Review Article

# The advantages of inhalational sedation using an anesthetic-conserving device versus intravenous sedatives in an intensive care unit setting: A systematic review

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**Abstract:**

**BACKGROUND:** Sedation is fundamental to the management of patients in the intensive care unit (ICU). Its indications in the ICU are vast, including the facilitating of mechanical ventilation, permitting invasive procedures, and managing anxiety and agitation. Inhaled sedation with halogenated agents, such as isoflurane or sevoflurane, is now feasible in ICU patients using dedicated devices/systems. Its use may reduce adverse events and improve ICU outcomes compared to conventional intravenous (IV) sedation in the ICU. This review examined the effectiveness of inhalational sedation using the anesthetic conserving device (ACD) compared to standard IV sedation for adult patients in ICU and highlights the technical aspects of its functioning.

**METHODS:** We searched the PubMed, Cochrane Central Register of Controlled Trials, The Cochrane Library, MEDLINE, Web of Science, and Sage Journals databases using the terms "anesthetic conserving device," "Anaconda," "sedation" and "intensive care unit" in randomized clinical studies that were performed between 2012 and 2022 and compared volatile sedation using an ACD with IV sedation in terms of time to extubation, duration of mechanical ventilation, and lengths of ICU and hospital stay.

**RESULTS:** Nine trials were included. Volatile sedation (sevoflurane or isoflurane) administered through an ACD shortened the awakening time compared to IV sedation (midazolam or propofol).

**CONCLUSION:** Compared to IV sedation, volatile sedation administered through an ACD in the ICU shortened the awakening and extubation times, ICU length of stay, and duration of mechanical ventilation. More clinical trials that assess additional clinical outcomes on a large scale are needed.

**Keywords:**

Anesthetic conserving device, inhalation sedation, intensive care unit, intravenous sedation, length of stay

Sedation is essential to provide comfort and prevent stress, anxiety, agitation, and patient-ventilator asynchrony in the intensive care unit (ICU).[1] The appropriate use of sedatives facilitates patient care and contributes to patient safety in critical care settings.[2] However, heavy sedation using intravenous (IV) benzodiazepine is associated with worse short-and long-term patient outcomes, including prolonged mechanical ventilation and delirium.[3-5]

Most recent guidelines recommend a minimum of sedation protocols in critically ill



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patients.[6,7] Recent evidence supports nonbenzodiazepine strategies with long-term outcomes and benefits.[8]

Theoretically, volatile anesthetic agents have many advantages compared to IV agents. Isoflurane and sevoflurane undergo pulmonary elimination, and have a low level of hepatic metabolism, and a rapid onset and offset of action, which allows for quick sedation onset and awakening.[9] Volatile anesthetics primarily act on the cerebral cortex and leave autonomic functions, such as temperature control, blood pressure regulation, and respiration, relatively undisturbed.[10] Inhalation sedation agents are short-acting drugs that are easily titratable to the targeted level from light-to-deep sedation. Volatile anesthetics are an available option for sedation in ICU settings.[11]

The use of these agents in the ICU increased during the coronavirus disease 2019 pandemic due to a surge in capacity plans and shortages of IV drugs.[12,13] One retrospective study found more ventilator-free days, hospital-free days, and decreased mortality in inhalational sedation using anesthetic-conserving devices (ACD) compared to patients receiving midazolam or propofol.[14]

## Anesthetic-conserving device: The AnaConDa

The ACD AnaConDa (Sedana Medical, Danderyd, Sweden) was marketed for ICU sedation with volatile anesthetic agents in 2005.[15] The AnaConDa is a modified heat moisture exchanger (HME), which is incorporated into the respiratory circuit between the Y-piece and the endotracheal tube instead of the usual HME. It has an internal volume (dead space) of 50 ml and may be used with any standard ICU ventilator. The device contains a miniature porous evaporator rod that converts the volatile anesthetic agent from a liquid to a vapor. The liquid anesthetic agent is continuously infused into the evaporator via an infusion pump that incorporates a syringe system. Activated carbon fibers interwoven with the HME adsorb, store, and release anesthetic vapors.[16]

During inspiration, the anesthetic vapor cloud that forms on the evaporator is picked up by the air–oxygen gas mixture from the ventilator and delivered to the patient. During expiration, 90% of the anesthetic vapor in the expired gas is adsorbed on the carbon layer and recycled to the patient in the next inspiratory cycle. The performance of the AnaConDa reflector is accurate when its capacity is not exceeded. The reflecting capacity of the device is 10 ml of anesthetic vapor contained in one expired breath (e.g., 1 Vol.% in 1000 ml or 2 Vol.% in 500 ml. Therefore, the infusion rates of volatile anesthetic agents must be increased with increases in minute ventilation to keep the end-tidal anesthetic concentrations constant. The resistance to gas flows at 60 L/min is 2.5 cm H2O/L/s, which is comparable to standard HME filters.

