


NARRATIVE REVIEW



Inhalational volatile-based sedation for COVID-19 pneumonia and ARDS

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Abstract

Hospitals worldwide are experiencing a shortage in essential intravenous sedative medications. This is attributable to high number and high sedative needs of COVID-19 critical care patients with disruption of drug supply chains. Inhaled volatile anesthetic agents are an abundant resource and readily implementable solution for providing ICU sedation. Inhaled volatile agents may also provide important pulmonary benefits for COVID-19 patients with ARDS that could improve gas exchange and reduce time spent on a ventilator. We review the use of volatile agents, and provide a technical overview and algorithm for administering inhaled volatile-based sedation in ICUs.

Keywords: Sedation, Volatile anesthetics, COVID-19, ARDS, Ventilation

Global shortage of essential intravenous sedatives and neuromuscular blocking agents has emerged to be a major problem in delivering safe care for critically ill patients during the COVID-19 pandemic. Government agencies and medical organizations are reporting major shortages of benzodiazepines, opioids, propofol and paralytics [1, 2]. Drug shortages may arise because of disrupted supply chains combined with increased demand from the large number of ventilated COVID-19 patients who exhibit high sedative requirements and commonly need neuromuscular blockade. Low drug stocks have wider impact beyond intensive care units (ICU) on other essential hospital services including operative surgery and end-of-life care. Resource scarcity has led to difficult ethical triaging of resources and re-introduction of older long-acting agents such as barbiturates in many jurisdictions.

During this crisis, many hospitals have moved to or are considering the use of sedation using inhaled volatile anesthetics to conserve intravenous sedatives agents.

However, evidence indicates that inhaled agents like isoflurane and sevoflurane offer more than just sedation and may be advantageous for patients with COVID-19 ARDS. These benefits may include anti-inflammatory effects and lower airway resistance via dose-dependent bronchodilatation [3–6]. Volatile agents also dilate pulmonary vascular beds, but the specific effect in ARDS and at low doses remains understudied. These combined benefits have shown moderate improvements in patient oxygenation, nonsignificant trend to increase ventilator free days, but studies lack sufficient power to show any mortality or ICU length of stay benefit [3]. Beyond ARDS studies, inhaled sedative regimens have shown modest benefits in faster extubation times upon drug discontinuation, which is attributable to their unique clearance via pulmonary exhalation with negligible systemic metabolism [7, 8].

There are several technical and personnel prerequisites when commencing inhaled volatile-based sedation in ICUs. Sevoflurane, desflurane or isoflurane can all be used, but isoflurane offers the greatest potency with the lowest dosing requirements for ICU patients. Volatiles are delivered using either an anesthesia machine or ICU ventilator with an in-line miniature vaporizer. The latter option provides high flow rates, more sophisticated ventilation options and better management of air leaks that would be preferable in severe ARDS patients with

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high minute volume requirements (15–25 L/min). Mini-vaporizers (for example, MIRUS or Anesthesia Conserving Device) are placed close to the endotracheal tube adding circuit dead space (50–150 ml) with minimal tidal volume requirements (200–350 ml, device dependent) to prevent re-breathing of carbon dioxide [6]. These vaporizers contain a reflector that recycles expired agent that allows sedation to be maintained using very low amounts of agent (i.e., isoflurane 2–5 ml/h, sevoflurane 3–8 ml/h). Devices also include humidification/anti-microbial filter, which filters over 99.9% of particles measuring at least 27 nm. This provides protection to the ventilator from SARS-CoV-2 which is a larger microbe measuring 120–160 nm. An additional filter could also be placed on the expiratory port of the circuit after discussion with the manufacturer. Delivering volatile agents must be performed in conjunction with scavenging of gas from the ventilator exhaust to keep occupational levels below recommended limits [6, 9]. Bedside end-tidal gas monitoring (correlate of cerebral concentration) can be used to ensure gas delivery, assess concentration of drug needed to achieve a specific clinical sedation endpoint, re-breathing of carbon dioxide and device obstruction. Monitoring can be performed using a portable monitor or gas module compatible with the ICU monitoring system. Practical management and regimen for inhaled sedation is summarized in Fig. 1. Given the differences of delivering volatile agents, institution of inhaled sedation regimens is often simpler in European ICUs that are staffed predominantly by anesthesiology-trained intensivists who are familiar with the physicochemical and delivery nuances of volatile agents. In North American ICUs where staffing models have a greater concentration of internal medicine-trained intensivists, optimal delivery of inhalational techniques may be better managed using a cross-disciplinary sedation team that encompasses an anesthesiologist, respiratory therapist or certified nurse anesthetist at least during early stages of implementation.

