Rethinking Sedation During Prolonged Mechanical Ventilation for Coronavirus Disease 2019 Respiratory Failure

To the Editor

We read with interest the recently published letter by Hanidziar and Bittner[1] reflecting on the sparse guidance regarding sedation in the mechanically ventilated coronavirus disease 2019 (COVID-19) patient and the thoughtful outline of the challenges and implications. The pattern of unusually high sedation requirements, often with multiple agents, along with reliance on relatively high doses of benzodiazepines, is unsettling for any intensivist. In our experience, this observation was not limited to the younger patients with minimal comorbidities. With the long durations of mechanical ventilation and possibility of critical drug shortages, alternative options and additional guidelines for sedation for the mechanically ventilated COVID-19 patient are desperately needed.

With the ubiquitous use of dexmedetomidine for sedation in critical care, the majority of patients are able to participate in neurologic assessments without the need for formal sedation vacations. Intubated COVID-19 patients are maintained at moderate to deep sedation/analgesia to facilitate ventilator synchrony, address pain, allow for neuromuscular blockade, and minimize the risk for self-extubation. Pending favorable respiratory mechanics, protocolized sedation vacations, and daily awakening trials will enable early assessment of delirium and initiation of targeted therapy with antipsychotics as opposed to increasing rates of opiate or benzodiazepine infusions to combat what may be worsening agitated delirium. One avenue that may minimize use and facilitate transition off intravenous sedatives is the use of an enteral α-2 agonist such as guanfacine. In comparison to clonidine, this agent is selective for the α-2A receptor, resulting in less hypotension,[2] but possibly at the expense of reduced analgesia. In addition to its sedative effects, guanfacine is an anxiolytic and may also be helpful in the treatment of insomnia and opiate withdrawal. Given its favorable hemodynamic profile and a relatively long half-life, guanfacine is a safe option for patients transitioning out of the intensive care unit (ICU) and may obviate the need for enteric opiate and benzodiazepine tapers for patients on prolonged infusions.

The 2018 SCCM Pain, Agitation/Sedation, Delirium, Immobility (rehabilitation/mobilization), and Sleep (disruption) (PADIS) guidelines have a conditional recommendation for the use of ketamine as an analgesic adjunct in postsurgical patients.[3] As such, this versatile agent has thus far been underutilized in the medical ICU. In addition to its amnestic, sedative, and opioid-sparing analgesic properties, ketamine decreases airway resistance, increases lung compliance, maintains airway reflexes, and has a favorable hemodynamic profile in low to moderate doses (0.25–1 mg/kg/h). There are emerging data that its use may prevent delirium in the medical–surgical ICU population.[4] Given the possibility of myocarditis or cardiomyopathy due to SARS-CoV-2, ketamine should be avoided in patients with hypertension, tachyarrhythmias, myocardial ischemia, and decompensated heart failure due to its sympathomimetic properties that may increase myocardial demand. Ketamine may additionally prolong the QT interval, which as the authors point out may be a significant concern in COVID-19 management due to the concomitant use of other pharmacological agents that additionally prolong the QT interval.[1]

Last, the considerable sedation and analgesic requirements in COVID-19 patients that persist several days into their ICU course despite improving respiratory failure warrant a comprehensive neurologic assessment. A recent study from Wuhan, China, reported that neurologic manifestations including cerebrovascular disease with impaired consciousness are perhaps more common than initially expected.[5] In 1 case series, SARS-CoV-2 infection was associated with encephalopathy, agitation, confusion, and corticospinal tract signs though unclear if this was a direct effect of the virus, proinflammatory mediators, or a consequence of long-term sedation with deliriogenic agents.[6] It is possible that difficult to control agitation might be a unique feature of severe COVID-19, and underlying neurologic pathology might be a driver of the sedation needs.

In summary, the prolonged course of respiratory failure in COVID-19, cumulative side effects, and dependency issues with commonly used sedative–analgesic infusions, along with strain on pharmacy inventories calls for innovative approaches including the use of multimodal analgesia (gabapentinoids, intravenous lidocaine infusions), ketamine for analgosedation, and the early use of enteral medications such as α-2 agonists, antipsychotics, and sleep-promoting agents. With emerging data, comprehensive neurologic evaluation must be performed before attributing severe encephalopathy and agitation to medications.

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