Each disposable AnaConDa device comes with a device-specific 50-mL keyed color-coded syringe and a 220-cm anesthetic supply line. The syringe barrel and plunger are made of polypropylene, and the piston is made of rubber. Other conventional plastic syringes and extensions must not be used because volatile anesthetic agents may dissolve these substances, which leads to the generation of potentially toxic products. Isoflurane and sevoflurane are drawn from their container bottles into the 50-ml syringes using special adaptors and then perfused continuously using standard infusion pumps into the evaporator rod, independent of the respiratory cycle. The manufacturer recommends changing the device every 24 h. An important caveat is that bubbles should not be present in the syringe because the liquid anesthetic agents will evaporate into these bubbles, which makes the bubbles grow and results in increased and unwanted high gas concentrations.[17,18]

A total volume of 1.2 ml is required for prefilling the system sample line. The infusion rates are generally started at approximately 5–10 mL/h for sevoflurane and 3–5 ml/h for isoflurane. A sampling port from the AnaConDa device allows the expired gas concentration to be continuously displayed via a side-stream measurement on the gas monitor. Once the monitor detects the anesthetic agent in the expired gas, the infusion rates can be titrated to achieve the desired level of clinical sedation. For sedation, the end-tidal anesthetic gas concentration should be slightly greater than one-third of the minimum alveolar concentration (MAC), i.e., slightly above MAC-awake. Rates of 2–5 ml/h (0.3–0.5 expired Vol.%) and 5–10 ml/h (0.5–1 expired Vol.%) for isoflurane and sevoflurane, respectively, provide acceptable light to moderate sedation.

The AnaConDa device has some limitations. First, not all volatile agents can be used with the device. For example, desflurane cannot be administered in the system due to its low boiling point and high vapor pressure. Second, ambient pollution of volatile anesthetics in the ICU is an additional concern. Although 90% of the anesthetic vapor is adsorbed onto the activated carbon fibers during expiration and recycled back to the patient, 10% of the vapor gas must be scavenged. Scavenging may be performed using an active or passive scavenging system connected to the expiratory outlet of the ventilator to minimize ambient pollution.

The current review summarizes the randomized control studies that compared inhalational sedation to IV sedation in adult ICU patients.

## Methods

### Search strategy

We conducted a systematic search of studies published over 10 years (2012–2022) in electronic databases (the PubMed, Cochrane Central Register of Controlled Trials, the Cochrane Library, MEDLINE, Web of Science, and Sage Journals databases). Two authors carry out the search using the terms "anesthetic conserving device," "AnaConDa," "inhalation sedation," "volatile sedation" and "intensive care unit" as keywords [Table 1]. In addition, the authors scanned the bibliographies of published studies, meta-analysis, and reviews for further possible references.

### Study selection

Two authors independently reviewed and checked the titles and abstracts to identify eligible articles. Study selection was limited to randomized controlled trials (RCTs), while other study designs were excluded. All articles meeting the inclusion criteria were included in the systematic review. Inclusion criteria were all RCTs performed on mechanically ventilated adult patients comparing (inhalation) volatile sedation using an ACD versus IV sedation in the ICU. Subsequently, full-text articles were obtained, and two authors independently assessed each study. Differences were resolved by a third author. The exclusion criteria were inhalation anesthesia not administered via ACD, retrospective studies, and isolated intraoperative use of inhalation anesthesia. The outcome measures for effectiveness were time to extubation, duration of mechanical ventilation, and ICU length of stay (LOS).

