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MedStar Pain, Sedation, and Neuromuscular Blockade Guidance for Vented Covid-19 Patients

- Initiate ABCDEF approach for mechanically ventilated patients[a]
- Optimize environment and treat pain first
- Titrate sedation to appropriate RASS score (RASS 0 to – 2, unless otherwise indicated)
- Include RASS endpoint in sedation orders with daily assessment of goal
- Avoid medications that may alter mental status (e.g., diphenhydramine, anticholinergics)
- Reevaluate continuation of medications used for pain, agitation or delirium prior to ICU transfer to floor

Is patient comfortable and sedation at goal?

NO

- Rule out and correct reversible causes
  (e.g., re-orientation, patient positioning, SSRI or other medication withdrawal)

YES

- Perform SAT/ SBT trials daily per site protocol(s), as appropriate
- Reassess sedation and analgesic requirements
- Maintain sedation goal with lowest effective dose of medications

Pain[b]

Analgesic Management (availability may dictate choices)

First-line: Hydromorphone OR fentanyl infusion, PLUS PRN boluses (titrate up infusion only after bolus dosing fails to control pain)
Second-line: Oral opioids (oxycodone OR morphine q4h scheduled + PRN) +/- hydromorphone/fentanyl infusion in patients tolerating enteral feeding OR morphine infusion
Refractory: ketamine infusion for pain OR lidocaine infusion OR oral methadone OR remifentanil infusion OR fentanyl patch (opioid tolerant patients only) – *call acute pain service (APS) or palliative care for refractory pain recommendations*

Agitation[b] (RASS>+1)

Sedation Management (optimize pain management, availability may dictate choices)

First-line: Propofol[c] OR dexmedetomidine (see considerations below)
Second-Line: Ketamine +/- dexmedetomidine OR benzodiazepines (for alcohol or benzodiazepine withdrawal or seizure OR for patients with contraindication to propofol or who are refractory to dexmedetomidine) OR ketamine (with lidocaine as adjuvant) – *call APS for lidocaine*
-If agitation still not controlled, consider adding lorazepam boluses OR clonazepam or an atypical antipsychotic as needed for rescue therapy
Refractory: Consider phenobarbital for sedation if agitation still uncontrolled

Dexmedetomidine: not to be used as the only sedative in a paralyzed patient, consider in the following patients:

a) Adjuvant therapy when unable to maintain RASS between 0 to -2 on propofol
b) Patients who continue to require sedation when propofol inhibits progress towards extubation
c) Patients who have a documented intolerance to other sedative agents or are currently experiencing adverse effects (e.g., triglycerides >500 mg/dL or elevated/upward trending myoglobin from propofol, QTc prolongation (>550 msec)

Paralysis[b]

Neuromuscular blocking agents (adequate sedation required prior to paralysis)

- Consider boluses over infusions to facilitate ventilation targets
- If proning with high peak plateau pressures and asynchrony, consider infusion for 24-48 hrs

NMB Selection (availability may dictate selection)

First-line: Vecuronium or rocuronium boluses IV q2h PRN vent asynchrony
Second-line: Cisatracurium infusion or vecuronium infusion
Drug Shortages: Rocuronium infusion or atracurium infusion
All paralyzed patients require an order for lubricant ophthalmic ointment or drops (e.g. Lacrilube™)

[a] ABCDEF: awakening and breathing coordination of daily sedation and ventilator removal trials, choice of sedative or analgesic exposure, delirium monitoring, early mobility and exercise, and family involvement
[b] Refer to other side for initial medication dosing recommendations. In presence of hepatic and/or renal impairment, dose adjustment should be considered
[c] Monitor triglyceride levels in patients receiving propofol for > 72 hours; consider discontinuing if > 500 mg/dL

Adapted from the UMMS Pain, Sedation, and Delirium Protocol, with permission

Dosing Recommendations

General principles for medication management during drug shortages:

- Attempt to reach goal with one medication.
- Availability of IV medications is always questionable. Attempt to use PO early after intubation to minimize IV medication use.
- We will attempt to predict shortages but be prepared to quickly switch to alternative medications. Utilize acute pain service or palliative care services for conversion recommendations.

