Is the Level of Sedation Depth in the Early Postintubation Period Associated With Worse Patient Outcomes?

TAKE-HOME MESSAGE

Compared with deep sedation, light sedation early in the postintubation course is associated with reduced mortality, decreased length of ICU stay, and fewer days of mechanical ventilation.

METHODS

DATA SOURCES

The Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, the Database of Abstracts of Reviews and Effects, EMBASE, MEDLINE, and Scopus were searched from inception through October 2016. A manual search of the reference lists of included articles and conference proceedings of major critical care, emergency medicine, surgery, trauma, and anesthesiology meetings was also performed. There were no language restrictions.

STUDY SELECTION

Studies were screened by 2 independent reviewers, with disagreements resolved by consensus with the addition of a third reviewer. Both randomized controlled trials and nonrandomized studies (including prospective and retrospective cohort analyses, cross-sectional studies, and before-after trials) were included. Studies included adult patients receiving invasive ventilation and had to report objective measures of sedation

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Editor's Note: This is a clinical synopsis, a regular feature of the *Annals'* Systematic Review Snapshot (SRS) series. The source for this systematic review snapshot is: **Stephens RJ, Dettmer MR, Roberts BW, et al. Practice patterns and outcomes associated with early sedation depth in mechanically ventilated patients: a systematic review and meta-analysis. Crit Care Med. 2018;46:471-479.**

Results

Summary of outcomes comparing early light versus deep sedation during mechanical ventilation.

Outcome	No. of Studies (No. of Participants)	Odds Ratio (95% CI)	Mean Difference (95% CI)	Heterogeneity (I^2), %
In-hospital mortality	9 (4,521)	0.34 (0.21 to 0.54)		71
Delirium frequency	6 (3,861)	0.50 (0.22 to 1.16)		95
Tracheostomy frequency	4 (673)	0.58 (0.29 to 1.16)		31
Mechanical ventilator days	9 (4,521)		−2.1 (−3.6 to −0.5)	99
ICU length of stay, days	7 (4,016)		−3.0 (−5.4 to −0.6)	88
Hospital length of stay, days	7 (4,016)		−5.9 (−13.8 to 2.0)	89

CI, Confidence interval.

The literature search identified 946 publications, of which 9 studies (n=4,521 patients) met the inclusion criteria. There were 2 randomized controlled trials, 3 prospective cohort studies, and 4 retrospective cohort studies. All studies were published between 2012 and 2017. The number of subjects in each study ranged from

depth (eg, the Richmond Agitation-Sedation Scale, the Glasgow Coma Scale [GCS]). The primary outcome was in-hospital mortality. Secondary outcomes included rates of delirium, duration of mechanical ventilation, hospital and ICU length of stay, and frequency of tracheostomy placement.

DATA EXTRACTION AND SYNTHESIS

Data were extracted with standardized forms. Quality was assessed with the Cochrane Collaboration Risk of Bias Tool for clinical trials, whereas observational studies were assessed with the Newcastle-Ottawa Scale. A random-effects model was used to calculate pooled effect sizes and corresponding 95% confidence intervals. Odds ratios were calculated for binary outcomes and overall effect estimates were generated with the z test. Heterogeneity was assessed with the I^2 statistic.

37 to 1,884 patients. Two studies included data on emergency department (ED) patients, whereas the remaining studies investigated only ICU patients. Seven studies defined deep sedation as a Richmond Agitation-Sedation Scale score less than or equal to −3, one study used a Richmond Agitation-Sedation Scale score less than or equal to −4, and one used a GCS score of less than 9. The deep sedation group comprised 34.7% of the patients (range 19.6% to 80.6%).

In-hospital mortality, number of days of mechanical ventilation, and ICU length of stay were lower in the light sedation group than in the deep sedation group (Table). There was not a statistically significant difference in the frequency of delirium, frequency of tracheostomy, or hospital length of stay. However, there was a trend toward improved outcomes for all of these in the light sedation group. All 7 observational studies were deemed high quality and both randomized studies were deemed at low risk of bias in 5 of 7 domains.

Commentary

Because hospitals are increasingly burdened with crowding, boarding of critically ill patients in the ED has become increasingly common.[1,2] Studies have shown that prolonged boarding of critically ill patients in the ED is associated with increased morbidity and mortality.[1,2] Moreover, among intubated patients, there is increasing recognition that the management of nonventilator components influences patient outcomes.[3] However, observational data have demonstrated that greater than 70% of intubated patients receive deep sedation during the first 48 hours of their care and that this is associated with adverse outcomes.[4,5] Because prolonged patient boarding and hospital crowding have led to increased management of these patients in the ED setting, it is important to be aware of the risks of light versus deep sedation in their early management.

The authors of this study identified that light sedation in the early period (defined as within 48 hours) was associated with reduced mortality, length of ICU stay, and number of days of mechanical ventilation. From a practical standpoint, providers could achieve this by using standardized protocols with sedation goals based on nursing-driven, objective measures of the patient sedation level (ie, Richmond Agitation-Sedation Scale score), as well as focusing on analgesics as the initial agent in place of more sedating agents.

However, it is important to consider several limitations with respect to this systematic review. First, the majority of included studies were observational, with only 2 randomized trials comprising 97 total patients. Additionally, several studies did not report the analgesics and sedatives used. Data were minimal for the ventilator settings (eg, tidal volumes, lung-protective ventilation strategies), which may also have influenced the outcomes. Moreover, the authors included studies using either a Richmond Agitation-Sedation Scale score or GCS score for sedation level. However, the GCS is intended to be used as a measure of brain damage and is not commonly used to assess level of sedation. Nonetheless, only one small study used GCS score to measure the level of sedation, so it is unlikely to have significantly influenced the outcomes. The majority of studies were conducted in the ICU setting and most defined early as within 48 hours, so it is difficult to determine how the ED portion of the care may have specifically influenced the outcomes. Finally, there was significant clinical and statistical heterogeneity between studies. However, the authors performed multiple sensitivity analyses and identified consistent outcomes after

removing multiple trials. Further randomized controlled studies are needed to determine the influence of light versus deep sedation early in the postintubation period, as well as the effect of care specifically within the ED setting.

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