## Results

The initial screening of the database, after the removal of duplicate articles, yielded 297 articles. Ultimately, nine randomized control studies were selected based on the assessed criteria and showed the benefit of the use of isoflurane or sevoflurane for ICU sedation using the AnaConDa device [Table 2]. Our random effects model showed that the awakening time was significantly shorter for volatile sedation than for IV sedation. A random effects model in five studies showed that volatile sedation significantly shortened the extubation time compared to IV sedation. Three studies showed that inhalation sedation significantly decreased mechanical ventilation duration. Four studies showed a lower duration of mechanical ventilation with inhalation than IV sedation.

**Table 1: Search strategy**

| Search term |
|---|
| Inhalation sedation/OR volatile sedation |
| Anesthesia conserving device/OR AnaConDa |
| Intensive care unit/critical care |
| Randomized control trials |

The included populations in the studies varied. All patients were mechanically ventilated adult patients in the ICU. Five studies evaluated postoperative cardiac surgery patients admitted to the ICU.[19-23] Two studies included patients with pulmonary disorders and acute respiratory distress syndrome (ARDS),[24,25] while two studies included medical-surgical ICU patients expected to be sedated for <48 h.[26,27]

Jerath *et al*.[19] performed a prospective RCT in a cardiac ICU. Sixty-six patients were randomly assigned to receive inhaled isoflurane, and 74 patients received IV propofol in the intra and postoperative period following coronary artery bypass graft (CABG) surgery. The results showed that patients sedated with inhaled sedatives had faster extubation time than the patients who received propofol (182 vs. 292 min, median). However, the ICU and hospital LOS were not statistically significant. Therefore, inhaled volatile anesthesia and sedation facilitated faster extubation times compared to IV propofol for patients undergoing CABG.[19]

Marcos-Vidal *et al*.[20] performed a prospective study on patients undergoing coronary or coronary and valve cardiac surgery to compare the potential beneficial effects of sedation with sevoflurane versus propofol on markers of myocardial injury (troponin T) and renal function after cardiac surgery using extracorporeal cardiopulmonary bypass. Sixty-two patients sedated with propofol, and 67 patients sedated with sevoflurane were analyzed. Troponin T levels showed differences at 12 and 48 h after admission. Therefore, postoperative sevoflurane in cardiopulmonary bypass is a valid alternative to propofol due to the decreased side effects related to kidney damage. The length of ICU stay was similar in both groups, while the duration of sedation was shorter in the sevoflurane group but did not reach statistical significance (285.82 min compared to 306.13 min).[20]

Guerrero Orriach *et al*.[21] studied the effects of intraoperative administration of halogenated agents on the myocardium in patients undergoing off-pump cardiac surgery. A prospective trial was performed with 60 patients undergoing CABG surgery divided into three groups according to the administration of the combination of hypnotic drugs into the intraoperative and postoperative periods (sevoflurane-sevoflurane, sevoflurane-propofol [SP], propofol-propofol). This study showed that extubation time was 4.5–6.3 h and sevoflurane administration in patients undergoing off-pump CABG in the ICU had reduced myocardial injury markers compared to patients who only received sevoflurane in the intraoperative period; however, the

**Table 2: Summary of the Randomized controlled studies comparing inhalational isoflurane or Sevoflurane inhalational sedation to IV sedation in the ICU**

