Review: Quality of sedation in the ICU is similar for propofol and midazolam, but propofol shortens the time to extubation

Ostermann ME, Keenan SP, Seiferling RA, Sibbald WJ. **Sedation in the intensive care unit. A systematic review.** JAMA. 2000 Mar 15;283:1451-9.

QUESTION

In patients who are mechanically ventilated in the intensive care unit (ICU), which sedatives are best for providing the optimal level of sedation (sedation quality) and reducing the time to extubation and length of ICU stay?

DATA SOURCES

Studies were identified by searching MEDLINE, EMBASE/Excerpta Medica, and the Cochrane Library (1980 to June 1998); reviewing bibliographies of relevant articles; contacting authors and 18 pharmaceutical companies; and searching personal files.

STUDY SELECTION

Studies were selected if they were randomized controlled trials (RCTs) that compared ≥ 2 sedative drugs in adults who were mechanically ventilated and required sedation and that reported data for sedation quality, time to extubation, or length of stay. Exclusion criteria were publication in abstract form and withdrawal of life support.

DATA EXTRACTION

The quality of study methods was assessed by using 8 criteria. Data were extracted in duplicate on follow-up, blinding, use of intention-to-treat analysis, baseline data, interventions, dosing schedules, and outcomes. Disagreements were resolved by consensus.

MAIN RESULTS

32 RCTs met the selection criteria. Studies were too heterogeneous to allow statistical pooling.

Short-term (≤ 24 h) sedation: In cardiac patients, pethidine (meperidine) and alfentanil led to similar sedation quality and time to extubation in 1 RCT. Propofol was better than midazolam for improving sedation quality in 2 of 7 RCTs and for shortening the time to extubation in 5 of 8 RCTs. Propofol shortened the duration of ventilation in 1 of 7 RCTs. Length of ICU stay was similar in the propofol and midazolam groups in 2 RCTs. In surgical patients or patients in the ICU, propofol was better than midazolam for improving sedation quality in 3 of 6 RCTs and for shortening the time to extubation in 3 of 3 RCTs. Midazolam and lorazepam did not differ for sedation quality in 1 RCT. Isoflurane was better than midazolam for improving sedation quality and shortening time to extubation in 1 RCT. Propofol and lytic solution (pethidine, promethazine, and dihydroergotamine) had a similar sedation quality, but propofol led to a shorter time to extubation.

Longer-term (> 24 h) sedation: In surgical patients or patients in the ICU, propofol and midazolam had a similar sedation quality in 3 of 6 RCTs. Sedation quality was better in the midazolam group in 1 RCT and in the propofol group in 2 RCTs. Time to extubation was shorter in the propofol group than in the midazolam group in 3 of 4 RCTs. Length of stay in the ICU was similar for the propofol and midazolam groups in 1 RCT. Midazolam and lorazepam had a similar sedation quality in 1 RCT. Time to extubation was shorter with isoflurane than with midazolam, but sedation quality and length of ICU stay were similar between groups (1 RCT). Alfentanil and propofol led to better sedation quality, shorter time to extubation, and shorter length of ICU stay than did morphine plus midazolam (1 RCT).

CONCLUSION

In patients who are mechanically ventilated in the intensive care unit (ICU), propofol is at least as effective as midazolam for sedation quality and shortens the time to extubation. Insufficient data exist to evaluate the effect on length of ICU stay.

Source of funding: University of Western Ontario and London Health Sciences Centre (Ontario).

For correspondence: Dr. S.P. Keenan, Centre for Health Evaluation and Outcome Sciences, St. Paul's Hospital, 620B-1081 Burrard Street, Vancouver, British Columbia V6M 2N8, Canada. FAX 604-269-0643.

COMMENTARY

Most ICU patients need pharmacologic assistance at some point to alleviate anxiety and pain, induce sleep, or manage the agitation of delirium (1). In 1995, the Society of Critical Care Medicine developed practice guidelines for sedation of ICU patients (2). Most of the guidelines were based on expert critical care opinion because RCTs on sedation in the ICU were few. Unfortunately, these problems persist. The key areas that make comparisons difficult are the heterogeneity of ICU populations, variation in drug regimens, disparity in rescue medications, and various sedation evaluation scales and evaluators.

After an extensive search of the literature between 1980 and 1998, Ostermann and colleagues were able to find only 49 RCTs on ICU sedation, and 17 were excluded because of failure to meet inclusion criteria. The authors noted that the studies were too clinically heterogeneous to permit statistical pooling. Therefore, the review's findings were often based on comparisons between 2 or 3 studies only. The authors' conclusions were neither new nor unexpected: Midazolam and propofol and lorazepam and midazolam were similarly effective in providing desired levels of sedation.

Despite the authors' attempts to shed more light on sedation in the ICU, too few well-done RCTs exist to determine the best ICU sedative regimens for any given situation. In the future, more emphasis must be placed on developing a standardized evaluation tool, defining patient populations better, and incorporating assessment of such outcome measures as cost expenditures and post-ICU satisfaction. This process will be difficult, but it is the only way that intensivists can obtain the evidence they need to provide optimal cost-effective sedation.

Eugene Y. Cheng, MD
Medical College of Wisconsin
Milwaukee, Wisconsin, USA

References

1. **Cheng EY.** The cost of sedating and paralyzing the critically ill patient. Crit Care Clin. 1995;11:1005-19.
2. **Shapiro BA, Warren J, Egol AB, et al.** Practice parameters for intravenous analgesia and sedation for adult patients in the intensive care unit: an executive summary. Society of Critical Care Medicine. Crit Care Med. 1995; 23:1596-600.