Reply to Murray and Newsome

From the Authors:

We appreciate the interest of Murray and Newsome in our recent 9-year evaluation of 4,017 adults in the ICU, in which we found daily opioid use to be associated with a dose-related increased risk of delirium the next day independent of pain (odds ratio, 1.45; 95% confidence interval, 1.24–1.69) (1). The authors hypothesize that the increase in the daily median (interquartile range) intravenous morphine equivalent opioid dose we report across the three study epochs (2011–2013: 0 [0–15] mg; 2015–2016: 2.5 [0–24] mg; 2017–2019: 5.3 [0–162] mg) represents a 9-year shift to lower use of γ-aminobutyric acid (GABA)-ergic (i.e., midazolam and propofol) sedatives.

A number of factors suggest this assumption may not be true. In any retrospective, uncontrolled study, it is not possible to know the specific reason(s) for opioid administration on each ICU day. It is therefore unclear whether opioids were used to treat pain, facilitate mechanical ventilation, treat agitation, or for other reasons. Although pain scores were not documented on 22% of the ICU days, the degree of pain score missingness was similar across the three epochs. Across the three epochs, the proportion of ICU days and the proportion of patients administered a GABA-ergic sedative, respectively, were similar (2011–2013, 33%/70%; 2015–2016, 34%/71%; 2017–2019, 33%/74%). Over the 9 years, the reduction in ICU days of midazolam use (2011–2013, 24%; 2015–2016, 15%; 2017–2019, 9%) is likely attributable to results from a 2015 study by our group showing that midazolam is associated with a 4% daily risk for a transition to delirium for every 5 mg of midazolam administered on the prior ICU day (2). The increase in ICU days of propofol use (2011–2013, 13%; 2015–2016, 25%; 2017–2019, 29%) across the epochs may be related to midazolam avoidance and a realization that propofol, even when compared with dexmedetomidine, is not associated with greater coma and delirium risk (3).

We agree with Murray and Newsome that important evidence gaps exist regarding the efficacy and safety of an analgosedation approach in mechanically ventilated adults. However, we do not feel the nonsedation randomized controlled trial (RCT) by Olsen and colleagues represents an analgosedation RCT given analgosedation was not evaluated as a distinct intervention (4). Among 12 published analgosedation RCTs comparing a continuously infused opioid to either "as needed" or "scheduled" GABA-ergic sedative therapy and "as needed" opoid therapy (5), we are aware of only one RCT in which a protocolized approach to maintain light sedation was used (6). This RCT found no difference in days spent free of mechanical ventilation at 28 days or 28-day mortality. The results from our report, and those of others, suggest ICU clinicians should be prudent with administering opioids and consider nonopioid analgesics when possible. Additional research is required to identify strategies to reduce opioid use and justify analgosedation approaches in critically ill adults. ■

Author disclosures are available with the text of this letter at www.atsjournals.org.

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