Long Term Volatile Anesthetic Sedation in Critically Ill Patients

Potential Emergency Use Protocol for the COVID-19 Pandemic

Introduction:

During the COVID-19 pandemic, critical care providers are facing numerous potential challenges in caring for a surge of critically ill patients, both with and without COVID disease. Preliminary epidemiologic studies and anecdotal reports have described high numbers of severely ill COVID-19 patients with severe hypoxia and ARDS requiring mechanical ventilation, at times with extremely high respiratory drive.[1,2] In hospital locations where ventilator resources are limited, and with anticipated shortages in intravenous sedative agents such as Propofol and Midazolam, consideration can be given to utilizing an anesthesia machine with a vaporizer capable of delivering the volatile anesthetic agents to both ventilate and sedate the critically ill patient.

Data Supporting Volatile Anesthetic ICU Sedation:

Historically, volatile anesthetic ICU sedation in the US has been employed largely in patients with refractory status asthmaticus, where their properties as bronchodilators can improve pulmonary mechanics and gas exchange.[3]

Long term volatile sedation would be an off-label use of these drugs in the US, according to the FDA. In Europe and Canada, critical care providers have been practicing long term volatile anesthetic sedation with either Isoflurane or Sevoflurane for nearly a decade. Experience in these locations suggests that both Iso and Sevo are effective sedatives with rapid on/offset and minimal metabolism and thus organ toxicity, even after multiple days of administration (Fig 1). Patients typically wake up quickly (even with Iso) and have shorter times to extubation after sedative discontinuation as compared to other sedatives including Propofol. This reduction in wake up and extubation times has been shown in isolated studies to translate to reduced ICU length of stay, although not consistently. A large scale randomized controlled trial in Germany has recently been completed, however results are not yet available.[4] A retrospective cohort study of 200 patients undergoing long term volatile sedation (>4 days) in Germany did not identify any increased risk of renal or hepatic injury with isoflurane, and actually reported a survival benefit.[5]

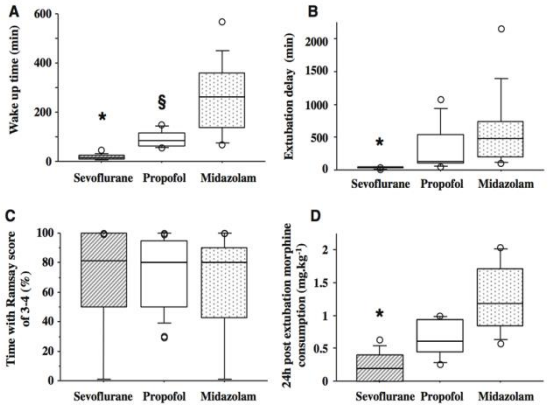
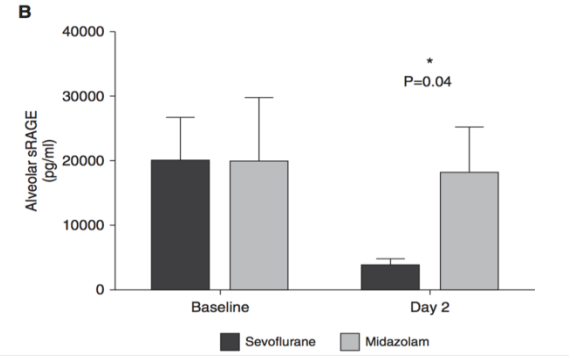


Figure 1: Sedation scores, wake up times, and morphine consumption in 60 patients receiving Sevoflurane sedation for 50-60 hours

Lung Protection from the Volatile Anesthetics:

In addition to their bronchodilatory properties, the inhaled anesthetics may prevent inflammatory lung injury from a number of exposures as demonstrated in multiple preclinical models.[6] In thoracic surgery, the use of sevoflurane as compared to Propofol has been shown to reduce lung inflammation and prevent postoperative pulmonary complications.[7] A pilot RCT of Sevoflurane vs Midazolam for 50 moderate to severe ARDS patients demonstrated lower concentrations of the inflammatory marker SRAGE and improved oxygenation on day 2 (Fig 2). Although the trial was not powered to detect differences in clinical outcomes, there were large non-significant differences in ventilator free days (13 vs 5.5d) and ICU length of stay (18 vs 23d) favoring the Sevoflurane group.



