Managing sedation in the mechanically ventilated emergency department patient: a clinical review

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Abstract
Managing sedation in the ventilated emergency department (ED) patient is increasingly important as critical care unit admissions from EDs increase and hospital crowding results in intubated patients boarding for longer periods. The objectives of this review are 3-fold; (1) describe the historical perspective of how sedation of the ventilated patient has changed, (2) summarize the most commonly used sedation and analgesic agents, and (3) provide a practical approach to sedation and analgesia in mechanically ventilated ED patients. We searched PubMed using keywords “emergency department post-intubation sedation,” “emergency department critical care length of stay,” and “sedation in mechanically ventilated patient.” The search results were limited to English language and reviewed for relevance to the subject of interest. Our search resulted in 723 articles that met the criteria for managing sedation in the ventilated ED patient, of which 19 articles were selected and reviewed. Our review of the literature found that the level of sedation and practices of sedation and analgesia in the ED environment have downstream consequences on patient care including overall patient centered outcomes even after the patient has left the ED. It is reasonable to begin with analgesia in isolation, although sedating medications should be used when patients remain uncomfortable and agitated after initial interventions are performed.

KEYWORDS
emergency, mechanical ventilation, sedation

1 | BACKGROUND

Emergency medicine clinicians are experts at airway management and should also consider themselves proficient in post-intubation sedation and analgesia. Approximately 240,000 patients require mechanical ventilation annually in United States emergency departments, and this figure is expected to continue to increase. Annual critical care unit admission from EDs in the US increased by 79% from 2001 to 2009. Increased ICU admission rates in combination with ED and hospital crowding means that the most critical patients are spending more time in the ED. Within the last 20 years, the median ED length of stay (LOS) for patients admitted to critical care units increased by at least 60 min, and approximately one-third of all critical care ED visits had an ED LOS >6 hours. Critically ill patients boarding for >6 hours in the ED have higher rates of inpatient mortality, possibly due to lack of continued resuscitative efforts and dedicated multidisciplinary care. In addition...
Existing evidence

A structured literature search and review of articles relevant to sedation in mechanically ventilated patients in EDs was performed. The PubMed database was electronically searched using keywords “emergency department post-intubation sedation,” “emergency department critical care length of stay,” and “sedation in mechanically ventilated patients.” The results were limited to English language articles and reviewed for relevance to the topic. Clinically relevant selections were reviewed by an author which led to additional selections identified in the references of those manuscripts. Our search found a total of 723 citations, including duplicates, when the multiple key words were searched. After duplicates were excluded and titles reviewed for relevance, 147 original publications met the criteria for managing sedation in ventilated ED patients. After excluding non-peer reviewed articles, case reports, case series, and opinion pieces, and including papers identified by detailed inspection of references, a total of 19 articles were selected and reviewed. The overall important takeaways from this review are presented in Table 1. The key characteristics about each study and summary of their findings are presented in Table 2.

Interruptions in sedation

The practice of sedation in mechanically ventilated patients has transformed considerably over the past 20 years, most notably with intermittent interruptions of sedation and targeting specific levels of sedation. Previously, it was standard to provide continuous infusions of analgesia and sedation throughout the duration of mechanical ventilation. Changes began with the noted benefits of decreased days on mechanical ventilation and decreases in overall LOS with the use of daily sedation breaks, also known as “sedation holidays.”

Although deep sedation may be necessary in certain situations such as status epilepticus or traumatic brain injury, the development of such intermittent interruptions in sedation have led to an increase in knowledge surrounding sedation strategies and the effects it has on patient outcomes. Light sedation in ventilated patients, when compared with deep sedation levels, allows patients to remember important moments more often, experience fewer adverse dreams after their illness, and trends toward less post-traumatic stress disorder. This means that as emergency clinicians, one must analyze sedation practices and consider downstream consequences of our choice of post-intubation sedation. This is even more likely to have an impact when considering prolonged patient boarding due to hospital crowding.

