Best evidence in critical care medicine

Daily interruption of sedative infusions in critically ill patients undergoing mechanical ventilation

Article appraised

Kress JP, Pohlman AS, O'Connor MF, Hall JB. Daily interruption of sedative infusions in critically ill patients undergoing mechanical ventilation. *N Engl J Med* 2000; 342: 1471–7.

Structured abstract

Question: Does daily interruption of sedative infusions in critically ill patients receiving mechanical ventilation decrease the duration of mechanical ventilation and length of stay in the intensive care unit (ICU) and hospital?

Population: This study investigated intubated patients in the medical ICU of the University of Chicago Hospital. The study coordinators enrolled 150 patients who required sedation for agitation or discomfort according to the treating ICU team. Amongst the 150 patients enrolled, the 128 patients who were ultimately included in the study were those who were still alive and intubated after the initial 48 hr in the ICU. The study excluded patients who were pregnant, already receiving sedatives upon transfer to the ICU, or who were post-cardiac arrest.

Intervention: Patients were randomly assigned to receive one of two sedation infusion strategies. The treatment group had sedation medications stopped daily. A study nurse then observed these patients until they awoke. A study physician was then summoned to restart the sedative medications at half their previous dose and then retitrate to the desired effect (Ramsay level 3–4 on a 1–6 scale). The control group received “routine care” of the rounding ICU team. Both of these treatment groups had their patients either assigned to midazolam or propofol as the sedative agent, making a total of four different treatment groups.

Outcomes of interest: The primary outcomes were the lengths of time with mechanical ventilation, in the ICU and in the hospital. Secondary outcomes included adverse events (e.g., premature self-extubation, reintubation, long-term ventilation, withdrawal of care and death).

FIGURE

For the daily interruption group, the number of days intubated and in the ICU was significantly lower, and there was a trend toward fewer hospital days (Figure). Furthermore, there were fewer diagnostic studies done for the intervention group to determine the cause of a change in mental status. Other secondary outcomes did not differ between the groups. No important differences were seen with regards to which sedative agent was used.

Conclusion: Intubated medical ICU patients who receive daily interruption of sedative infusions have shorter times on the ventilator and in the ICU.

Commentary by T. Gorman, F. Bernard, F. Marquis, P. Dagenais, and Y. Skrobik

Background

Sedative infusions in the intensive care unit (ICU) are very useful, but are an independent risk factor for prolonged intubation/ICU time, as well as unnecessary diagnostic studies for decreased levels of mental status.¹ The study by Kress *et al.*² underscores such risks, demonstrating earlier extubation for patients who have daily interruption and retitration of their sedative infusions.

Design

The study was relatively well-designed. Randomization of enrolled patients seemed well-performed and subsequently preserved by an intention-to-treat analysis. While there was some inevitable contamination in the study (with some control patients having their sedation stopped daily), there seemed to be no significant crossover. Follow-up was not mentioned, but was presumably 100% given the study's design.

There are three major problems with the validity of the study. First, the control group was treated to a Ramsay sedation level of 3 to 4, which may represent oversedation by today's standards. Secondly, the study group may have been less likely to tolerate extubation at baseline, given it ended up having a much higher proportion of patients who stayed in a coma and/or eventually required long-term ventilator support. Thirdly, it is highly unlikely the study was truly blinded. The study group patients had a research nurse sitting by them daily, who called a study physician to retitrate the sedative infusions. Surely, the regular team rounding on their patients would be aware of the intervention. It is conceivable that they would have been more diligent in their care overall of the treatment patients, leading to faster extubations as a confounding effect.

Applicability

We are not told exactly how or how many patients were screened to come up with the final pool of 150 enrollees. We must therefore assume that inclusion criteria covered all medical ICU admissions, and that the enrolled patients might be similar to our own intubated patients. We are also not told what their protocol was for weaning ventilator support and extubating. Another major problem comes from the complexity of the intervention. Despite the fact that daily interruption of sedatives may lead to earlier extubations (which may ultimately lead to lower overall costs), it is hard to imagine that any ICU could afford this intensive intervention of one study nurse and physician to only take care of sedation.

Summary

Despite its flaws, the study has had an impact on critical care practice today. It served as a reminder that our therapies and best intentions (in this case continuous sedation) can often have silently harmful results. We can take from this study the concept that daily "lightening" of sedation for reevaluation of a patient's neurologic status makes good sense. The study served as an important factor in the latest Society of Critical Care Medicine guidelines³ on sedation in the ICU,

which recommend the use of intermittent benzodiazepines for sedation. If infusions are chosen, the guidelines clearly suggest daily interruption with retitration toward a specific Ramsay goal. Individual intensivists will have to draw their own conclusions as to how to accomplish this within their own systems' logistic constraints.

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- 3 Jacobi J, Fraser GL, Coursin DB, et al. General practice guidelines for the sustained use of sedatives and analgesics in the critically ill adult. *Crit Care Med* 2002; 30: 119–41.