Management of Sedation and Paralysis

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KEYWORDS

• Mechanical ventilation • Sedation • Paralysis • Patient ventilator dyssynchrony (PVD)

KEY POINTS

- Minimizing sedation in mechanically ventilated patients, which can be facilitated by using validated scales and or protocols, has been linked with improved intensive care outcomes.
- Benzodiazapines are associated with adverse effects when used as a sedative in mechanically ventilated patients and the routine use should be abandoned in most cases.
- Patient–ventilator dyssynchrony (PVD) is a common, but harmful, occurrence in sedated patients and can be decreased with increasing doses of opioids and/or propofol.
- Muscle relaxants have a survival benefit in acute respiratory distress syndrome and can also play a role in managing PVD in the mechanically ventilated patient.

Endotracheal intubation and mechanical ventilation can lead to significant patient anxiety and agitation, which are associated with adverse outcomes.[1–3] These symptoms were prevented previously with the routine use of sedatives in most mechanical ventilated patients, whereas paralysis was limited to patients with severe hypoxemic respiratory failure or significant patient–ventilator dyssynchrony (PVD). However, based on more recent evidence suggesting improvement in patient outcomes with lighter degrees of sedation, the use of sedative drugs has assumed a more limited and specific role in the mechanically ventilated patient.[2,4–6] This review discusses the goals of sedation and paralysis in the mechanically ventilated patient, the evidence behind these goals, as well the pharmacologic characteristics impacting the selection of frequently used agents.

Although it is now recommended that sedation and paralysis should be used as sparingly as possible based on recent clinical trials,[4,5,7–9] in selected patients sedatives and paralytics can be invaluable in ensuring synchronous patient–ventilator interactions, especially in patients with cases of severe acute respiratory distress syndrome (ARDS).[10–16] This review discusses the advantages and disadvantages of the various sedative and paralytics drugs and provides an outline of when and how these medications should be administered.

PRINCIPLES OF SEDATION AND ANALGESIA

Sedatives and analgesics are administered to mechanically ventilated patients to decrease discomfort associated with endotracheal intubation, protect against self-injury, minimize pain during procedures and care in the intensive care unit (ICU), decrease inadvertent removal of supportive lines or tubes, or to improve patient–ventilator interactions. To achieve these objectives, analgesics and sedatives are administered either individually or in combinations and titrated to targets based on patient assessment or according

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to a protocol that has been shown to reduce duration of mechanical ventilation and ICU length of stay (LOS), although definitive data are still needed.[2,5,17–21]

The shift to lighter sedation targets gained traction with data in 1998 and 2000 suggesting that increased durations of mechanical ventilation with continuous sedation and reduction in ventilator days by the use of daily sedation interruptions (DSI) in mechanically ventilated patients.[8,22] In Kress and associates' landmark trial, DSIs lead to a decrease in use of sedative medications and duration of mechanical ventilation and ICU LOS.[8] However, in 2014 a Cochrane Review of the subject was unable to identify outcome benefits when pooling 9 trials comparing sedation strategies with and without DSI.[23] Their negative results may reflect a trend toward fewer sedatives being administered in mechanically ventilated patients, because drug administration was not significantly different in the 2 arms of the review. This finding suggests that the initial benefit of DSIs may have been in their ability to prompt reduction of depth of sedation compared the amount of drug administered.[23] Although physician and nurse perceptions of DSIs, which are often not evidence based, frequently dictate their use,[24] deference of daily DSIs should certainly be considered in situations where they may cause harm, for example, in patients with increased intracranial pressure, refractory seizures, or severe PVD, and should not be performed on paralyzed patients.

Although the use of continuous sedatives for the majority of mechanically ventilated patients is often considered standard of care in some institutions, current practice is highly variable by region and institution,[25] and the alternative strategy of intermittent bolus sedation may be an equivalent or even superior strategy.[26–28] A clinical trial in Denmark randomized 140 patients and found that patients given only intermittent sedatives, analgesics, or antipsyhcotics (unless continuous agents were determined essential to prevent patient injury, or to control PVD or agitation) had a shorter duration of mechanical ventilation than those randomized to receive continuous sedation with daily awakening trials; a larger, multicenter trial is currently ongoing.[26,27] A similar study, however, failed to identify any patient-oriented benefits of intermittent versus continuous sedation, although patients in the intermittent group received fewer opioids and sedatives.[28] Further on-going research will reveal how the practice of intermittent sedation compares to the use of protocol-based targeted to light sedation goals.

MONITORING SEDATION AND PROTOCOLS

Over 40 years ago, Ramsay and coworkers[29] introduced the use of a standardized scale as a tool to monitor a patient's level of consciousness during ICU sedation with alphaxalone and alphadolone. Since their initial publication, multiple scales have been introduced and prospectively validated[29–36]; however, the Richmond Agitation–Sedation Scale (RASS) and Sedation–Agitation Scale have emerged as the most frequently used tools in literature for assessing and guiding depth of sedation.[2] Whichever scale is implemented, it should be easy to use within a multidisciplinary group, have clear and discrete criteria for each level, contain a sufficient number of levels to allow for drug titration, include a mechanism to assess for agitation, and be designed with interuser reliability and prospective validation.[37] The ability of a sedation scale to assess for agitation is of paramount importance, because up to 46% of critically ill patients exhibit severe or potentially dangerous agitation at some point in their ICU stay.[1,38] Separate from these scales should be a delirium assessment, because it is an often misidentified condition that can worsen if managed with delivering more sedatives.[39,40] Algorithm-based systems of assessment and management of sedation, which are typically multidisciplinary, have been demonstrated to decrease the amount of sedative medications administered, while being cost effective.[17,41,42] For instance, the I-SAVE group reported a savings of $750 USD per patient after the deployment of multidisciplinary sedation–agitation–delirium protocol in their tertiary ICU, while decreasing ICU LOS and ventilator days, and improving pain scores.[41]

CHOICE OF SEDATION

Sedative agents used in the ICU can be classified based on their pharmacodynamic properties such as amnestic, anxiolytic, analgesic, antipsychotic, and hypnotics. Many drugs have multiple properties and overlapping effects depending on the dosage used (**Table 1**). Amnestic agents, such as some benzodiazepines, inhibit anterograde memory formation. Anxiolytic drugs, including benzodiazepines and barbiturates, induce a state of calmness through activation of λ-aminobutyric acid (GABA) receptors. Many classes of drugs hold analgesic properties; however, opioids are the most widely used class of pain-relieving drugs in the ICU and can also be administered for their sedative properties.[46,52] Antipsychotic drugs, such as haloperidol, risperidone, ziprasidone, and quetiapine, which are primarily used for the