Medication	Adult Dosing*	Comments
PAIN THERAPY		
Fentanyl	Continuous infusion 25 – 300 mcg/hr IV Bolus: 25 – 50 mcg q1 hr PRN procedural breakthrough pain only Patch: 12.5-100 mcg/hr topically (Contact APS or palliative care to start patch)	• PRN to be used for procedural breakthrough pain and for bolus dosing for patients on an infusion • Prefer fentanyl for CrCl < 15
Hydromorphone	Continuous infusion 0.5-4 mg/hr IV Bolus: 0.5 – 1 mg IV q 3-4 hrs-4PRN PO: 2 – 4 mg PO q 3 to 4 hr PRN or scheduled	• Use lower doses in opioid naïve patients. • Active metabolites can accumulate in severe renal impairment • Prefer hydromorphone over morphine for CrCl </= 30 due to neurotoxicity risk
Morphine	Continuous infusion 2-20 mg/hr IV Bolus: 2-4 mg IV q 4 hr PRN or scheduled PO tablets: 7.5 (1/2 tab) - 15 mg (1 tab) q 4 to 6 hr PRN or scheduled PO solution: 6 - 10 mg q 4 to 6 hr PRN or scheduled ([limit to "even" doses since solutions come as 1 mg/mL or 20 mg/mL])	• Use lower doses in opioid naïve patients. • Active metabolites can accumulate in severe renal impairment – avoid in these patients if feasible • Use liquid for enteral tube administration when feasible/available • Prefer morphine over hydromorphone for CrCl > 30 to preserve hydromorphone
Oxycodone	PO: 2.5 – 10 mg PO q 4 hr PRN or scheduled	• Use liquid for enteral tube administration when feasible/available
Ketamine (for pain)	Continuous infusion 0.1 mg/kg/hr, increase by 0.1 mg/kg/hr every 60 mins, maximum dose 1 mg/kg/hr (maximum weight 100kg)	• Provider must titrate (not nurse titrated) • Follow MedStar Clinical Practice Guideline, link here.
Lidocaine	Continuous infusion 0.5 mg/kg/hr, increase to 1 mg/kg/hr (usual dose), maximum rate 2 mg/kg/hr	• Provider must titrate (not nurse titrated) • Follow MedStar Clinical Practice Guideline, link here.
Remifentanil	Continuous infusion 0.1 – 0.15 mcg/kg/min, maximum dose 0.2 – 0.4 mcg/kg/min	• Rapid offset with interruption or discontinuation
ADJUNCTIVE/ALTERNATIVE		
Acetaminophen	PO: 1000 mg q8h scheduled (preferred) or 650 – 1000 mg PO q 4 to 6 hr PRN	• Consider as adjunct or as an alternative to an opioid analgesic • Maximum 4000 mg/day • Monitor hepatic function
Gabapentin	300 mg – 1200 mg three times daily (CrCl ≥ 60 mL/min) 200-700 mg twice daily (CrCl > 30 to 59 mL/min) 200 -700 mg once daily (CrCl > 15 to 29 mL/min) 100-300 mg once daily (CrCl ≤ 15 mL/min)	• Preferred therapeutic option for neuropathic pain only • Monitor renal function

