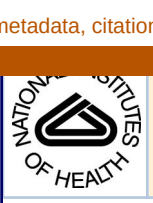

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Effectiveness of Implementing a Wake up and Breathe Program on Sedation and Delirium in the Intensive Care Unit

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Abstract

Objective—Mechanically ventilated critically ill patients receive significant amounts of sedatives and analgesics that increase their risk of developing coma and delirium. We evaluated the impact of a 'Wake-up and Breathe Protocol" at our local intensive care unit (ICU) on sedation and delirium.

Design—A Pre-Post implementation study design.

Setting—A 22 bed mixed surgical and medical ICU.

Patients—702 consecutive mechanically ventilated ICU patients from June 2010 to January 2013.

Intervention—Implementation of daily paired spontaneous awakening trials (daily sedation vacation plus spontaneous breathing trials) as a quality improvement project.

Measurements and Main Results—After implementation of our program, there was an increase in the mean Richmond Agitation Sedation Scale (RASS) scores on weekdays of 0.88 ($p <$ 0.0001), and an increase in the mean RASS on weekends of 1.21 (p: < 0.0001). After adjusting for age, race, gender, severity of illness, primary diagnosis, and ICU unit, the incidence and prevalence of delirium did not change post implementation of the protocol (incidence: 23% pre

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versus 19.6% post; *p*: 0.40; prevalence: 66.7% pre versus 55.3% post; *p*: 0.06). The combined prevalence of delirium/coma decreased from 90.8% pre protocol implementation to 85% post implementation (Odds ratio: 0.505; 95% CI: 0.299-0.853; *p*: 0.01).

Conclusion—Implementing a "Wake-up and Breathe Program" resulted in reduced sedation among critically ill mechanically ventilated patients, but did not change the incidence or prevalence of delirium.

Keywords

intensive care unit; sedation; delirium; quality improvement; acute brain dysfunction

Introduction

Five million Americans are admitted to Intensive Care Units (ICU) annually due to life-threatening illnesses,[1] and approximately 36% of these critically ill patients receive mechanical ventilation during their ICU stay,[2] that is usually associated with significant amounts of sedative and analgesic use.[3] An optimal sedation strategy is highly desirable, as inadequate sedation can lead to patient-ventilator asynchrony, patient agitation, and unplanned extubations, while excessive sedation can result in an increased duration of mechanical ventilation, a higher length of ICU and hospital stay,[4] and can predispose the patient to delirium.[5]

Sedation strategies in the ICU have seen a change over the last two decades with the publication of studies showing the efficacy of sedation vacation,[6] along with the pairing of sedation and ventilator-weaning protocols,[7] in reducing duration of mechanical ventilation and ICU length of stay. Both randomized controlled trials showed a decrease in benzodiazepine use among intervention patients, suggesting that the favorable outcomes could be attributed to the reduction in sedation under well-controlled conditions. In March 2011, as a response to the evidence on the efficacy of the sedation vacation and spontaneous breathing practice, we localized and implemented the "Wake up and Breathe Protocol" developed by Girard et al.[7] to reduce variations in sedation levels across our ICU care teams, especially on the weekends.

Since 2009, the Indiana University Delirium study group has been actively conducting a randomized controlled trial: the Pharmacological Management of Delirium (PMD) (clinical trial.gov identifier: NCT00842608)[8] in the same ICU. To identify eligible participants for the trial, ICU patients are regularly screened for level of sedation, coma, and delirium. The access to this large collection of screening data allowed us to assess the effect of our awakening and breathing protocol in decreasing sedation levels and acute brain dysfunction (coma/delirium) in a pre/post implementation study design. The primary hypothesis of our study was that implementation of a "wake up and breathe program" in a real-world setting will decrease sedation levels among critically ill mechanically-ventilated patients. The secondary hypothesis was that such a program will also reduce the burden of coma and delirium in our ICU.

Methods

Study Setting and Patient Population

The study was approved by the Institutional Review Board of the Indiana University Purdue University at Indianapolis. Patients admitted to the ICU services of Wishard Memorial Hospital (WMH) from June1, 2010 to January 8, 2013 were included in the study. WMH is a 457-bed; university-affiliated, urban public hospital with an average of 1200 ICU admissions/year. It has an 8-bed surgical ICU (SICU), and a 14-bed medical and coronary ICU (MICU). The medical and surgical ICUs are staffed identically at a nurse/patient ratio of 1:2 and 1:1 when necessary. There were no changes in the patients' characteristics or staffing practices of these ICUs during the study period.

