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REVIEW ARTICLE

Airway

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.[1] Annual critical care unit admission from EDs in the US increased by 79% from 2001 to 2009.[2] 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.[2] 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.[3] In addition

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TABLE 1 Key Clinical Review Findings

Using standardized measures of sedation such as RASS leads to more reliable and consistent sedation practices
EDs are increasingly caring for ventilated patients as well as initiating analgesia and sedation
Early deep sedation has been consistently shown to lead to poorer long-term outcomes
Evidence is building that sedation practices in the ED have downstream consequences for sedation in the ICU setting as well as patient-oriented outcomes throughout the hospital length of stay

to, and likely of equal importance to increased ICU boarding, growing evidence suggests that critical care protocols initiated in the ED have downstream consequences in patient-centered outcomes.[4,5] Although efforts to decrease the rates of ED and hospital crowding are being explored, it is vital that emergency clinicians continue to improve the quality of care provided to critically ill patients in the ED. One area of improvement is the management of sedation of ventilated patients in the ED. The objectives of this review are 3-fold: (1) describe the historical perspective of how sedation of the ventilated ED 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.

1.1 | 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 the ventilated ED patient. 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.

1.2 | 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."[6] Although sedation holidays are not usually needed in the ED setting, 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.[7] 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.

1.3 | 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).[8] 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).[9] 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,[10–12] However, over sedation is common and may occur as often as 40% to 60% in ventilated patients.[10] 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.[13,14] 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.[5] 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.[4] A deeper ED RASS score has also been associated with increased patient mortality.[15] 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.[4] Although deep sedation may be necessary in certain situations such as status epilepticus or traumatic brain injury,[16] this is not the case in all situations requiring mechanical ventilation.

TABLE 2 Studies investigating sedation practices in the ICU and ED

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

(Continues)

TABLE 2 (Continued)

Author	Study type	Patient population	Intervention	Result
Stephens et al. (2017)	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. (2019)	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 analgosedation protocol	Implementation of an analgosedation protocol was associated with lighter level of sedation, shorter mean ventilator duration, and a reduced use of continuous infusion sedatives
Devlin et al. (2018)	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. (2018)	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. (2011)	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 frequented medications for ventilated patients in the ED are fentanyl, midazolam, and propofol;with less use of ketamine, dexmedetomidine, and morphine.[4,15] This is consistent with medication choices in the ICU.[5,13,15] 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%.[4,15] 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 hypotension
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]

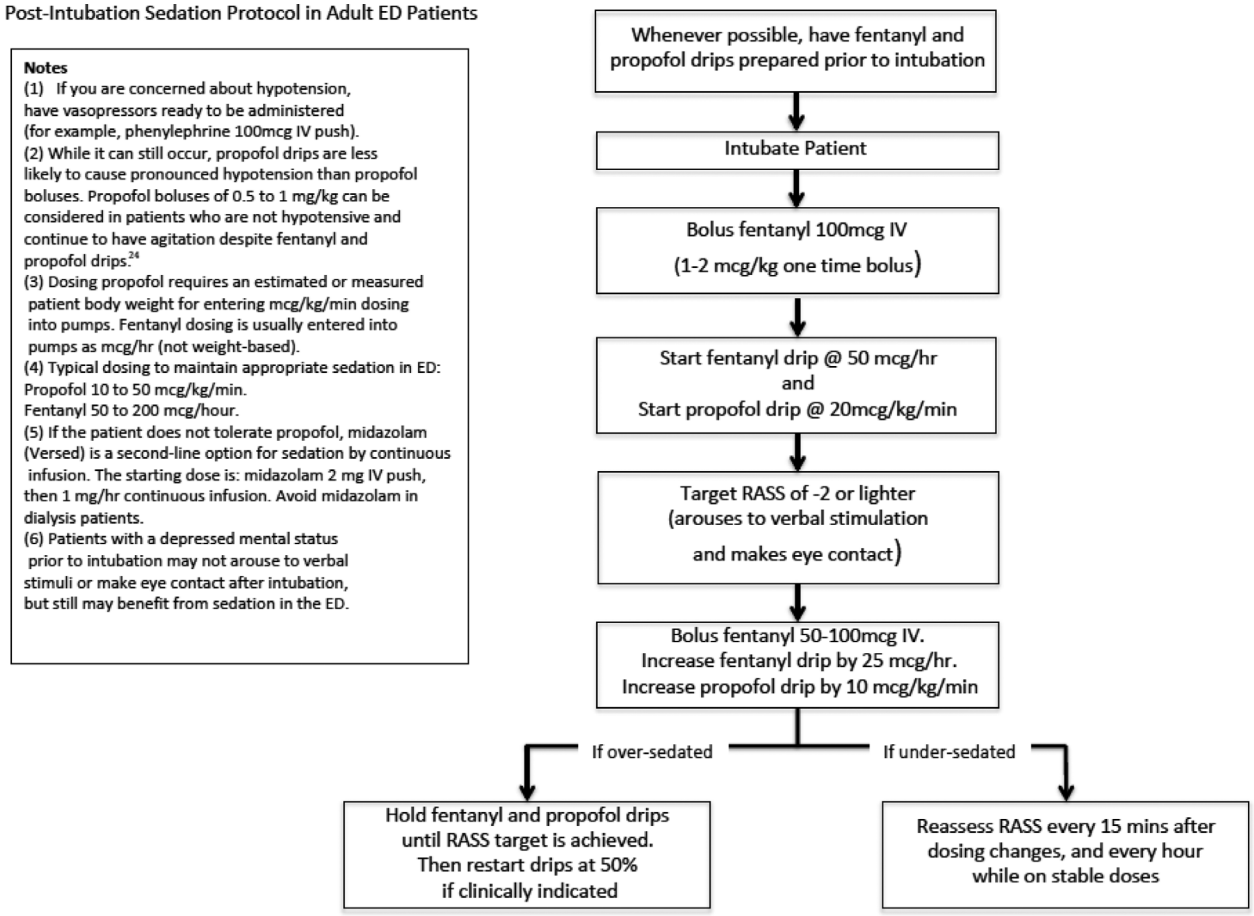

FIGURE 1 Example of post-intubation sedation path

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.[8] A desirable goal is to maintain a RASS score of 0.[21] 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.[20] When compared with benzodiazepine infusions, propofol use has provided shorter times to light sedation as well as shorter times to extubation.[20] 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,[20] and propofol should be used cautiously in hypotensive patients.[23] 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.[24]

2 | CONCLUSIONS

Post-intubation sedation and analgesia of mechanically ventilated patients in the ED is increasingly becoming a core skill of emergency medicine. Current literature continues to suggest 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. Care should be taken to ensure that sedation levels are appropriate, and this should be protocolized using reliable means of patient evaluation and medication titration. 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.

CONFLICT OF INTEREST

CLF and CSE have nothing to disclose. TWB is the Site Investigator for Portola Pharmaceuticals and is a Paid Consultant for Red Bull GmbH.

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