Overall Principles to Analgesia/Sedation/NMBA Use

- Sedation is measured using the Richmond Agitation Sedation Scale (RASS), which spans from +4 to -5. Positive scores represent agitation and negative scores represent sedation. The degree of agitation/sedation increases the further away the score moves from zero.
- Light sedation, RASS of +1 to -2, is generally indicated in critically ill adults. However, patients on high ventilator settings may require deeper levels of sedation (RASS -3 to -5) to promote ventilator synchrony.
- Any patient being paralyzed with a neuromuscular blocking agent (NMBA) should be deeply sedated to RASS -4/-5 prior to NMBA initiation. Do not decrease sedative/analgesic infusions while paralyzed.

Analgesics

	Mechanism	Dose	Half Life (hours)	Metabolism	Clinical Pearls
Fentanyl (IV)	Mu agonist	12.5-200 mcg/hr	2-4	Hepatic (De-alkylation and CYP3A4)	- Half life may become prolonged with continuous use - Consider hyperalgesia with prolonged use of high rates
Hydromorphone (IV)		0.25-3 mg/hr	2-3	Hepatic (Glucuronidation)	- Consider hyperalgesia with prolonged use of high rates
Morphine (IV)		2-20 mg/hr	2-4	Hepatic (De-methylation, multiple CYP enzymes) *Active metabolite renally cleared	- Histamine release -> hypotension - Accumulation with renal dysfunction - Reserve only if unable to use fentanyl/hydromorphone or is patient is comfort care
Oxycodone (PO)		5-20 mg Q3-6H	3-6	Hepatic (CYP3A4, CYP2D6)	- Consider hyperalgesia with prolonged use of high rates
Hydromorphone (PO)		1-4 mg Q4H	2-3 hours	Hepatic (glucoronidation)	- Consider hyperalgesia with prolonged use of high rates
Morphine (PO)		7.5-30 mg Q4-6H	2-6 hours	Hepatic (De-methylation, multiple CYP enzymes) *Active metabolite renally cleared	- Histamine release -> hypotension - Consider hyperalgesia with prolonged use of high rates

Sedatives

	Mechanism	Dose	Half Life (hours)	Metabolism	Clinical Pearls
Propofol	$GABA_a$ agonist	5-80 mcg/kg/min	1.5-12	Hepatic (CYP2B6)	- Can cause hypotension and bradycardia - Mixed in lipid emulsion-> hypertriglyceridemia. - Check triglyceride levels every 24 hours for COVID patients. Reduce or avoid propofol exposure when triglycerides are >750
Midazolam	$GABA_a$ agonist	1-20 mg/hr	3-12	Hepatic (CYP 3A4) *Active metabolite 1-hydroxymidazolam glucuronide is renally cleared	- Lipophilic – accumulates in fat tissue with prolonged use (especially obese patients) - No hemodynamic effects - Associated with delirium - Difficult to maintain light levels of sedation – emphasize daily awakening trials
Lorazepam (IV)	$GABA_a$ agonist	1-20 mg/hr	10-20	Hepatic (glucuronidation)	- Hydrophilic – less accumulation; longer half-life, so longer onset compared to midazolam - Diluent is propylene glycol- accumulates in renal dysfunction (cleared with iHD/CRRT). Causes metabolic acidosis. Can check for accumulation with osmolar gap
Dexmedetomidine	α-2 agonist	0.2-1.5 mcg/kr/hr	2-4	Hepatic (glucuronidation, methylation, CYP2D6)	- Can cause hypotension and bradycardia - Do not administer via IV bolus due to high rates of hypotension and bradycardia - Does not provide deep sedation. Should not be used as monotherapy for sedation in patients receiving neuromuscular blockade.
Ketamine	NMDA antagonist	0.2-2 mg/kg/hr infusion or 0.5-1 mg/kg IV bolus as needed for breakthrough agitation	2.5-3	Hepatic (CYP3A4, CYP2D6)	- Can cause hypertension and arrhythmias - Use cautiously in patients with decompensated heart failure or active acute coronary syndrome - Use cautiously in patients with psychiatric history - Emergence reactions may be managed with PRN benzodiazepines
Phenobarbital	$GABA_a$ agonist	65 or 130 mg IV bolus as needed for breakthrough agitation	50-100	Hepatic (CYP2C9)	- Potent CYP enzyme inducer. Assess for drug interactions if multiple doses used - Likely avoid with remdesevir due to drug interaction
Lorazepam (PO)	$GABA_a$ agonist	1-6 mg Q4-6H	10-20	Hepatic (glucuronidation)	- Hydrophilic – less accumulation; longer half-life, so longer onset compared to midazolam

Neuromuscular Blocking Agents (NMBAs)

	Mechanism	Dose	Half Life	Metabolism	Clinical Pearls
Cisatracurium	Acetycholine receptor agonist Acetylcholine	3-10 mcg/kg/min	20-30 minutes	Hoffman Elimination	- No relevant drug-related side effects
Atracurium		5-30 mcg/kg/min	20 minutes	Hoffman Elimination	- Histamine release- can case hypotension
Vecuronium		1-2 mcg/kg/min or 0.1 mg/kg bolus	50-75 minutes (infusion)	Hepatic *Active metabolite 3-deacetyl vecuronium is renally cleared	- Renally cleared- can accumulate in renal dysfunction - No histamine release – hemodynamically neutral - Duration of action following IV bolus is only 20-35 minutes
Rocuronium		0.6-1.2 mg/kg bolus	15 minutes (IV bolus)	Renal	- Generally used for rapid sequence intubation or PRN bolus dosing for ventilator synchrony - Duration following IV bolus is approximately 30 minutes, but higher doses >1 mg/kg may result in longer activity

Michigan Critical Care Collaborative Network

Material Attribution

Author(s): Adult ICU Directors and Nick Farinas

Institution or Source: Michigan Medicine

Notes/Summary