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Sedation and Analgesia: Optimizing Care for the Critically Ill

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Editorial

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Sedation and Analgesia Agents

Pharmacotherapy for sedation is an essential component of the management of critically ill patients in the intensive care unit (ICU). Sedation agents, such as benzodiazepines and propofol, can target light or deep sedation levels and eliminate the patient's awareness of the environment during mechanical ventilation (MV). Those agents can also facilitate procedures such as tracheal intubation, prone position, wound care, or minor surgical procedures. Historically, benzodiazepines (e.g., midazolam, lorazepam) and propofol have been the medications of choice to facilitate mechanical ventilation (MV) in North America [1,2]. In the past decade, dexmedetomidine (DEX) was introduced for procedural sedation and sedation during MV. DEX is a highly selective alfa2-receptor agonist with sedative and mild analgesic/opioid-sparing properties [3,4]. Its pharmacology is distinct from propofol and benzodiazepines in that its mechanism of action is not mediated by agonism or binding to the gamma-aminobutyric acid receptors; thus, reducing respiratory depression risk. This property made DEX the preferred agent when light sedation and rapid extubation are planned [5]. DEX is not recommended when deep sedation is required or for managing conditions such as status epilepticus or when neuromuscular blocking agents are used.

The 2018 SCCM PADIS guidelines required routine pain assessment and treatment before considering initiating sedative agents [2]. Current practice utilizes intravenous administration of fentanyl over morphine sulfate or newer agents such as remifentanil. In addition to providing pain control, analgesics can optimize patient-ventilator synchrony to improve MV outcomes.

Sedation and Analgesia Strategies

More important than choosing the specific agent is to determine the strategy for medication administration. The current literature supports three approaches: a) protocolized sedation (PS), b) PS plus daily sedation interruption (DSI), and c) analgesia-first strategy. The 2018 SCCM PADIS guidelines provide a conditional (vs. a strong) recommendation for the use of analgosedation in critically ill adults, which is further supported by recent a clinical trial that demonstrated that an RCT comparing sedation strategies including the applicability of the AFS is feasible in North America [2,6].

Protocolized Sedation with Daily Sedation Interruption

Protocolized sedation permit nurses to achieve and maintain a predetermine targeted sedation base on a valid sedation scale such as the Richmond Agitation-Sedation Scale (RASS) and Sedation-Agitation Scale (SAS). Daily sedation interruption (DSI) delineates a set time for the sedative to be discontinued, allowing the patients to wake up to undergo neurological evaluation with a RASS score range of -1 to +1 or SAS score of 4 to 7 [2].

Brook AD, et al. performed a randomized, single-center, clinical trial; comparing protocol-directed sedation versus non-protocol-directed sedation in 321 mechanically ventilated patients. Patients were assigned to two groups, protocol-directed sedation or non-protocol-directed sedation. The study demonstrated that protocol-directed sedation significantly reduced MV time (89.1±133.6 hrs. vs. 124.0±153.6 hrs; p =.003) [7]. The adoption of protocolized

sedation leads to studies supporting the utilization of daily sedation interruption (DSI).

The seminal study published by Kress et al. in 2000 was a randomized, single-center, clinical trial to evaluate daily interruption of continuous infusion of sedation. The study included 128 mechanically ventilated patients requiring sedation via continuous intravenous infusion. The results showed a 2.4 days reduction in MV time for the daily interruption group [8]. The significant finding led to a strong recommendation to adopt a sedation strategy that incorporates a DSI [1].

Strategies for Protocolized Sedation without DSI

Mehta et al. examined the role of DSI when protocolized sedation is performed. They conducted an RCT to compare protocolized sedation (PS) to PS plus DSI with time to extubation as the primary outcome. The sedation goals were SAS 3 or 4 or RASS -3 to 0. The study concluded that both strategies are equipoise. However, they noted that the nurse workload was higher in the PS plus DSI group [9].

Analgesia-First Strategy

Concern over over-sedation prompted Strom et al. to evaluate approaches focusing on controlling pain first and then administering anxiolytics when needed; an analgesia-first approach. They conducted a single-center randomized control trial comparing a strategy of no sedation to sedation strategy incorporating DSI. The average time without ventilation was higher in the no-sedative (13.8 days) than in DSI group (mean 9.6 days). Yet, they identified a higher rate of agitated delirium in the intervention group (20% vs. 7%, p=0.04) [10]. The authors concluded that the higher rate of delirium might be related to the ability to conduct delirium assessment in less sedated patients. In a more recent study, the investigator has concluded that that 90-day mortality was not different between the two groups [11]. Result of our randomized trial comparing sedation strategies showed a higher perceived nurse workload with the analgesia-first strategy [6].

Including Dexmedetomidine in sedation strategies

The PADIS guidelines recommended propofol or dexmedetomidine over benzodiazepines for sedation in critically ill mechanically ventilated adults. The SPICE III trial performed a multinational, open-label, randomized controlled trial to investigate DEX as the sole or primary sedative agent to be administer in patients undergoing mechanical ventilation [12]. The researchers compared Dexmedetomidine to usual care. The results demonstrated equal outcomes; the death rate from any cause at 90 days was similar in both groups; however, the DEX group had more bradycardia and hypotension. Results also suggested that often DEX alone was insufficient and required supplemental sedation to reach the desired goal in the first 24 hours. Propofol was the most frequent additive sedation (64.7%) follow by midazolam (2.9%), and in some cases, both were administered (6.9%).

Knowledge of the pharmacological principles alone is not sufficient to yield favorable MV outcomes from the sedative agents. The PADIS guidelines permit for more than one sedation strategy while emphasizing the benefits of light sedation. The ideal implementation of a given strategy is to select one of the validated options and adhere to the recommended goals [12]. Considering the nuances of the different strategies, each organization must use an interdisciplinary approach to implement the strategy that best fits its setting and resources. The optimum strategy should account for institutional resources and clinical practice restraints.

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