Measures of sedation

A pivotal shift in understanding how to measure sedation involved the development of a reliable and valid measure of sedation such as the Richmond Agitation-Sedation Scale (RASS). The RASS score is a validated measure ranging from −5 (unarousable) to +4 (combative), with a score of 0 corresponding to alert and calm (Table 3). Although it is vital for providers to minimize stress, anxiety, and pain in ventilated patients, sedation is not without patient risk. Both forms of suboptimal sedation (under and over) have been described and should be avoided. However, over sedation is common and may occur as often as 40% to 60% in ventilated patients. Early deep sedation, most often defined as RASS −3 to −5, has been associated with increased delirium, prolonged ventilator days, ICU stays, hospital LOS, renal replacement therapy, and tracheostomy occurrence. Although likely dependent on sedation throughout an entire patient’s course through an ICU stay, lighter sedation in the first 48 hours of ventilation is associated with decreases in mortality, ICU LOS, and total days requiring ventilation. This is not an isolated ICU issue, and sedation practices initiated in the ED often carry over into ICU care. Deep sedation in the ED setting alone has been shown to increase delirium rates. A deeper ED RASS score has also been associated with increased patient mortality. Up to 70% of ventilated patients arrive at the ICU in a state of deep sedation, and approximately 75% and 69% of patients who arrive at the ICU deeply sedated remain so on days 1 and 2, respectively.
| Author                  | Study type               | Patient population                                                                 | Intervention                                                                                                                                                                                                 | Result                                                                                                                                                                                                 |
|-------------------------|--------------------------|-------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Easter et al. (2011)    | Retrospective review     | 3.6 million ED visits from 1993–2007                                                | Reviewed the epidemiology of mechanical ventilation in United States EDs                                                                                                                                         | Patients undergoing mechanical ventilation have high in-hospital mortality rates; LOS is sufficient for evidence based ventilator interventions                                                                |
| Herring et al. (2013)   | Retrospective analysis   | ED patients admitted to critical care units found in the National Hospital Ambulatory Medical Care Survey between 2001 and 2009 | Analyzed publical available data                                                                                                                                                                            | Annual critical care unit admission from United States EDs increased from 1.2 to 2.2 million; ED LOS increased from 185 to 245 min for critical patients                                                          |
| Mathews et al. (2018)   | Retrospective cohort     | 854 ED patients for whom the ICU was consulted for admission in a single tertiary care hospital | Analysis of ICU admission delays                                                                                                                                                                             | Prolonged ED boarding times are associated with worse patient outcomes                                                                                                                                  |
| Kress et al. (2000)     | Randomized, controlled trial | 128 patients receiving mechanical ventilation and continuous infusions of sedative drugs in medical ICU | Sedative infusions were interrupted until patients were awake on a daily basis                                                                                                                                 | The median duration of mechanical ventilation and ICU LOS were improved in the intervention group                                                                                                      |
| Treggiari et al. (2009) | Randomized control trial | 129 adult ICU patients requiring intubation and expected to receive mechanical ventilation for at least 12 h | Patients were randomized to receive either light or deep sedation                                                                                                                                               | Light sedation reduces ICU stay and duration of ventilation without negatively affecting patient mental health or safety                                                                             |
| Ely et al. (2014)       | Prospective cohort       | 38 medical ICU patients for reliability testing and 275 patients receiving mechanical ventilation for validity testing | Analysis of interrater reliability                                                                                                                                                                           | RASS demonstrates excellent interrater reliability and criterion, construct, and face validity                                                                                                          |
| Sessler et al. (2002)   | Validation study         | 192 ICU patient encounters                                                           | Evaluated interrater reliability after implementation of RASS into a medical ICU                                                                                                                             | Demonstrated RASS to have good interrater reliability and validity                                                                                                                                      |
| Jackson et al. (2009)   | Systematic review        | Multiple reliable databases were searched for studies using the terms ICU, sedation, sedation quality management, and suboptimal sedation | Literature review involving over sedation among ICU patients and sedation scoring systems used for determining sedation quality management                                                                         | Available data suggest a high incidence of oversedation in ICUs, potentially present at 40% to 60% of assessments                                                                                       |
| Tanaka et al. (2014)    | Secondary analysis of prospective cohort study | 322 patients in 45 Brazilian ICUs that required ventilator support and sedation in the first 48 h of ICU admission | Sedation depth was evaluated after 48 h of mechanical ventilation; multivariate analysis was used to identify variables associated with hospital mortality | Early deep sedation is associated with adverse outcomes and constitutes an independent predictor of hospital mortality in mechanically ventilated patients |
| Balzer et al. (2015)    | Retrospective analysis   | 1884 patients admitted to one of four ICUs in a tertiary university hospital between 2007 and 2012 | Analyzed the impact of early deep sedation within the first 48 h of admission on in-hospital and 2-y follow-up survival                                                                                       | Early deep sedation during the first 48 ho of intensive care treatment was associated with decreased in-hospital and 2-y follow-up survival                                                           |
| Stephens et al. (2018)  | Systematic review and meta-analysis | Nine studies (n = 4521 patients) published between 2012 and 2017 were included       | Defines and quantifies the impact of deep sedation within 48 h of initiation of mechanical ventilation, as described in the world’s literature                                                                 | Deep sedation in mechanically ventilated patients was associated with increased mortality and LOS                                                                                                         |
| Fuller et al. (2018)    | Prospective cohort       | 324 mechanically ventilated adult ED patients from EDs and ICUs of 25 medical centers | All data involving sedation were recorded                                                                                                                                                                     | Early deep sedation in the ED is common, carries over into the ICU, and may be associated with worse outcomes                                                                                           |
**TABLE 2 (Continued)**

