Intubation Drugs

Neuromuscular Blocking Agents (NMBAs) a.k.a. Muscle Relaxants

At the NMJ, ACh molecules released by the arrival of a nerve impulse diffuse across the synaptic cleft and can bind in pairs to the the post-synaptic nicotinic receptors to cause muscle fibre contraction. ACh in the cleft is hydrolysed by end-plate acetylcholinesterase and recycled to the nerve terminal. NMBAs can either stimulate the nicotinic receptor whilst blocking it (depolarising blockers e.g. suxamethonium) or competitively antagonise at the receptor (non-depolarising muscle relaxants). Non-depolarising blockers also act presynaptically to inhibit release of further ACh. Giving an anticholinesterase (e.g. neostigmine) increases cleft ACh by inhibiting acetylcholinesterase action (& stimulating more ACh release) and can surmount a non-depolarising block. Neostigmine inhibits plasma cholinesterase too and thus could potentially prolong the effect of suxamethonium (if given quickly enough). Paradoxically giving too much anticholinesterase leads to excess ACh and a depolarising block (resembling that of suxamethonium). Antibiotics (esp. aminoglycosides) and LA may enhance neuromuscular blockade. Non-depolarising NMBAs antagonize depolarising blockers, so a small dose pre-intubation was suggested (but rarely used) to reduce fasciculation when using suxamethonium.

Depolarising NMBA

Suxamethonium

ACh dimer that binds for a prolonged time @ ACh receptor, inactivating & desensitising it

Onset: 30-60s

Duration: 5-10min - hydrolysed by plasma & liver pseudocholinesterases (not by end-plate acetylcholinesterase)

Cons:

- Myalgia - from fasciculations
- Bradycardia - esp in children or rpt doses (muscarinic effect).
- Transient ↑IOP & ↑ICP
- Masseter spasm - esp in children
- ↓LOS sphincter & intra-gastric pressure → risk of aspiration.
- ↑[K^+] - caused by ACh receptors beyond NMJ. May be significant if:
    - Burns, crush or intra-abdominal sepsis: CI >5 days post onset 'til resolution/healed
    - Denervation (spinal cord injury, stroke): CI >5 days post onset for 6mo
    - Neuromuscular disease (ALS, MS, malignant hyperthermia): CI always
    - Renal failure: if already ↑[K+], ok if [K^+] normal.
    - [K^+] rise reduced by thiopentone, ketamine, pancuronium, salbutamol
- Prolonged effect - (apnoea & paralysis) genetic/ acquired abnormality of plasma pseudocholinesterase
    - Genetic: two autosomal allelomorphic genes with 4 variants: normal (N), dibucaine resistant (D), fluoride resistant (F), and silent (S). 94% are normal (NN), most common abnormality is ND with mildly increased Sux sensitivity.
    - Acquired pseudocholinesterase deficiency: Pregnancy, malnutrition, chronic debilitating diseases, severe burns, organophosphate exposure, drugs (incl. MAOI, OCP, chlorpromazine, neostigmine)
- Malignant hyperthermia - masseter spasm an early sign

Dosage: 1-1.5mg IV Adults, 2mg/kg IV in children<10yr

Non-Depolarising NMBAs

Chemical structure is multi-ringed (all but atracurium, an isoquinoline are based on steroids) with quaternary nitrogen groups.

