Critical Care Drug Recommendations for COVID-19 During Times of Drug Shortages

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Because of the COVID-19 pandemic, many institutions throughout the country are anticipating or currently experiencing shortages of vital anesthetic drugs that are also commonly used in intensive care units (ICU). When institutions approach capacity status in their ICUs and have concerns regarding the availability of sedating and paralytic drugs, anesthesiologists should strive to conserve vital drugs for use in ICUs. Shortages of particular concern include propofol, dexmedetomidine, midazolam, and neuromuscular blocking agents.

This document is meant to help anesthesiologists proactively make changes to avoid shortages of these vital drugs and preserve supplies for the duration of the pandemic.

Surgeries that are performed in the operating room should avoid use of total intravenous anesthetics (TIVA) whenever possible to preserve the supply of intravenous agents. Efforts should be made to employ the use of regional anesthetic techniques wherever suitable.

In the event that intravenous sedation agents are unavailable, inhalational anesthetics have the potential to be used for sedation when anesthesia machines are being used for prolonged periods as ICU ventilators. This application should be utilized with caution due to issues with scavenging, excessive inhalational agent consumption, moisture buildup, and limited data on their use in Adult Respiratory Distress Syndrome (ARDS) in general and COVID-19 in particular. Use of these agents mandates the continuous presence of a trained anesthesia professional on a 24/7 basis in order to facilitate their use.

Use best clinical judgment if more than one adjunct from each category is felt to be necessary.

Propofol Conservation Model

1. **Propofol**
   a. Primary sedative for ventilated patients
   b. Start ONE OR MORE Primary Adjuncts (noted below) at the time of starting propofol
   c. Limit maximum propofol maintenance dose to 50 mcg/kg/min
      i. Allow higher doses for up to 2 hours to allow for adjunct sedation to take effect
2. Primary Adjuncts
Start primary adjuncts at the time of starting propofol infusion

**Opioids**

a. **Fentanyl** 50-100mcg q1hr IV PRN, AND start infusion fentanyl 50-200 mcg/hr.
b. **Hydromorphone** 0.25-1.0 mg q1hr IV PRN, AND start infusion 0.5 to 2 mg/hr.
c. If concern for shortage of IV opioid or high daily requirement: start an enteral opioid to replace part of the past 24-hour IV opioid. Transdermal patch is an alternative if enteral route is not clinically indicated
   i. Fentanyl IV 100 mcg/hr. x 24hrs: start oxycodone 30 mg PO q8hrs (preferred) OR Fentanyl TTS patch 12.5mcg/hr. (could escalate based on prior IV infusion requirements)
   ii. Hydromorphone IV 1 mg/hr. x 24 hrs.: start oxycodone 30 mg PO q8hrs (preferred) OR fentanyl TTS patch 12.5mcg/hr. (could escalate based on prior IV infusion requirements)
   iii. Consider addition of PO methadone

3. Antipsychotics

a. **Quetiapine** 25-50 mg PO q8hrs scheduled (max 400mg/day)
   i. **Alternative: Olanzapine** 10mg PO q24hrs (max 30 mg/24 hours)
b. **Haloperidol** 2 mg IV now x1; escalate to 5 mg IV if needed
c. 12 lead EKG daily while on antipsychotics, reduce dose if QTc >500 ms
   i. Baseline EKG if on other QTc prolonging agents (i.e. azithromycin, hydroxychloroquine).

4. Secondary Adjuncts

a. Reserve for patient with sedation/ventilator synchrony requirements refractory to **Propofol AND Opioid infusion AND scheduled antipsychotics**
b. Secondary Adjunct Options
   i. **Phenobarbital** 10mg/kg IV q24 hours
      • Check level at 24 hours (dose to 15-20mcg/mL)
      • 130 mg PO twice daily may prove particularly useful in setting of alcohol withdrawal syndrome to reduce benzodiazepine use
   ii. **Dexmedetomidine**: 0.1 to 1.2 mcg/kg/hr. IV
      • Restricted use in adult critical care requires attending intensivist approval
   iii. **Clonidine**: 0.2-0.4 mg PO q 8hrs
      • Alternative to Dexmedetomidine for adult patients

5. Third Line Adjuncts

a. Reserve for patient with sedation/ventilator synchrony requirements refractory to **propofol AND opioid infusion AND scheduled antipsychotics AND barbiturate/dexmedetomidine/clonidine**
b. Option:
i. **Ketamine**: 0.15 to 2.0 mg/kg/hr.

ii. Benzodiazepines are not required to reduce psychomimetic-side effects if propofol or dexmedetomidine infusion is used concomitantly
   - Note: will not be able to titrate sedation to EEG/BIS if using ketamine

iii. **Benzodiazepines**
    Choices
    - **Midazolam** 2 mg IV PRN x1 and start 1-5mg/hr. IV infusion
    - **Lorazepam** 2 mg IV PRN x1 and start 1-5mg/hr. IV infusion

iv. **Neuromuscular Blocking Agent (NMBA) Conservation Model**
    - If NMBA is indicated, start with intermittent bolus regimen first, before starting NMBA infusions
    - If NMBA infusion is required, consider lower doses and titrating to a Train-Of-Four (TOF) of 3-4

6. **Additional Agents**
   a. **Buffered Lidocaine**: Dosing suggestion: Buffered 2% lidocaine (lidocaine 2% with 8.4% sodium bicarb at 9:1 mL ratio) instilled into endotracheal tube cuff until no leak occurs at 20 cm H2O of positive pressure. (4-6 mL). May allow reduction of sedation to very low levels as patients seem to tolerate the presence of the endotracheal tube much better.
   b. **Methadone**: Due to the very high intraindividual bioavailability of oral methadone and the variability in time to onset and peak, IV methadone is preferred as a first choice followed by po if IV is in short supply or after an IV “load” is on board.
      i. Oral is not ideal due to the length of time to onset (0.5 – 1hr) and the high variability in time to peak (1-7 hr.)
      ii. IV < 10 min for onset, respiratory depression even from a large IV dose is expected to be resolved in 30-45 minutes secondary to redistribution.
      iii. Recommend monitoring QTc in the same fashion as antipsychotics especially if both are used together.
   c. **Inhalational Anesthetics**: Inhalational anesthetics may potentially be used for sedation when there is a continuous presence and availability of trained member of the anesthesia care team. However, little is known about the physiologic consequences of the volatile anesthetics when used for long periods in patients who are infected with Covid-19. Additionally, anesthesia machines being used for prolonged periods as ICU ventilators may present challenges pertaining to scavenging, excessive inhalational agent consumption, and moisture buildup. Devices are able to administer volatile anesthetics without an anesthesia machine but are not available for use in the US at this time.