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Exploring the impact of augmenting sedation assessment with physiologic monitors

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ABSTRACT

Background: Pharmacological sedation is a necessary tool in the management of critically ill, mechanically ventilated patients. The intensive care unit (ICU) sedation strategy is to use the least amount of medication to meet safety and comfort goals. Titration of pharmacological agents is currently guided by clinical assessment tools. The purpose of this study was to determine whether the addition of a neurophysiological monitor, bispectral index (BIS), aided the ICU nurse in reducing the amount of drug used, compared to a clinical tool alone, in a general critical care population.
Methods: In this prospective clinical trial, mechanically ventilated adults ($N = 300$) were randomised to sedation assessment using only the observational assessment tool (RASS) or a combination of observational and physiologic measures (RASS + BIS). Subjects were enrolled from a medical ICU ($N = 154$), a trauma ICU ($N = 72$) and a general mixed-use ICU ($N = 74$).
Results: BIS-augmented sedation was only associated with the reduction of drug use when patients were sedated with propofol or narcotic agents (propofol [1.61 mg/kg/h vs. 1.77 mg/kg/h; $p < 0.0001$], fentanyl [54.73 mcg/h vs. 66.81 mcg/h; $p < 0.0001$], and hydromorphone [0.97 mg/h vs. 4.00 mg/h: $p < 0.0001$] compared to RASS alone. In contrast, patients sedated with dexmedetomidine or benzodiazepines were given higher doses under the BIS-augmented dexmedetomidine [0.46 mcg/kg/h vs. 0.33 mcg/kg/h; $p < 0.0001$], lorazepam [4.13 mg/h vs. 3.29 mg/h $p < 0.0001$], and midazolam [3.73 mg/h vs 2.86 mg/h; $p < 0.0001$]) protocol compared to clinical assessment alone.
Conclusion: The clinical evaluation of depth of sedation remains the most reliable method for the titration of pharmacological sedation in the critical care unit. However, BIS-augmented assessment is helpful in reducing the amount of propofol and narcotic medication used and may be considered an adjunct when these agents are utilised.

Introduction

Patients in the intensive care unit (ICU) often receive sedative medications to facilitate periods of mechanical ventilation (MV), as well as prevent recall of unpleasant events and maintain a safe environment.[1,2] The term sedation has a variety of definitions such that 'sedation' is both a verb (the administration of sedative medications) and a noun (a state of decreased responsiveness). Oversedation has been associated with delayed weaning from MV, increased length of stay and increased prevalence of delirium.[3–7] On the other hand, undersedation may result in patient recall of unpleasant events, ventilatory dysynchrony, or haemodynamic instability.[3,8,9] Thus, the clinician must balance the need to provide

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patients with an adequate amount of sedative to achieve the medical goals of providing critical care and meeting patient comfort while at the same time using the lowest dose of sedative to achieve this endpoint.[3,10–15] In response, practitioners have sought tools to define best-practice for sedation during MV.

Clinical physiological markers such as blood pressure, heart rate and respiratory rate have not been shown to be consistent and reliable enough to be of use in monitoring the adequacy of sedative or analgesic medications.[16,17] As such, various clinical scales have been developed to provide an evaluation of the depth of sedation.[15,18–21] Prominent amongst these is the Richmond Agitation Sedation Scale (RASS), a single-item scale with mutually exclusive definitions for each of 10 levels of sedation (range: −4 to +5).[18,19] Sedation scales, along with a standardised sedation algorithm for the care of a critical care patient, have been shown to provide a more consistent approach to sedation management resulting in reduced prevalence of delirium, as well as facilitating liberation from MV.[22–24] However, clinical evaluation tools such as the RASS score only provide intermittent assessments of sedation status and are subject to some degree of inconsistency due to the interrater and intrarater reliability of each respective scale. In addition to the use of sedation scales, several sedation strategies have been explored. Daily 'wake-ups' have been associated with decreased duration of MV and overall length of hospital stay.[24,25] Some guidelines now support stopping sedative medications at least once each day, although a variety of patients are ineligible for this treatment (e.g., patients who require deep sedation, or chemical paralysis).[24,26,27] Recently, Mehta et al.[28] found no association between sedation interruption and weaning from MV.