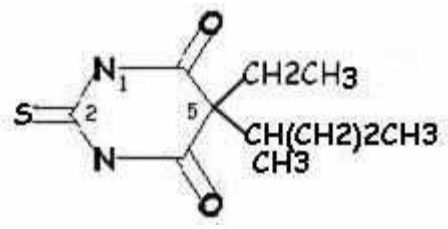
Reversal agent: **sugammadex**

Drug	Onset	Duration	Elimination	Pros	Cons	Usage	Dosage (IV)
Rocuronium	60-90s	20-45min	Biliary>>urinary excretion	Fairly fast onset, short duration.	May ppt with thiopentone.	Modi. RSI, ongoing paralysis	0.6-1.2mg/kg
Vecuronium	2-3min	20-60min	Biliary>>urinary excretion	Short duration, rapid offset. No histamine release. Little CVS effect.	Slow onset for RSI. May ppt with thiopentone.	Maintenance paralysis, modified RSI, elective intubation	0.3mg/kg for intubation, 0.1mg/kg for maintenance
Atracurium	3min	20-30mins.	Hofmann degradation. Some liver ester hydrolysis. Mainly biliary excretion.	Useful in renal or liver failure.	Histamine release. Occ. anaphylactoid reaction. Needs to be kept cold and at low pH.	Modified RSI, elective intubation	0.4-0.5mg/kg
Cisatracurium	a stereoisomer of atracurium, relies more on spontaneous Hofmann degradation & releases less histamine.						
Pancuronium	3-4min	45+min	Hepatic metabolism & primarily renal excretion	Good for prolonged paralysis - retrievals. No histamine release. No ganglia block.	Slow onset. HR (mild cardiac vagolytic effect), – BP, salivation. Rare anaphylaxis. May ppt with thiopentone	Maintenance of paralysis	0.1mg/kg

Induction Agents

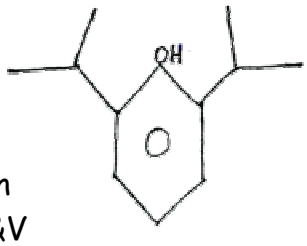
- Sedation for responsive/conscious patients
- Augment NMBAs to improve intubating conditions
- Rapid onset to coincide with maximal muscle relaxation
- Attenuate adverse responses to intubation

Thiopentone



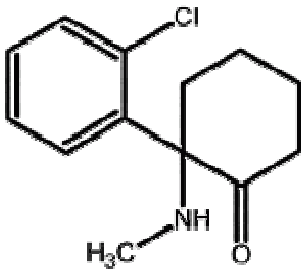
- Short acting barbiturate
- *Pharm:* Protein bound & lipophilic. Vd 2.5L/Kg. Very rapid onset (<30s) to high blood flow tissues (brain) then to rapid redist to muscle & fat.
- *Action:* Increase $GABA_A$-mediated inhibition in CNS and, at higher doses, directly activate GABA receptor
- *Duration:* 10-20min but long elim $t_{\frac{1}{2}}$ (9 days) - rate 12-16%/hr.
- *Pros:* ↓cerebral metabolic rate, ↓ICP rise with intubation
- *Cons:* ↓BP (myocardial depression & venodilatation), ↓RR, histamine release, phlebitis, skin necrosis if extravasation/intra-arterial, laryngospasm, mild ↓cerebral flow, rash, rare anaphylactoid reaction, neuronal demyelination with pophyria, low dose pain perception.
- *Usage:* General RSI, useful in HI, status epilepticus. Avoid in asthmatics or hypotensive.
- *Presentation:* Reconstitute 500mg powder+20ml water (may precipitate with NS).
    - Currently difficult to obtain as main producer has stopped manufacture.
- *Dosage:* 3-5mg/kg. May need slightly more in young children. Reduce in elderly/hypovolaemic/premedicated (1-3mg/kg). Can also decrease in obesity.

Propofol



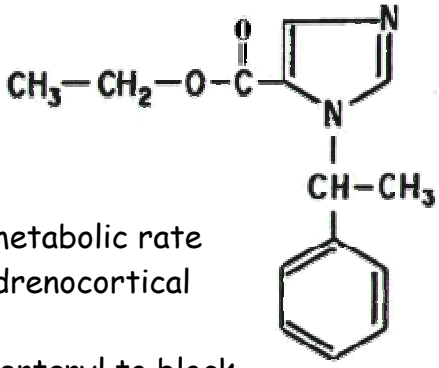
- Very short acting alkylphenol derivative.
- *Pharm:* Insoluble in water. Rapid onset (15-45s) & redist t1/2 2-3min
- *Action:* Enhances inhibitory effect of GABA receptors
- *Duration:* Short (5-10min). Elim $t_{\frac{1}{2}}$ 1hr via hepatic conj & renal excretion
- *Pros:* Short duration of action, ↓ICP rise with intubation, uncommon N&V
- *Cons:* CI in Egg allergy. Marked ↓BP (by 25-40%) & CPP, pain on injection (may ↓ if mixed with 2ml 1% lignocaine), resp depression (apnoea in ~25-40% on induction), dreaming, ↑tone/myoclonic jerks (rel CI in epilepsy), hypersensitivity, hiccoughs, ↓HR, acidosis & sequelae in children with prolonged use, cost.
- *Usage:* Procedural sedation, GA (slower onset than thiopentone), sedation while intubated
- *Presentation:* 200mg/20ml or 500mg/50ml ampoules of white emulsion incl. propofol 1%, soybean oil 10%, egg phophatide 1.2% & glycerol 2.25%
- *Dosage:* 1-3mg/kg for induction, 1-10mg/kg/hr for maintenance. 0.25-0.5mg/kg boluses or 1-3mg/kg/hr for sedation.