Volatile agents are effective in complex and high-sedation-need patients with significant reduction or removal of intravenous sedatives. Volatile agents possess mild muscle relaxation properties and may lower usage of paralytic agents, but neuromuscular blocking agents will likely still be required for patients with severe ARDS. Volatile agents possess little analgesic effect and are typically co-administered with intravenous opioids. Inhaled volatile agents show similar pharmacodynamics properties to intravenous sedative, i.e., dose-dependent hypnosis, respiratory depression and hypotension. Prolonged use of volatile agents has

shown good safety with equivalent hemodynamic stability, no hepatorenal toxicity and possibly less agitation compared to intravenous agents [3, 8, 10]. Prolonged use of sevoflurane may be associated with diabetes insipidus in some rare cases [11]. Rare adverse effects include malignant hyperthermia within genetically susceptible individuals, which is identified by hyperthermia, hypercarbia and hemodynamic instability. These hypermetabolic symptoms need to be separated from more common ICU problems such as new sepsis and deteriorating lung function.

Several important technology and drug features need to be considered using these systems. Device changes may be more frequent (<24 h) in patients with high-volume secretions. Addition of miniature vaporizers mildly elevates circuit resistance (and airway pressures) that is partially lowered by infusing volatile agent. During weaning or sedation holidays when volatiles are discontinued, removal of mini-vaporizers from the circuit is vital to minimize work of breathing [12]. Overlapping good management of delirium and pain while tapering off volatile agents will help transition to a more successful weaning process. Recently, Gattinoni et al. have suggested two COVID-19 lung phenotypes with different physiological features and ventilation recommendations; type-L (low lung recruitability with high tidal volumes >6 ml/kg and lower PEEP ventilation) and type-H (high lung recruitability with low tidal volumes and higher PEEP ventilation) [13]. Patients with either phenotype may exhibit high ventilatory ratio indicating increased dead space [14]. Maintaining adequate sedation is determined clinically (i.e., sedation score, motor activity) as end-tidal gas monitoring maybe an inaccurate measure of alveolar and cerebral concentration in the presence of significant ventilation–perfusion mismatch. Patients with a deterioration in lung function and/or new sepsis may show a reduction in tidal volumes below the recommended device thresholds that can lead to re-breathing and hypercarbia. Optimizing ventilation settings to increase tidal volumes will overcome this issue, but inability to provide sufficient tidal volumes should lead to device removal unless patients are commenced on extracorporeal support where external gas exchangers or sweep gas efficiently removes carbon dioxide [15].

In conclusion, trained teams can safely deliver inhaled volatile sedation regimens with a good sedation profile that may have benefits in the lung while easing pressure on essential sedative medications.