| Author             | Study type                              | Patient population                                                                 | Intervention                                                                                      | Result                                                                                             |
|--------------------|-----------------------------------------|-------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------|
| Stephens et al.    | Cohort Study                            | 1414 ED mechanically ventilated adult patients from a single academic medical center | Analyzed a prospectively compiled ED registry to describe ED sedation practices                   | Early deep sedation is common in mechanically ventilated ED patients and is associated with worse mortality |
| Lembersky et al.   | Retrospective analysis                   | 11,748 patients’ records collected from the NEAR database from 25 EDs from January 2016 to December 2017 | Analyzed the frequency of receiving post-intubation sedation and associated factors               | Post-intubation sedation rates are higher than previously reported and multiple factors are associated with higher odds of receiving post-intubation sedation |
| Dale et al. (2013) | Retrospective cohort                    | 19,561 mechanically ventilated cardiac surgery patients from all Washington state non-federally funded hospitals | Assess the relationship between a hospital’s pain, agitation and delirium order set quality and the average duration of mechanical ventilation of its cardiac surgery patients | Cardiac surgery hospitals with more guideline-adherent analgesia, sedation, and delirium order sets have patients with shorter mean durations of mechanical ventilation than hospitals with lower order set quality scores |
| Faust et al. (2016)| Retrospective study                     | 79 patients were included in the post-implementation group and 65 in the pre-implementation group in a 24-bed medical ICU | Analyzed the duration of mechanical ventilation before and after implementation of an analgesedation protocol | Implementation of an analgesedation protocol was associated with lighter level of sedation, shorter mean ventilator duration, and a reduced use of continuous infusion sedatives |
| Devlin et al.      | Clinical practice guideline development; expert panel review | Adult patients in the ICU                                                             | Content experts, methodologists, and ICU survivors were represented in each of the five sections of the guidelines; each section created questions and recommendations based on perceived clinical relevance; the guideline group then voted their ranking, and patients prioritized their importance | Substantial agreement among a large, interdisciplinary cohort of international experts regarding evidence supporting recommendations, and the remaining literature gaps in the assessment, prevention, and treatment of pain, agitation/sedation, delirium, immobility, and sleep in critically ill adults |
| Shehabi et al.     | Prospective longitudinal cohort          | Critically ill patients expected to be ventilated for longer than 24 h                 | RASS and pain were assessed every 4 h; delirium and mobilization were assessed daily using the Confusion Assessment Method of ICU and a standardized mobility assessment, respectively | Sedation intensity independently predicted increased risk of death, delirium, and delayed time to extubation |
| Harlow et al.      | Randomized trial                         | 140 critically ill adult patients who were undergoing mechanical ventilation and were expected to need ventilation for >24 h | Patients were randomly assigned to receive sedation with daily interruptions until awake or no sedation | No sedation of critically ill patients receiving mechanical ventilation is associated with an increase in days without ventilation |