| Study name (Trial name) | Intervention | Sample size | Objective and study population | Outcome | | | | | | conclusion |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Time to extubation | | Duration of mechanical ventilation | | ICU Length of stay | | |
| | | | | Mean/Median\ (Minutes) (SD/IQR/Range) | *P* | Mean/Median (Minutes) (SD/IQR/Range) | *P* | Mean/Median (SD/ IQR/Range) | *P* | |
| Jerath 2015[19] | Isoflurane or Sevoflurane | R: 67 | To assess the differences in extubation times in a cardiac surgical patient who were anesthetized and sedated using IV or inhaled sedation | 182 (140-255) | <0.001 | NA | | 25.17 hours (22.33-49.83) | 0.34 | Inhaled volatile anesthesia and sedation facilitated faster extubation times compared to IV in cardiac surgery patients |
| | Propofol | C: 74 | | 291 (210-420) | | | | 24.88 hours (20.92-44.83) | | |
| Jabaudon, 2017[24] | Sevoflurane | R: 25 | To evaluate whether sevoflurane improved gas exchange and inflammation in ARDS | NA | | 12.5 days (5.8-17.3) | 0.3 | 18 days (10–37) | 0.9 | Use of inhaled sevoflurane improved oxygenation and decreased levels of a marker of epithelial injury and of some inflammatory markers |
| | Midazolam | C: 25 | | | | 17 days (6-30.0) | | 23 days (9–43) | | |
| Marcos-Vidal, 2014[20] | Sevoflurane | R: 67 | To compare the potential beneficial effects on myocardial injury and renal function between sevoflurane vs. propofol after cardiac surgery | NA | | NA | | 44.1 hours (SD 30.4) | 0.625 | Use of sevoflurane after cardiac surgery is a valid alternative to propofol. It did not increase the number of side effects related to kidney damage, and it reduced troponin T levels. |
| | Propofol | C: 62 | | | | | | 46.8 hours (SD 31.4) | | |
| Orriach, 2013[21] | Sevoflurane | R: 20 | To evaluate the benefits of intraoperative administration of halogenated agents in patients undergoing cardiac surgery | 4.25 hours | | NA | | NA | | Sevoflurane administration in cardiac patients decreased levels of myocardial markers compared to propofol |
| | Propofol | C: 20:20 | | 6.30 hours | | | | | | |
| Soro, 2012[22] | Sevoflurane | R: 36 | To assess cardioprotective effect of sevoflurane in cardiac surgical patients if administration during anesthesia continued until weaning from mechanical ventilation. | NA | | NA | | 71.0 hours 48.0 hours | 0.771 | There were no significant improvements in the extent or time course of myocardial damage biomarkers compared to propofol |
| | Propofol | C: 37 | | | | | | 76.0 hours 69.0 hours | | |
| Steurer, 2012[23] | Sevoflurane | R: 46 | To assess whether volatile anesthetics used for postoperative sedation had any beneficial effects on cardiac surgery patients after on-pump valve replacement. | NA | | NA | | ICU length of stay was 0.005 days less in the Sevoflurane group (CI 0.6-0.6 day) | >0.05 | Late postconditioning with the volatile anesthetic sevoflurane may provide cardiac protection. |
| | Propofol | C: 56 | | NA | | | | | | |
| Hellstrom, 2012[26] | Sevoflurane | R: 49 | Use of intravenous sedation in ICU may contribute to altered consciousness and prolonged mechanical ventilation. | (10-100) | <0.001 | 185.0 minute (1.2-3.8) | 0.056 | 22 hours (SD 5) | | Use of sevoflurane led to shorter wake-up times and quicker cooperation compared to propofol. No differences were seen in ICU stay. |
| | Propofol | C: 50 | | 25 (21-240) | | 215.0 minute (1.8-17.6) | | 22 hours (SD 4) | | |

*Contd...*

**Table 2: Contd...**

| Study name (Trial name) | Intervention | Sample size | Objective and study population | Outcome | | | | | | conclusion |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Time to extubation | | Duration of mechanical ventilation | | ICU Length of stay | | |
| | | | | Mean/Median\ (Minutes) (SD/IQR/Range) | *P* | Mean/Median (Minutes) (SD/IQR/Range) | *P* | Mean/Median (SD/ IQR/Range) | *P* | |
| Turktan, 2019[25] | Sevoflurane Dexmedetomidine | R: 15 C: 15 | Assess intravenous and volatile agents used for sedation ICU patients with pulmonary disorders. | NA | | NA | | NA | | Sevoflurane and dexmedetomidine are suitable sedative agents in ICU patients with pulmonary diseases. |
| A. Meiser 2021[27] | Isoflurane | R: 150 | Examined whether sedation with isoflurane was inferior to sedation with propofol in adult ICU patients who are expected to need at least 24 h of sedation. | 30 min (10-136) | 0.0011 | 30-day ventilator-free days was 24 days (2-27) | 0.751 | 30-day ICU free days was 17 (0-24) | 0.344 | The outcome supports the use of isoflurane in invasively ventilated patients who have a clinical need for <48 hours of sedation. |
| | Propofol | C: 151 | | 40 min (18-125) | | 30-day ventilator-free days was 26 days (2-27) | | 30-day ICU free days was 14 (0-24) | | |

ARDS; Acute Respiratory Distress Syndrome, IV=Intravenous, SD=Standard deviation, IQR=Interquartile range, NA=Not available, ICU=Intensive care unit, CI=Confidence interval, R=Inhalation group, C=Intravenous sedation group

study was not powered to study major clinical outcome. Therefore, the clinical data were not included in the Table 2.[21]

