CRITICAL CARE

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Pushing the envelope to reduce sedation in critically ill patients

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Expanded Abstract

Citation

Strom T, Martinussen T, Toft P: A protocol of no sedation for critically ill patients receiving mechanical ventilation: a randomized trial. *Lancet* 2010, 375:475-480 [1].

Background

Standard treatment of critically ill patients undergoing mechanical ventilation is continuous sedation. Daily interruption of sedation has a beneficial effect, and in the general intensive care unit of Odense University Hospital, Denmark, standard practice is a protocol of no sedation. We aimed to establish whether duration of mechanical ventilation could be reduced with a protocol of no sedation versus daily interruption of sedation.

Methods

Of 428 patients assessed for eligibility, we enrolled 140 critically ill adult patients who were undergoing mechanical ventilation and were expected to need ventilation for more than 24 h. Patients were randomly assigned in a 1:1 ratio (unblinded) to receive: no sedation (n = 70 patients); or sedation (20 mg/mL propofol for 48 h, 1 mg/mL midazolam thereafter) with daily interruption until awake (n = 70, control group). Both groups were treated with bolus doses of morphine (2.5 or 5 mg). The primary outcome was the number of days without mechanical ventilation in a 28-day period, and we also recorded the length of stay in the intensive care unit (from admission to 28 days) and in hospital (from admission to 90 days). Analysis was by intention to treat. This study is registered with ClinicalTrials.gov, number NCT00466492.

Findings

27 patients died or were successfully extubated within 48 h, and, as per our study design, were excluded from the study and statistical analysis. Patients receiving no sedation had significantly more days without ventilation (n = 55; mean 13.8 days, SD 11.0) than did those receiving interrupted sedation (n = 58; mean 9.6 days, SD 10.0; mean difference 4.2 days, 95% CI 0.3–8.1; p = 0.0191). No sedation was also associated with a shorter stay in the intensive care unit (HR 1.86, 95% CI 1.05–3.23; p = 0.0316), and, for the first 30 days studied, in hospital (3.57, 1.52–9.09; p = 0.0039), than was interrupted sedation. No difference was recorded in the occurrences of accidental extubations, the need for CT or MRI brain scans, or ventilator-associated pneumonia. Agitated delirium was more frequent in the intervention group than in the control group (n = 11, 20% *vs.* n = 4, 7%; p = 0.0400).

Interpretation

No sedation of critically ill patients receiving mechanical ventilation is associated with an increase in days without ventilation. A multicentre study is needed to establish whether this effect can be reproduced in other facilities.

Commentary

Critically ill patients who require mechanical ventilation are often given continuous intravenous sedative infusion to maintain comfort, improve patient-ventilator interaction, decrease pain and anxiety, avoid self injury and allow safe completion of invasive procedures [2]. Unfortunately, administration of continuous sedative infusion has been associated with unintended consequences. These consequences include but are not limited to longer duration of mechanical ventilation, longer intensive care unit (ICU) length of stay, ventilator-associated complications and cognitive deficits, such as delirium and post traumatic stress disorder [3]. In 2000, Kress et al. clearly demonstrated that daily interruption of sedative drug infusion decreased the duration of mechanical ventilation and the length of intensive care unit stay [4]. The last two decades have been marked by studies aimed at decreasing sedation for critically ill patients using validated sedation scales to titrate therapies and new pharmacological agents such as dexmedetomidine [5,6].

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In a first of its kind, single-center randomized controlled study, Strom et al. aimed to establish whether the duration of mechanical ventilation could be reduced with a protocol of no sedation versus daily interrupted sedation. It is important to point out that, although the authors refer to the intervention group as 'no sedation' group, this group received 2.5-5 mg boluses of morphine, which may have caused some sedation. In contrast, the continuous sedation group received 20 mg/ml propofol for 48 hours followed by 1 mg/ml of midazolam with daily sedation interruption. There were 27 patients who died or were successfully extubated within 48 hours and were excluded from the study. Patients who receiving only morphine boluses, on average had 4.2 fewer days without mechanical ventilation compared to the group with continuous sedation. Furthermore; the intervention group was associated with a shorter ICU stay by 9.7 days and hospital stay by 24 days than the control group. Agitated delirium was more frequent in the intervention group than the control group (20% vs. 7%) and haloperidol was used more frequently in the intervention group (35% vs. 14%). There was no difference recorded between the groups in the incidence of accidental extubations, the need for CT or MRI brain scans, or ventilator-associated pneumonia.

This study is innovative as it attempts to push the envelope to reduce sedation in critically ill patients. This approach of using analgesia alone and avoiding sedation, unless necessary, has been the standard of care in the author's ICU in Denmark since 1999. Another strength of the study was inclusion of both medical and surgical patients, and thus these results are more generalizable.

Despite its innovative approach, there are several limitations of this study. A careful evaluation of patients baseline characteristics, shows a slightly increased severity of illness in the control group (based on SAPS II: 46 vs. 50) and SOFA score (7.5 vs. 9). This may have biased results towards the experimental group. Another concerning aspect is the choice of sedation agent in the control arm. Propofol was switched to midazolam which, has a longer clearance time especially in the setting of liver or renal failure and increase duration of mechanical ventilation [7]. Another noteworthy limitation that challenges the generalizability of this study is the use of 1:1 nurse to patient ratio and patient comforters. This suggests that successful completion of this protocol requires more staff presence which is often not available in most ICUs. Any deviation from this required staffing would seem to compromise patient safety and may defeat the intended purpose of this study. Interestingly, the intervention group had more reported agitated delirium, though the significance of this result is questionable as the DSM IV criteria was used rather than the well validated CAM-ICU or RASS scale [8,9]. Post-traumatic stress disorder (PTSD) is common in survivors of critical illness and is an important outcome in studies that attempt to reduce sedation [10]. Future studies to assess the risk of PTSD would be helpful to understand long-term sequelae of this sedation strategy.

The implementation and titration of ICU sedation is one that is a balancing act to minimize sedation associated complications and improving patient comfort. This study suggests that analgesics should be considered first before instituting continuous sedation. Furthermore, using more comfortably modes of mechanical ventilation may reduce the need for sedation. It remains to be seen how these novel ways of decreasing sedation complications will impact practice patterns and work load for ICU physicians, nurses and respiratory therapists.

Recommendation

A conservative approach of less sedation does not appear to cause harm in critically ill mechanically ventilated patients. This is an important proof of concept study. Larger, multicenter trials are necessary to determine the feasibility and safety of this approach.

Competing interests
The authors declare that they have no competing interests.

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