ED, emergency department; LOS, length of stay; RASS, Richmond Agitation-Sedation Scale

**1.4 Medications used**

Emergency clinicians are comfortable with a wide variety of medications when providing sedation and analgesia in the ED. The most frequently used medications for ventilated patients in the ED are fentanyl, midazolam, and propofol; with less use of ketamine, dexmedetomidine, and morphine. Sedation levels across all agents are variable; rates of ventilated patients with no analgesia in the ED ranges from 14.3% to 28.4% and rates of no sedation range from 15.2% to 21.3%. Pre-and post-intubation hypotension is associated with lower odds of post-intubation sedation. Patients intubated for medical indications when compared with traumatic, and patients who receive succinylcholine rather than rocuronium have higher rates of post-intubation sedation.
### TABLE 3  Richmond Agitation-Sedation Scale

| Score | Term | Description |
|-------|------|-------------|
| +4    | Combative | Overtly combative or violent; immediate danger to self |
| +3    | Very agitated | Pulls or removes tube(s) or catheter(s) or has aggressive behavior toward staff |
| +2    | Agitated | Frequent nonpurposeful movement or patient-ventilatory dyssynchrony |
| +1    | Restless | Anxious or apprehensive but movements not aggressive or vigorous |
| 0     | Awake and alert | |
| −1    | Drowsy | Not fully alert, but has sustained (>10 s) awakening with eye contact to voice |
| −2    | Light sedation | Briefly (<10 s) awakens with eye contact to voice |
| −3    | Moderate sedation | Any movement (but no eye contact) to voice |
| −4    | Deep sedation | No response to voice, but any movement to physical stimulation |
| −5    | Unarousable | No response to voice or physical stimulation |

Summarized from Sessler et al.9

administration in the ED.17 Table 4 provides a summary of the common analgesic and sedative medications used in intubated and mechanically ventilated ED patients.

### 1.5 Recommended sedation pathway

Providing appropriate sedation and pain control for ventilated patients in EDs will require intentional changes in daily practice. It is common for inadequate sedation and pain control as well as inappropriately deep sedation to take place in the ED, and both have downstream consequences for sedation practices in the ICU and on patient-centered outcomes such as mortality, ICU days, and ventilator days.9–11 We recommend EDs provide a standardized multidisciplinary framework for all ventilated patients to receive appropriate medication status post-mechanical ventilation initiation. This is best achieved through protocols such as the one outlined in Figure 1, as well as order sets via electronic records, and may be best driven by nursing professionals.18,19 High-quality order sets are associated with decreased ICU days for ventilated patients.19 It is also likely that nursing protocolized targeted sedation will achieve a lighter level of sedation.20 For consistent sedation levels from patient to patient and despite changing providers, monitoring of sedation must be reliable. The RASS has interrater reliability and is superior to Glasgow Coma Scale when measuring sedation levels in ventilated patients.8 Levels of light sedation have not been clearly defined in literature, although levels of −3 to −5 are generally considered deep sedation. Initially it was believed that a RASS goal of −2 was ideal, although it is likely that this is deeper than required, and goal of zero may be more appropriate.20,21