Ketamine



- Dissociative anaesthetic related to phencyclidine (PCP)
- *Pharm:* Onset ~1min IV or 3-8min IM,
- *Action:* Blocks excitatory glutamate NMDA-receptors +/- some opioid receptors. Catalepsy, amnesia & analgesia, preserves airway reflexes & resp. Eyes may remain open/moving.
- *Duration:* 5-15min IV or 10-30min IM. Complete recovery longer.
- *Pros:* Bronchorelaxation (asthma), analgesic, amnesia, short acting
- *Cons:* Release of endogenous catacholamines → HR & BP (systolic pressure by 20-30mmHg), ICP, IOP, transient ↓RR/apnoea if given rapidly, salivation & bronchorrhoea, laryngospasm (usually have resp), dysphoria/emergence reactions (adults>children - Rx BDZ)
- *Usage:* Bronchoconstriction (asthma), short painful procedures, hypotensive patients. Avoid in pts with IHD or HI.
- *Presentation:* 200mg/2ml ampoule.
- *Dosage:* 1-2mg/kg IV or 6-10mg/kg IM for induction. Procedural sedation: 0.5-1mg/kg IV or 2-4mg/kg IM. Can be given with atropine (20mcg/kg IV) to ↓secretions. Can be given orally for sedation (5-10mg/kg) - ?unpredictable effect.

Etomidate



- Carboxylated imidazole
- *Pharm:* Rapid onset (15-45s)
- *Action:* ?At GABA receptors
- *Duration:* Short (3-12min). Hepatic metabolism.
- *Pros:* Minimal resp & myocardial depression. ↓ICP, ↓cerebral metabolic rate
- *Cons:* Myoclonic jerks, N&V, painful injection, not analgesic, adrenocortical suppression, hiccoughs, thrombophlebitis.
- *Usage:* Good for hypovolaemic or HI/ICP. May be given with fentanyl to block stimulation of laryngoscopy.
- *Presentation:* Not available in Australia. Where avail mixed with propylene glycol as insoluble/unstable in water.
- *Dosage:* 0.3mg/kg halved if haemodynamically unstable.

Midazolam

- Water soluble short-acting benzodiazepine
- *Pharm:* Mod. rapid onset (2min IV, 15-30min PO/IN/IM/PR).
- *Action:* GABA receptor
- *Duration:* Elim $t_{½}$ 1- 4hrs. Protein bound. Hepatic metabolism to active metabolite and then conj for renal excretion.
- *Pros:* Anxiolytic, anterograde amnesia, anticonvulsant, reversible (flumazenil), ↓ICP, centrally-acting muscle relaxation
- *Cons:* Resp depression (potentiated with opioids), hallucinations, mod ↓BP, not analgesic, variable dose required
- *Usage:* Procedural sedation, Induction (more often an adjunct to reduce dose of another induction agent), sedation while intubated
- *Presentation:* 5mg/5ml or 15mg/15ml ampoules
- *Dosage:* 0.1-0.3mg/kg IV/IM (0.25-1mcg/kg/min IV for maintenance sedation), 0.25mg/kg PR/IN, 0.5-1mg/kg PO.

Opioids

- *Pharm:* Slow-rapid onset, lipophilic & short-acting opioids such as fentanyl & alfentanil may be used
- *Usage:* Most often used as an adjunct to other induction agents. Occasionally used as main induction agent. Useful for procedural sedation, analgesia.
- *Pros:* Blunts sympathetic response to laryngoscopy esp. useful in ICP, IHD, aortic dissection etc. BP maintained.
- *Cons:* Resp depression/apnoea esp if used with BDZ. Chest wall rigidity.
- *Dose:* Fentanyl - Analgesia/Premed: 1-6mcg/kg IV (reduced in children), Induction 50-100mcg/kg

Other

- Neuroleptic anaesthesia: droperidol + fentanyl - pt is detached & unable to obey, no LOC.