Methadone	Contact APS or palliative care to start methadone	• Consider for opioid-sparing effects as an adjunct • Need to monitor QTc, serum K, and serum Mg. • Avoid use in patients with unstable hepatic function. • Avoid titrating methadone doses up no more frequently than every 3 days. • Do not recommend IV methadone due to risk of QTc prolongation, hypotension and bradycardia.
AGITATION THERAPY		
Propofol	5-50 mcg/kg/min (or higher if tolerated)	• No loading dose or bolus for sedation, intubation only • Monitor for propofol-related infusion syndrome • Monitor triglyceride and CPK levels in patients receiving propofol for > 72 hours; consider discontinuing if triglyceride > 500 mg/dL
Dexmedetomidine	Intubated: 0.1-1.5 mcg/kg/hr (or higher if tolerated) Non-intubated: 0.1-1 mcg/kg/hr	• No loading dose or bolus due to concern for hypotension or bradycardia • Should not be used for deep sedation or alone with paralytics or for severe agitation • Hold drip if HR < 60 or MAP < 60
Clonazepam	PO/SL: 1-2 mg q12h (initial)	• If no response to propofol and/or dexmedetomidine
Lorazepam	1 – 4 mg IV q 2 to 4 hr PRN for acute agitation	• If no response to propofol and/or dexmedetomidine
Midazolam	Bolus 2 mg IV q 5 minutes to goal RASS (up to 12 mg), then continuous infusion 2 mg/hr. Rate may be increased by 1 mg/hr q 30 minutes to maximum 12 mg/hr	• May cause hypotension • Accumulation can occur with prolonged use, and in the elderly or those with hepatic or renal impairment. This may result in delayed emergence from sedation
Ketamine (for sedation)	Continuous infusion 0.3-0.5 mg/kg/hr. Increase rate by 0.1-0.25 mg/kg/hr every hour to RASS goal. Maximum dose 3 mg/kg/hr (maximum weight 100kg) Continuous infusion 5-8 mcg/kg/min. Increase rate by 2-4 mcg/kg/min every hour to RASS goal. Usual dose 25 mcg/kg/min. Maximum dose 50 mcg/kg/min. (maximum weight 100kg)	• **Sedation dosing regimen for intubated patients only** • Attempt to wean down or titrate off continuous opioids (e.g. fentanyl) when a patient is on a ketamine continuous infusion • Usual dose 1.5-2 mg/kg/hr but may be lower with concomitant sedation use • If refractory despite propofol, dexmedetomidine, and/or benzodiazepines • Dosing for sedation differs significantly from dosing for pain management • Provider must titrate (not nurse titrated) • Consider PRN lorazepam and glycopyrrolate to manage adverse effects
Phenobarbital	***ETOH withdrawal protocol (adult patients, weight > 80kg):*** LOAD: Phenobarbital 220mg IM x 1 now, then in 3 hours Phenobarbital 165mg IM x 1, then in 3 hours Phenobarbital 165mg IM x 1. TAPER: Phenobarbital 32.4mg Q12H x 4 doses, then 32.4mg PO daily x 2 doses. PRN MAINTENANCE: Phenobarbital 65mg IM Q6H PRN for 2 or more of the following: SBP>160, DBP>100, HR>110, diaphoresis, tremors, hallucinations, significant agitation.	• Patient should NOT receive IV Phenobarbital as there is an increased risk of respiratory depression due to rapid absorption • Check level in AM
NEUROMUSCULAR BLOCKING THERAPY (Use ideal body weight (IBW) or adjusted body weight (AdJBW) in obese patients)		
Vecuronium	Continuous infusion: 0.8 – 1.2 mcg/kg/min IV Bolus: 0.1-0.2 mg/kg	• Active hepatic and renal metabolites
Rocuronium	Continuous infusion: 8-12 mcg/kg/min IV Bolus: 0.6 mg/kg	• Usually used for rapid sequence intubation • Transient tachycardia (vagolytic effects) • Fecal and urinary elimination, minimal hepatic metabolism

Cisatracurium	Continuous infusion: 1-10 mcg/kg/min IV Bolus: 0.15-0.2 mg/kg	• Hoffman elimination • Transition rare bradycardia, hypotension or bronchospasm
Atracurium	Continuous infusion: 4-15 mcg/kg/min IV Bolus: 0.4-0.5 mg/kg	• Hoffman elimination • Histamine release at high dose with potential for flushing, bradycardia and hypotension • Tachyphylaxis may occur at doses greater than 10 mcg/kg/min
ATYPICAL ANTIPSYCHOTICS (for treatment of delirium)		
Quetiapine	50 – 100 mg PO q 6 to 12 hr	• EKG should be obtained at baseline and at least once weekly – more frequent monitoring may be necessary initially or when patient is on additional QTc prolonging medications or has an underlying arrhythmia
Ziprasidone	10 – 20 mg IM q 2 to 4 hr	• EKG should be obtained at baseline and at least once weekly – more frequent monitoring may be necessary initially or when patient is on additional QTc prolonging medications or has an underlying arrhythmia
Olanzapine	5 - 10 mg PO q 12 to 24 hr (age 18-65 yo) 2.5 - 5 mg PO q 12-24 hr (age > 65 yo)	• Concurrent IM olanzapine use with IM/IV BZDs not recommended (risk of hypotension, bradycardia, hypoventilation, and death)
Risperidone	0.5 - 1 mg PO q 12 to 24 hr (age 18-65 yo) 0.25 - 0.5 mg PO q 12 to 24 hr (age > 65 yo)	

***Consider starting at lower end of dosing range for patients > 65-year-old**