Patients are screened for the PMD study if they are: 1) admitted to the WMH ICUs; 2) age ≥ 18 years; and 3) able to speak English. Patients are excluded if they are 1) not English speaking; 2) hearing impaired; 3) legally blind; 4) admitted with alcohol intoxication; 5) prisoners; or 6) diagnosed as having an Axis 1 Psychiatric disorder. Consecutively admitted mechanically ventilated patients with the above screening criteria are included for the evaluation of the Wake Up and Breathe program.

Procedures and Data Collection

Outcome Measures—The Richmond Agitation Sedation Scale (RASS)[9] was used to assess the level of sedation. RASS is a valid and reliable sedation assessment scale with items ranging from -5 to +4, with negative items denoting deeper levels of sedation. A RASS score of -4 or -5 is indicative of coma; -3 and-2 depict moderate and light sedation respectively; -1 equal drowsiness; 0 depicts alert and calm state; and the positive items from +1 to +4 indicate various degrees of restlessness and agitation. Confusion Assessment Method for the ICU (CAM-ICU) was used to screen for delirium for patients with a RASS score ≥ - 3.[10] Patients were identified as delirious if their RASS score was -3 (responsive to verbal stimuli) or greater and had a positive CAM-ICU result. Incident delirium was defined as a positive CAM-ICU after an initial negative result. Prevalent delirium was defined as any CAM-ICU positive result during the ICU stay. Patients who were either delirious or comatose at any time point were classified as having acute brain dysfunction. The RASS and CAM-ICU data were collected by trained research personnel who conducted two sedation/ delirium assessments each day, once in am and once in pm. Patients were assessed within 24 hours of ICU admission and then daily until they become delirious, died, or were discharged.

Wake Up and Breathe Protocol—Our protocol (appendix 1) was adapted from the Awakening and Breathing Controlled (ABC) trial.[7] Prior to the protocol implementation, the sedation practices involve continuous analgesics and sedatives infusions based on physicians' discretion. The protocol mandated patients' sedatives to be discontinued at seven am after they pass the safety screen. Once awake, a spontaneous breathing trial is initiated. If patients tolerate the breathing trial for one hour, attending physicians are notified. In cases of intolerance of sedation interruption or spontaneous breathing, sedatives are restarted at half of the previous dose and patients are returned to assisted ventilation. Multidisciplinary

weekly group sessions over a period of three months were organized to develop the protocol and to train the ICU personnel.

Other data collection—Baseline demographics such as: age, sex, and race; patients' severity of illness, principal diagnoses, duration of mechanical ventilation, and length of hospital stay were also recorded.

Statistical Analysis

Descriptive data are expressed as counts (%) for categorical variables, medians (IQR) for skewed variables, and means (SD) for symmetric variables. We used Chi-square tests to compare incident and prevalent delirium, coma, acute brain dysfunction, and hospital mortality rates between the pre/post-protocol cohorts. Logistic regression was used to adjust for potential confounders such as age, race, gender, severity of illness, principal diagnosis, and ICU unit as described in Table 1. Linear mixed models, with appropriate contrasts, were used to assess changes in daily RASS scores. Poisson regression was used to assess differences in number of days on mechanical ventilation between the pre/post-protocol cohorts while adjusting for potential confounders. The Wilcoxon rank sum test was used to compare hospital length of stay between the pre- and post-cohorts. Statistical significance was defined as $p<0.05$. All analyses were performed using SAS version 9.3 (SAS Institute, Cary NC).

