In Response

We appreciate the interest of Drs Madhok and Mihm[1] in our article[2] and their suggestions on how to optimize sedation management in coronavirus disease 2019 (COVID-19) patients. The authors point out the interrelated problems of prolonged mechanical ventilation, choice of sedative drugs, and sedation depth[1] that we would like to further address.

A recently published analysis from 2 academic hospitals in Boston[3]—one of the most affected regions in the United States—revealed median duration of invasive mechanical ventilation of 16 days in COVID-19 patients who were successfully extubated. Given these prolonged periods of sedation and immobility, there clearly is a need to implement sedation approaches that would facilitate lung-protective ventilation but that would also limit the rates of oversedation, delirium, sedation-related encephalopathy, and subsequent functional disability in COVID-19 survivors. Older and frail patients are especially susceptible to these adverse outcomes.

Propofol, ketamine, dexmedetomidine, and intravenous opioids have been the typical components of the multimodal regimen used across the 10 ICUs dedicated to treatment of COVID-19 within our institution. This benzodiazepine-free approach has not been uniformly attainable in all patients with COVID-19. The addition of midazolam is typically seen in patients with rising triglyceride levels (due to propofol), rising creatine kinase levels (due to propofol), worsening QT interval prolongation (due to haloperidol, ketamine, azithromycin, and hydroxychloroquine), insufficient sedation depth during paralysis, and in patients with hemodynamic instability. Once introduced, we believe that benzodiazepines should be administered at lowest doses that are sufficient to achieve sedation targets and that allow regular neurologic assessments. Benzodiazepines should also be the first agents discontinued due to their deliriogenic effects and prolonged context-sensitive half time. As mentioned by Drs Madhok and Mihm,[1] management of sedation that allows neurologic assessments in patients with COVID-19 is critical given the reports of acute neurologic complications such as cerebrovascular accidents.[4]

Escalation of the doses of benzodiazepines over the course of the ICU stay without appropriate neuromonitoring in place should be discouraged, and alternative solutions should be sought. It must be emphasized that further deepening the levels of sedation with propofol or benzodiazepines in already adequately sedated patients is unlikely to improve patient-ventilator synchrony, and a bolus dose of neuromuscular blockers might be more appropriate to achieve ventilator synchrony.

The use of oral adjuncts (eg, quetiapine, propranolol, clonidine, gabapentin) has been proposed to reduce the doses and side effects of intravenous sedatives and to mitigate shortages of intravenous drugs. In our own experience, utility of these oral agents in critically ill COVID-19 patients has been limited due to high prevalence of ileus,[5] intolerance of enteral feeding, and unreliable absorption. We propose that these oral agents might be useful during ventilator and intravenous sedation weaning in patients who manifest signs of withdrawal (hypertension, tachycardia, and delirium), are not on vasopressor support, and in whom bowel function has returned. We have frequently been introducing these enteral agents in patients with COVID-19 who require intermittent or prolonged mechanical ventilation after undergoing a tracheostomy.

Finally, we propose that sedation management should be individualized based on respiratory variables. It has been established that COVID-19 ARDS is a heterogeneous entity.[6] While deeper levels of sedation might be indicated in patients with severe hypoxemia and poor lung compliance (eg, during proning, paralysis, high levels of PEEP), patients with well-preserved compliance might tolerate spontaneous modes of ventilation and lighter sedation levels (eg, dexmedetomidine alone). Bedside assessments of respiratory mechanics might be useful to identify patients with ARDS in whom high respiratory drive and larger tidal volumes are not injurious[7] so that they are not exposed to deep sedation and prolonged controlled ventilation unnecessarily. A proactive practice of tailoring sedation and ventilator support might reduce the length of mechanical ventilation and improve long-term outcomes in patients with COVID-19.

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