose ('heavy' or hyperbaric bupivacaine) bupivacaine hydrochloride 5 mg.ml⁻¹ (0.5%) with glucose 80 mg.ml⁻¹ (specific gravity = 1.026).

Clinical indications

- Intrathecal spinal anaesthesia in children and adults undergoing urological, abdominal and lower limb operations. **P**
- It is especially useful for perineal surgery due to the dense saddle block it can offer.

Alternative drugs or techniques

- Racemic bupivacaine.
- Hyperbaric prilocaine.

General comments

- An amide local anaesthetic.
- The addition of glucose produces a solution that is hyperbaric relative to cerebrospinal fluid. Intrathecal spread can be influenced by patient positioning.

Essential? Necessary? Critical?

- One of the recommendations in the recent National Hip Fracture Database Anaesthesia Sprint Audit of Practice⁷ was that hyperbaric bupivacaine should be used when spinal anaesthesia is performed for patients with a fractured neck of femur. **E N**

⁷ <http://www.aagbi.org/news/asap-anaesthetic-sprint-audit-practice-2014>

Drug used for local anaesthetic overdose

Drug name and formulation

Lipid emulsion (Intralipid™ 20%).

Clinical indications

- Severe local anaesthetic toxicity with cardiovascular or neurological impairment. **P**

Alternative drugs or techniques

- 10% solution.
- 30% solution.

General Comments

- The AAGBI has published a Safety Guideline on the treatment of severe local anaesthetic toxicity⁸.

Essential? Necessary? Critical?

- A unique agent for management of severe local anaesthetic toxicity, to be at hand whenever higher dose local anaesthetic is being administered. **E**
- Life-saving. **N**
- Shortages have been reported. **C**

⁸ http://www.aagbi.org/sites/default/files/la_toxicity_2010_0.pdf

Anti-emetics: dexamethasone

Drug name and formulation

Dexamethasone sodium phosphate injection 4 mg.ml⁻¹ and 3.3 mg.ml⁻¹ in 1 ml or 2 ml.

Clinical indications

- Prevention of post-operative nausea and vomiting (PONV).
- Suppression of inflammatory and allergic disorders. **P**
- Treatment of cerebral oedema. **P**

Alternative drugs or techniques

- There is a range of anti-emetics available of the classes serotonin antagonists and dopamine antagonists.
- Histamine antagonists and anticholinergics.

General Comments

- In shortage, dexamethasone should not be used as a perioperative anti-emetic.

Essential? Necessary? Critical?

- Established safety record and efficacy in reducing risk of PONV by 25%. PONV is one of the most common causes of patient dissatisfaction post surgery and may delay day case patient discharge. **E**

Anti-emetics: ondansetron

Drug name and formulation

Ondansetron hydrochloride dihydrate 2 mg.ml⁻¹ in 2 ml or 4 ml.

Clinical indications

- The prevention and treatment of postoperative nausea and vomiting (PONV).

Alternative drugs or techniques

- There is a range of anti-emetics available of the classes serotonin antagonists and dopamine antagonists.
- Histamine antagonists and anticholinergics.
- In shortage of injectables, consider use of enteral route of administration if safe.

General comments

- In shortage, use another injectable serotonin antagonist or consider the wide range of anti-emetic alternatives.

Essential? Necessary? Critical?

- Established safety record and efficacy in decreasing risk of PONV by 25%. Postoperative nausea and vomiting are common causes of patient dissatisfaction after surgery and may delay day case patient discharge. **E**

Pressors given by bolus: phenylephrine

Drug name and formulation

Phenylephrine 10 mg.ml⁻¹ (1%) in 1 ml, to be administered intravenously after dilution to at least 1 mg.ml⁻¹.

Clinical indications

- Anaesthesia-induced hypotension. **P**

Alternative drugs or techniques

- Metaraminol.
- Ephedrine.

General comments

- Phenylephrine is a synthetic sympathomimetic amine with alpha-agonist effects, causing a rapid increase in systemic vascular resistance via vasoconstriction, and an increase in blood pressure. It has no effect on beta adrenoreceptors.
- It is slightly safer to use in presence of monoamine oxidase inhibitors than indirectly acting sympathomimetics such as ephedrine and metaraminol, although caution should still be taken.
- It is used primarily for hypotension associated with general anaesthesia or regional anaesthesia.
- Most frequently used as a bolus or infusion in obstetric theatre after spinal anaesthesia (**P**) and to treat epidural-related postoperative hypotension (**P**).
- Can be safely given as a short-term peripheral intravenous infusion.

Essential? Necessary? Critical?

- Established safety record and clinician familiarity. **E**

Pressors by bolus: metaraminol

Drug name and formulation

Metaraminol 10 mg.ml⁻¹ (1%) in 1 ml, to be administered intravenously after dilution to at least 1 mg.ml⁻¹.

Clinical indications

- Anaesthesia-induced hypotension. **P**

Alternative drugs or techniques

- Ephedrine.
- Phenylephrine.

General comments

- Indirectly acting sympathomimetic of longer duration of action.
- Less tachycardia than ephedrine.

Essential? Necessary? Critical?

- Widely used in the UK with an established safety record and clinician familiarity. **E**

Pressors by bolus: ephedrine

Drug name and formulation

Ephedrine 3 mg.ml⁻¹ in 10 ml or 30 mg.ml⁻¹ in 1 ml.