On the other hand, a neurophysiological monitor such as the electroencephalogram (EEG) is capable of providing a continuous standardised measure of the electrical function of the brain and has been shown to be highly sensitive to the effects of sedating drugs.[29] Interpretation of the EEG requires extensive training and as such, the use of "raw" EEG waveforms as a tool to guide sedation administration is not practical. To address this limitation, devices such as the bispectral index (BIS) and Entropy monitor have been developed. The BIS index uses processed scalp EEG to provide a single value between 0 and 100, where lower values reflect lower levels of consciousness.[30,31] The addition of BIS monitoring has been shown to be of benefit in evaluating depth of sedation in the operating room setting[31,32] for neurocritical care patients,[3] cardiac surgical patients,[33] and trauma patients.[34] However, there have been limited studies regarding the use of the combination of BIS and sedation scales in the ICU. The guidelines recently published by Barr et al.[35] summarise that 15 studies which included objective monitors of sedation found that they provided benefit as adjuncts to sedation and five additional studies found no benefit of incorporating objective measures. In a secondary analysis of data from the Entropy monitor, Walsh et al. found that the frontal electromyography (EMG) signal could be used to predict responsiveness during sedation.[36]

The purpose of this study was to determine if there was benefit to combining electrophysiological measures with the clinical assessment of sedation in a general critical care population. Previous work had examined the combination of electrophysiological measures and clinical tools compared to clinical tools alone, finding that the combination of tools was superior to clinical judgement alone.[3] However, the study involved a single ICU and was limited to neurological/neurosurgical patients being sedated with a single agent (propofol). Based on recent literature, our hypothesis was that combining observational and physiologic sedation assessment tools (intervention group) would result in lower sedative use compared to use of observational sedation assessment tools alone (control group) when applied to a general population of critically ill, sedated patients.

Methods

This was a prospective randomised clinical trial (clinicaltrials.gov identifier NCT00734409) to determine whether the addition of a neurophysiological monitor (BIS) aided the ICU nurse in reducing the amount of sedation drugs used compared to a clinical tool alone in a general critical care population. Unlike previous studies that considered the use of only one agent (propofol), multiple sedation options were possible for this study. Mechanical ventilator days, length of stay, and ICU survival were additional outcome measures collected in order to determine if a difference existed between the intervention and control group.

Subjects

Subjects ($N = 300$) were recruited from three ICUs at two hospitals: a surgical ICU and medical ICU in a university based hospital, and a mixed-bed adult ICU at a regional community-based hospital. Prior to enrollment, all study protocols and procedures were approved by the Institutional Review Boards at the participating hospitals. Consent was obtained from the patient's legally authorised representative as subjects were unable to self-consent due to concurrent intravenous (IV) sedation. Sample size calculations were performed using tables from Lipsey et al.,[37] and are based on data from a previous study by our group.[3] This analysis estimated a sample size of 270 subjects based on an effect size of 0.80, a two-tailed alpha level of 0.05, and a desired power of 0.90. Between May 2008 and April 2011, 300 adults (age 18 years or older) were enrolled within 24 h of endotracheal intubation and mechanical ventilation with IV sedation. Patients were excluded if they were prisoners, had a bifrontal brain injury, had no available skin area on the forehead to place the BIS sensor (e.g. de-gloving trauma), were receiving continuous EEG monitoring for seizures or barbiturate coma therapy, were moribund and death was an expected event within 24 h, or if they did not recover consciousness after cardiac arrest. Prior to subject recruitment, the nursing and medical staff in each of the ICUs was provided with education on the sedation protocol, use of BIS monitors, and RASS scores during unit-based staff meetings.

Following consent, subjects were randomised to one of two sedation assessment groups: the control group that received sedation assessment with RASS as the standard of care, and the intervention group that received the standard of care (RASS) plus physiologic monitoring (BIS). Randomisation was performed using a random number generator and randomisation without replacement. There was no effort to blind subjects, family, or staff to group assignment. When sedation was required, nurses adjusted sedation dosages as determined by the subject's randomisation. Nurses assigned to subjects in the control group adjusted sedation to a goal RASS of −2. Nurses caring for subjects in the intervention group were instructed to adjust sedation to a goal RASS of −2, and then after the clinical goal was reached, the sedating drug was titrated to achieve a goal BIS of 60–70. Protocol required that RASS scores be documented at a minimum of once every 4 h, and BIS values were recorded once per hour. The respiratory care protocol included coordinating a daily wake-up and spontaneous breathing trial. During the study period, all sedative and analgesic medications were recorded and the mean hourly doses were calculated. Data were abstracted from the subject's medication record for the total hourly dose of sedative/analgesic medications used. The primary ICU care team determined the drug or drug combination for each subject as they felt necessary for the individual. Drugs used in these ICUs for sedation and analgesia included dexmedetomidine, propofol, fentanyl, hydromorphone, lorazepam, midazolam and morphine.

Subjects remained in their randomised group until discharge from the ICU. All statistical analyses were performed using SAS v