A double-blind, randomized study by Soro *et al*.[22] compared the cardioprotective effects of SP during anesthesia and the postoperative period in CABG. Seventy-five adult patients were randomly assigned to receive anesthesia and postoperative sedation with propofol ($n$ = 37) or sevoflurane ($n$ = 36). Necrosis biomarkers increased significantly in the postoperative period in both groups with no significant differences at any time. Inotropic support was needed in 72.7% and 54.3% of patients in the propofol and sevoflurane groups, respectively. Therefore, continuous administration of sevoflurane did not improve the extent or time course of myocardial damage biomarkers compared to propofol in patients undergoing bypass graft surgery.[22]

Steurer *et al*.[23] performed a RCT to investigate whether volatile anesthetics used for postoperative sedation provided beneficial effects on myocardial injury in cardiac surgery patients after on-pump valve replacement. Anesthesia was performed with propofol after arrival in the ICU, and 117 patients were randomized for at least 4 h of sedation with propofol or sevoflurane. Fifty-six patients were analyzed in the propofol arm, and 46 patients were analyzed in the sevoflurane arm. The results indicated that late postconditioning with sevoflurane may provide cardiac protection; however, secondary outcomes, including pulmonary complication postoperatively, ICU and hospital LOS did not significantly differ. Time to extubate from sedation stop and the duration of mechanical ventilation were not the primary outcomes.[23]

Jabaudon *et al*.[24] performed a randomized controlled study at three ICU in a French university hospital. This study included 50 patients with ARDS and evaluated whether sevoflurane improved gas exchange and inflammation in ARDS if administered within 24 h of ARDS onset for 48 h compared with midazolam infusion. The results indicated that the use of inhaled sevoflurane improved oxygenation and decreased the levels of a marker of epithelial injury and some inflammatory markers in patients with ARDS compared to midazolam. The weaning and extubation times were not assessed as primary outcomes; however, there was a reduction in mechanical ventilation duration and ICU LOS in the sevoflurane group compared to the midazolam group but did not reach statistical significance due to the small sample size [Table 2].[24]

Türktan *et al*.[25] performed a randomized study that investigated the effect of sevoflurane and dexmedetomidine on pulmonary mechanics in ICU patients with the pulmonary disorder who needed

short-time sedation. Thirty patients had pulmonary disorders, including chronic obstructive pulmonary disease, pneumonia, pulmonary contusions, and pneumothorax, between the ages of 18 and 65 years. Sevoflurane and dexmedetomidine were suitable sedative agents in ICU patients with pulmonary diseases. The $CO_2$ levels were higher in the sevoflurane group (50.10 ± 13.30 mmHg Compared to 37.93 ± 7.66 mmHg, $P = 0.004$), while the effect on lung mechanics was comparable between the two groups. The results indicate inhalation anesthesia through ACD should be used in caution with patients with underlying lung disease who might not tolerate hypercapnia. The clinical outcome was not analyzed due to the small sample of the included patients.[25]

Hellström *et al*.[26] examined whether IV sedation in the ICU contributed to a short wake-up time, altered consciousness, and prolonged mechanical ventilation. Patients in this study underwent coronary artery bypass surgery with cardiopulmonary bypass. One hundred patients were randomized to sedation with sevoflurane via an ACD or propofol postoperatively in the ICU. Patients who received sevoflurane sedation after cardiac surgery had shorter wake-up times and quicker cooperation compared to propofol. No differences were observed in ICU stay, adverse memories, or recovery events in the short-term sedation group.[26]

In a recent phase-3 multicenter RCT, Meiser *et al*.[27] compared sedation with isoflurane with propofol in 24 ICUs in Germany and Slovenia. This randomized, controlled, open-label noninferiority trial evaluated the efficacy and safety for 48 h (range 42–54 h) of isoflurane compared with propofol in adults (aged ≥18 years) who were invasively ventilated. Of the studied population, 40% were admitted to the ICU for medical indication compared to 56% for surgical admission. In addition, 65% were admitted through the emergency room. The outcome difference between the two treatment groups in sedation levels reached, median extubation time at sedation stop was not statistically significant, indicating that isoflurane was noninferior to propofol sedation, in invasively ventilated patients with a clinical need for sedation. The median for significant secondary outcomes, such as vasopressor uses, delirium-free days, ICU-free days, and 30-day mortality, were comparable in both groups.[27]