Clinical indications

- Hypotension in obstetric anaesthesia. **P**
- Anaesthesia-induced hypotension.

Alternative drugs or techniques

- Metaraminol.
- Phenylephrine.

General comments

- Ephedrine is a synthetic sympathomimetic with alpha-agonist and beta-agonist properties, increasing heart rate, force of contraction and blood pressure. Exhibits tachyphylaxis as a result of its indirect effects, as stores of noradrenaline (norepinephrine) at nerve endings are depleted.
- Used commonly for hypotension in obstetric anaesthesia as it may maintain uterine and placental blood flow more efficiently than some other sympathomimetics. In shortage, it should be reserved for this indication.
- Can be given as an oral preparation in a dose of 30 mg if the parenteral route is not available, resulting in a longer duration of action.

Essential? Necessary? Critical?

- Established safety record and clinician familiarity.

Pressors by infusion: noradrenaline (norepinephrine)

Drug name and formulation

Noradrenaline 1 mg.ml⁻¹ (as noradrenaline acid tartrate 2 mg.ml⁻¹) in 2 ml, 4 ml and 20 ml, to be diluted before administration.

Clinical indications

- Antihypotensive agent, given by infusion. **P**

Alternative drugs or techniques

- Dopamine.
- Vasopressin.
- Terlipressin.

General comments

- Dopamine causes more tachycardia than noradrenaline.
- Phenylephrine and metaraminol are longer-acting pressors that can be given by intermittent bolus.
- The V1 agonists vasopressin and terlipressin are often effective in hypotensive states but their safety is not fully assessed.

Essential? Necessary? Critical?

- Hypotension is harmful and noradrenaline is the pressor of choice. **E**
- Shortages are reported. **C**

Pressors by infusion: adrenaline (epinephrine)

Drug name and formulation

Adrenaline 1 : 1000 and 1 : 10000 in ampoules and prefilled syringes. The 1 : 1000 preparation can be used for intramuscular and subcutaneous administration, or for dilution before intravenous infusion. Patients at risk of anaphylaxis are given “pen” devices.

Clinical indications

- Cardiac arrest situations as part of the Advanced Life Support algorithm. **P**
- For inotropic support in the critically ill with circulatory failure, either by intravenous bolus or infusion. **P**
- Anaphylaxis. **P**
- Nebulised to decrease symptoms associated with acute upper airway obstruction, post-intubation swelling and infectious croup.
- Prolongs the action of local anaesthetics by decreasing local blood flow.
- Topical haemostatic agent, e.g. used for peptic ulcers during endoscopy.

Alternative drugs or techniques

- Dopamine (inotropic support).
- Dobutamine (inotropic support).

General comments

- Adrenaline is presented in different concentrations, leading overdose errors when the stronger solution is used instead of the more dilute.
- Noradrenaline (norepinephrine) appears to be as effective as adrenaline in the treatment of cardiac arrest.
- In critical care practice a combination of noradrenaline and dobutamine is often preferred to adrenaline alone, giving greater control over heart rate and blood pressure.
- Dopamine has a mixed alpha and beta profile comparable to adrenaline when infused to increase heart rate and pressure.

Essential? Necessary? Critical?

- Life-saving. **E N**
- Shortages reported. **C**

Magnesium sulphate

Drug name and formulation

Magnesium sulphate 20% (4 g in 20 ml; 0.8 mmol.l⁻¹) or 50% (2.0 mmol.l⁻¹) in 2 ml, 4 ml, 5 ml or 10 ml.

Clinical indications

- Seizure prevention and control when caused by pre-eclampsia or eclampsia. **P**
- Severe Tetanus. **P**
- Magnesium sulphate is valued as an adjunctive agent during anaesthesia. It is thought to improve analgesia, relaxation and to protect against cardiac arrhythmia.

Alternative drugs or techniques

- None.

General comments

- Hypomagnesaemia is common after surgery and usually corrects itself.

Essential? Necessary? Critical?

- Established safety record and clinician familiarity in a wide variety of contexts. **E**
- Pre eclampsia. **N**
- Severe tetanus. **N**

Appendix - Summary

Drug name	Essential?	Alternatives	Necessary?	Critical?
Adrenaline	✓		✓	✓
Air & oxygen	✓		✓	
Atracurium	✓	✓		
Atropine	✓	✓		
Dantrolene	✓		✓	✓
Dexamethasone	✓	✓		
Ephedrine	✓	✓		
Fentanyl	✓	✓		✓
Flumazenil	✓			
Glycopyrronium	✓	✓		
Hyperbaric bupivacaine	✓	✓	✓	
Levobupivacaine	✓	✓	✓	
Lidocaine	✓	✓		
Lipid emulsion	✓		✓	✓
Magnesium sulphate	✓		✓	
Metaraminol	✓	✓		
Midazolam	✓	✓		
Morphine	✓	✓		✓
Naloxone	✓			
Neostigmine	✓	✓		
Noradrenaline	✓	✓		✓
Ondansetron	✓	✓		
Paracetamol	✓	✓		
Phenylephrine	✓	✓		
Propofol	✓	✓		✓
Rocuronium	✓	✓		✓
Sevoflurane	✓	✓		
Sugammadex	✓	✓		
Suxamethonium	✓	✓		✓

N.B. on p5, section 4, paragraph 2, line 2, the word 'lower' was corrected to 'higher' on 11/05/2015.