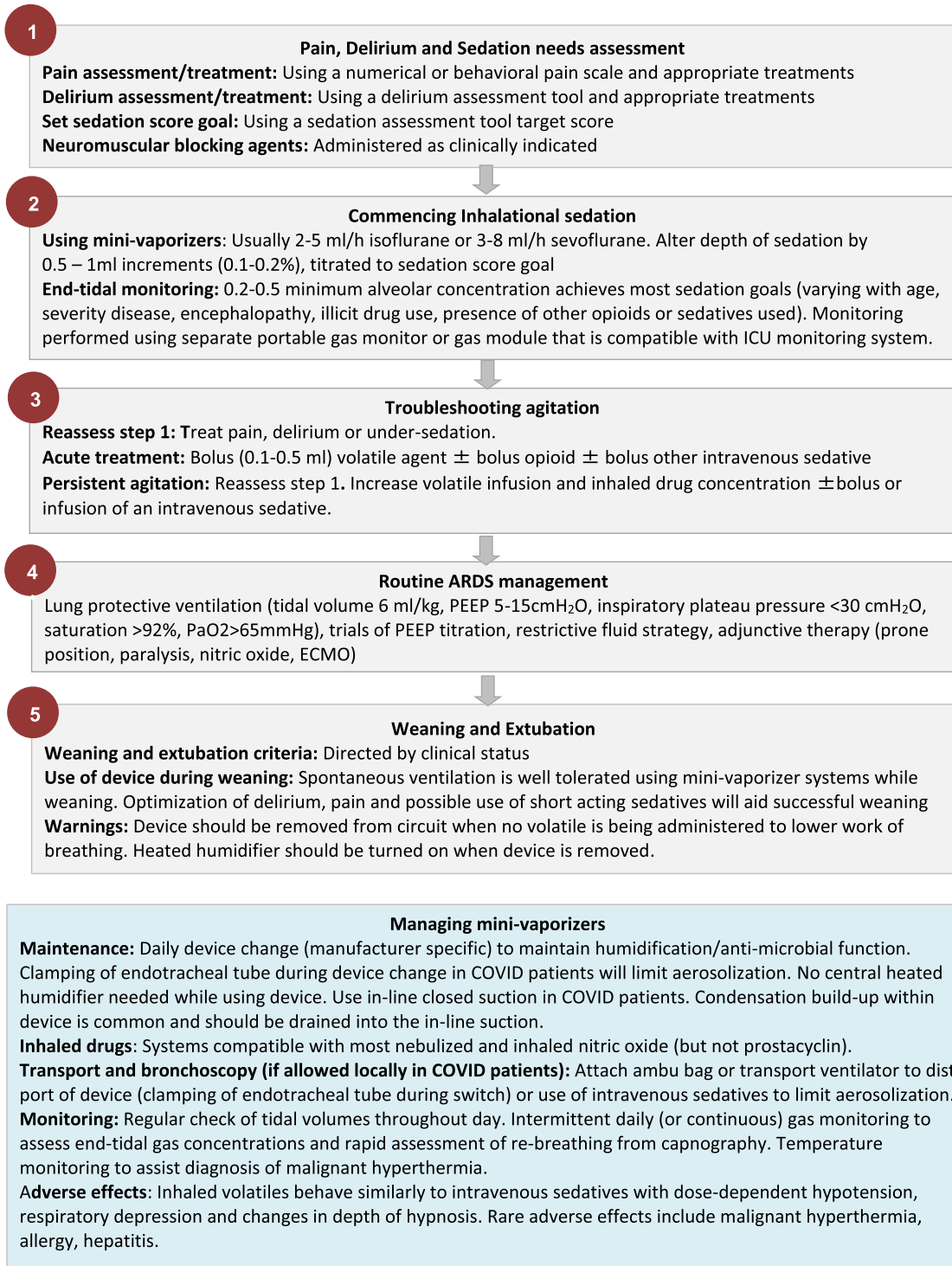


Fig. 1 Algorithm for initiating and commencing inhaled volatile-based sedation regimen for ARDS

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Compliance with ethical standards

Conflict of interest

AJ and NDF have consulted for Sedana Medical, Sweden. NDF has received fees from Getinge and Xenios. AJ and BC have received funds from the Innovation Fund of the Alternative Funding Plan for the Academic Health Sciences Centres of Ontario.

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