## Discussion and Future Prospective

Inhaled sedation with halogenated agents is now feasible in ICU patients using dedicated equipment and staffing systems. These agents have ideal pharmacological properties that allow an efficient, well-tolerated depth of sedation. These agents also provide clinical benefits that are especially relevant in ICU patients. We limited our review to studies that utilized ACD for the administration of inhalational sedation and excluded traditional applicators, for example, through masks, to avoid the effect of variability in the effective delivery of the medication along with the safety evaluation might be caused by leakage or inaccurate delivered dosage as a result. Our review summarized the current best available evidence supporting inhaled sedation delivered via ACD as a viable alternative to IV sedation.

On January 27, 2022, the National Institute of Health and Care Excellence (NICE) issued medical technology guidance recommending Sedaconda ACD for enabling the delivery of inhaled sedation in adults in an intensive care setting as an alternative to IV sedation.[18] This guideline is the first time that NICE has recommended the use of a device for inhaled sedation in the ICU in England. A technical review of AnaConDa uses by Farrell *et al*.[28] found that when the device had an HME filter combined into one airway component, the device reflected moisture back to the patient but also reflected 90% of the anesthetic by adsorbing and releasing the drug using a proprietary carbon filament reflecting medium. This reflection reduced the total amount of anesthetic needed and the amount exhausted or scavenged upon exhalation. The device may be used for 24 h of sedation and fits most current critical care ventilator circuits without modifications. This result supports the potential use of this technique in the ICU.[28] Bomberg *et al*.[29] performed a comparative study in which a test lung constantly insufflated with $CO_2$ was ventilated with a tidal volume of 500 ml at 10 breaths/min. End-tidal $CO_2$ partial pressure was measured using 3 different devices, a heat-and-moisture exchanger (HME, 35 ml), ACD-100, and ACD-50 under. The study concluded that isoflurane reflection remained sufficient with ACD-50 at clinical anesthetic concentrations, and $CO_2$ elimination was improved. The ACD-50 should be practical for tidal volumes as low as 200 mL and allow lung-protective ventilation even in small patients.[29]

This systematic review demonstrated the reduction in time to extubation and mechanical ventilation duration despite the heterogeneity of the population of RCTs included in the study. These findings are consistent with earlier published systematic reviews.[30]

No clear relationship was found with statistically significant ICU LOS in the individual studies. In surgical patients, especially following cardiovascular surgeries, it is the norm to have a short duration of ICU stay; therefore, this factor has a significant effect on the outcome. However, there is a trend toward shorter stays with inhalation sedation which might be more evident in future studies of mechanically ventilated medical

patients. Important literature supports the overall safety of administering inhaled sedation to ICU patients without the risk of tolerance, withdrawal, or major adverse effects. Some limitations exist in the included studies in this review. First, the duration of application of the ACD was <96 h limiting the generalization of the safety of its use beyond this duration. Second, blinding to the study sedation was limited in many studies due to the nature of the ACD and the difficulty of hiding the connection and adjustment by the treating teams. In addition, we could not report long-term outcomes as mortality as it was inconsistently reported in the included studies. However, multiple areas of uncertainty persist, and large-scale studies are necessary to further confirm the efficacy and safety of these agents. Some considerations could be perceived as limitations to the use of inhalational anesthesia, such as the healthcare-related cost of inhaled sedation compared to IV sedation, while few old studies reported the cost of inhalation anesthesia utilization in the ICU,[31,32] there is no recent literature that evaluates the direct and indirect cost-benefit evaluation of inhalation anesthesia including ACD monitoring, change, and application to the financial impact of the beneficial outcomes including the reduction of LOS. Environmental pollution and risk to ICU staff are also major issues when performing inhaled sedation in the ICU, and all should be the focus of future research, which must be answered via large-scale future studies.

## Conclusion

Using halogenated agents for inhaled sedation is gaining popularity in the ICU. Due to technological advancements in volatile vaporizers, the current best available evidence suggests that inhalational sedation agents shorten extubation time, ventilator days, and ICU stay. However, because the included studies were small with high heterogeneity, additional large, high-quality prospective clinical trials are needed to validate these findings.

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### Conflicts of interest

There are no conflicts of interest.

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