It is necessary to begin analgesic treatment as soon as mechanical ventilation is begun, particularly when long-acting paralytics are used for intubation, because patients may be unable to exhibit signs of discomfort. It is reasonable to consider analgesia alone in ventilated patients. Over three-quarters (77%) of patients report moderate to severe pain during their ICU stays, meaning it is critical to provide them relief as soon as possible.21 It is also likely that early treatment of pain will help patients to achieve a level of light sedation before the use of chemical sedatives.21 Sedation strategies that have focused on analgesia alone, with efforts to minimize continuous sedating medications, have resulted in shorter ICU and total hospital duration times.22 Such treatment strategies are also associated with lighter overall levels of sedation and fewer patients found to suffer from deep sedation when defined as RASS −3 to −5.21

### TABLE 4  Common analgesic and sedative medications used in intubated and mechanically ventilated ED patients

| Agent       | Bolus dosing | Infusion dosing | Benefits/advantages                  | Adverse effects                                      |
|-------------|--------------|-----------------|--------------------------------------|------------------------------------------------------|
| Analgesics  |              |                 |                                      |                                                      |
| Fentanyl    | 0.5–1.0 µg/kg q30 min | 1.0–2.0 µg/kg/h | Less hypotension quick onset          | Respiratory depression                                |
| Morphine    | 2–4 mg q 1–2 h | 2–30 mg/h       | Widely available                      | Histamine release hypotension accumulation in renal/hepatic impairment |
| Hydromorphone| 0.2–0.6 mg q 1–2 h | 0.5–3.0 mg/h | Widely available                      | Accumulation in renal/hepatic impairment              |
| Analgesics/sedative |         |                 |                                      |                                                      |
| Ketamine    | 0.1–0.5 mg/kg | 0.05–0.4 mg/kg/h | Less hypotension attenuates tolerance to opiates | Hallucinations psychological disturbances tachycardia/hypertension |
| Sedatives   |              |                 |                                      |                                                      |
| Propofol    | 5 µg/kg/min   | 5–50 µg/kg/min  | Quick on/quick off                    | Hypotension propofol infusion syndrome pain at injection site |
| Midazolam   | 0.01–0.05 mg/kg | 0.02–0.1 mg/kg/h | Quick on/quick off                    | Respiratory depression                                |
| Dexmedetomidine | 1 µg/kg over 10 min | 0.2–0.7 µg/kg/h | Generally, less respiratory depression | Bradycardia hypotension                              |

Dosing ranges summarized from Barr et al. (2013).25
When it is necessary to provide sedating medications it is essential that the patient be assessed frequently via a valid and reliable scale such as the RASS. A desirable goal is to maintain a RASS score of 0. When given the choice, it is preferred that non-benzodiazepine medications such as propofol and dexmedetomidine be used for sedation in ventilated patients because they may decrease ICU LOS, duration of ventilation, and occurrence of delirium. When compared with benzodiazepine infusions, propofol use has provided shorter times to light sedation as well as shorter times to extubation. When dexmedetomidine is compared with benzodiazepines, there is not a large benefit, although dexmedetomidine is still preferred because of known side effects of benzodiazepines. Dexmedetomidine may be associated with decreased rate of delirium at 48 hours when compared to propofol; however, there is likely no difference in time to patient extubation. We provide no significant recommendations when choosing between these two medications. It should be noted, however, that dexmedetomidine should not be used when deep sedation is required, and propofol should be used cautiously in hypotensive patients. Last, although the use of long-acting paralytics in sedated and mechanically ventilated patients have specific indications such as ventilator desynchrony, in general, we would recommend against use of neuromuscular-blocking agents like vecuronium in the ED because of the challenges in monitoring levels of sedation in such settings.
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