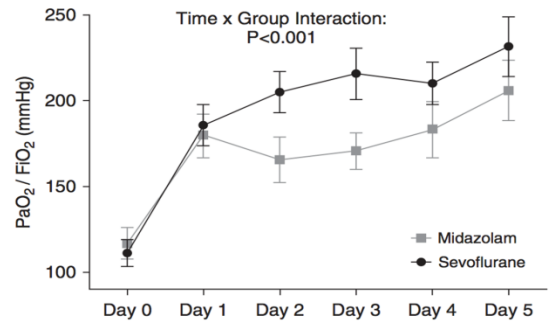


Figure 2: Reductions in alveolar inflammatory biomarkers and improvement in oxygenation with Sevoflurane sedation in ARDS patients

Proposed Guidelines for Long Term Volatile Anesthetic Sedation in Critically Ill Patients

Patient Selection

Indications:

- Mechanical ventilation with need for sedation
- Preference to avoid, conserve, or unavailability of, intravenous sedatives

Contraindications:

- Personal or family history of Malignant Hyperthermia (MH)[8]
- Known or suspected elevation in intracranial pressure
- Severe shock unresponsive to vasopressors
- No ability to scavenge anesthetic gases

Dosing and Monitoring

Agent Selection

- Both Isoflurane and Sevoflurane have been used for long term sedation
- Our study group here would prefer Sevoflurane as the majority of the preliminary studies have been conducted using Sevoflurane

Dosing

- The conventional dosing method in the OR is to follow the end tidal anesthetic concentration % (ie MAC)
- In the ICU, dosing is typically titrated to effect
    - Target sedation score (RASS, Ramsey score, etc)
    - Ventilator synchrony
    - Patient comfort

Agent	Surgical Anesthetic Dose	ICU sedation range[9]
Isoflurane	1.2%	0.2 – 0.7%
Sevoflurane	2%	0.5-1.4%

Monitoring

- A gas monitor can and should be used to monitor end tidal gas concentrations and carbon dioxide where available
- Temperature monitoring (MH)
- Hemodynamic monitoring as per usual ICU care
- Daily serum Cr and LFT checks in long term patients

Wake Up

- Turn the vaporizer to zero and increase gas flows as per usual practice.
- Patients typically able to be assessed/extubated within 10-15 minutes.

Scavenging

- Use of the volatile agents should only be considered in locations where adequate scavenging has been established
- All OR locations have scavenging, all other locations will require an adapter to fit to wall suction
- If there are any questions regarding the scavenging abilities in your location, contact your local anesthesia biomedical engineers

QUESTIONS?????
Contact Brian O'Gara MD p34895 bpogara@bidmc.harvard.edu
And/or the Anesthesia Quality and Safety Division

References

1) Wang. *JAMA.* 2020;323(11):1061-1069. doi:10.1001/jama.2020.1585
2) Yang *Lancet 2020.* https://doi.org/10.1016/S2213-2600(20)30079-5
3) Schutte *BJA 2011.* https://doi.org/10.1093/bja/aet257
4) SED001 trial. https://www.clinicaltrialsregister.eu/ctr-search/trial/2016-004551-67/SI
5) Bellgardt *EJA* 2016 10.1097/EJA.0000000000000252
6) O'Gara *ICM* 2016. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4992441/
7) DelaGala *BJA* 2017. https://academic.oup.com/bja/article/119/4/655/4100575
8) https://www.uptodate.com/contents/malignant-hyperthermia-diagnosis-and-management-of-acute-crisis