Results

3902 RASS assessments were performed on 702 unique ICU (262 pre- and 440 post-implementation) admissions from June 1, 2010 to January 8, 2013. Among these unique admissions, 443 (141 pre- and 302 post-implementation) had at least one CAM-ICU assessment and were used as the cohort for estimating prevalence of delirium. Of those assessed, 229 (61 pre- and 168 post-implementation) were negative for delirium at the first CAM-ICU assessment and were used as the cohorts for estimating incidence of delirium. The Wake up and Breathe protocol was initiated on March 1st, 2011. Patients admitted during the nine months prior to protocol implementation (n=262) were selected as control, whereas those admitted during the 22 months after implementation (n=440) were selected as the intervention cohort. Table 1 describes the patients' characteristics of the study cohorts. The median RASS score was -4 (IQR -5 to -3) for the overall study population on weekdays and -4 (IQR -5 to -4) on weekends [mean RASS -3.6 (SD=1.65) on weekdays and -3.9 (SD=1.36) on weekends]. The incidence of delirium was 20.5% (47/229), and the prevalence was 58.9% (261/443) for the overall study period. The prevalence of coma was 75.2%. (528/702); and that of acute brain dysfunction (coma/delirium) was 87.2% (612/702).

Prior to the protocol implementation, patients had a median RASS of -4 (mean -3.74) on weekdays and -5 (mean -4.4) on weekends [adjusted mean difference: -0.44 ($p < 0.0001$)]. After implementation of the protocol, there was an increase in the mean RASS on weekdays of 0.88 ($p < 0.0001$), and on weekends of 1.20 ($p < 0.0001$). Both SICU and MICU showed similar trends. Figure 1 shows the mean daily RASS score for mechanically-ventilated patients in the MICU and SICU pre/post implementation of the protocol.

The incidence of delirium in the pre-protocol period was 23.0% (14/61) and the prevalence was 66.7% (94/141). Post protocol, the incidence and prevalence of delirium were 19.6% (33/168) and 55.3% (167/302), respectively. Although incidence did not change significantly, prevalence changed significantly from pre to post-protocol implementation periods (incidence; *p*: 0.58; prevalence; *p*: 0.02). Coma prevalence did not decrease significantly [pre-protocol: 78.2% (205/262), post-protocol: 73.4% (323/440); *p*: 0.15]. When both delirium and coma were considered together as acute brain dysfunction, the prevalence decreased from 90.8% (238/262) in the pre-protocol period to 85% (374/440) in the post-protocol phase (*p*: 0.02; unadjusted odds-ratio=0.571). After adjusting for age, race, gender, severity of illness, primary diagnosis, and ICU unit, the odds-ratios post-protocol relative to pre-protocol were: incident delirium 0.718 (95% CI: 0.326-1.578; *p*: 0.40); prevalent delirium 0.650 (95% CI: 0.413-1.022; *p*: 0.06); coma 0.659 (95% CI: 0.446-0.974; *p*: 0.04); acute brain dysfunction 0.505 (95% CI: 0.299-0.853; *p*: 0.01). The number of days on mechanical ventilation post-protocol was higher compared to pre-protocol (median pre: 4; post: 5; mean pre: 6.1, post: 7.1, adjusted *p*: ≤ 0.01). There were no differences in hospital length of stay (median pre: 14 days; post: 14 days, *p*: 0.56), and in-hospital mortality (pre: 19.5%; post: 19.6%, *p*: 0.97).

Discussion

Implementation of a “Wake Up and Breathe Program” at our local hospital resulted in an improvement in overall RASS scores, the primary target that the implementation team wanted to achieve. The program was not able to reduce incidence or ICU-acquired delirium, but showed a trend towards reducing prevalent delirium among mechanically ventilated critically ill patients. Even though coma prevalence decreased after implementation of the protocol; the duration of mechanical ventilation was increased. These results demonstrate that implementing a sedation vacation and spontaneous breathing program as pioneered by Girard et al.[7] may be feasible in a real world setting, but may not be able to provide similar results as seen in the original trial. The effect sizes of interventions found in tightly controlled research environments could be substantially attenuated when implemented in a complex clinical setting.

Critical illness subjects patients to extreme stressors both directly through physiological derangements, and indirectly through life-sustaining interventions such as mechanical ventilation. To reduce the anxiety and pain associated with critical illness, sedation and analgesia are frequently employed in mechanically ventilated patients for patient comfort, ease of care, and safety.[3] A liberal sedation strategy results in an overuse of these agents with an increase in oversedation, acute brain dysfunction, and ICU and hospital length of stay.[4-7] Instituting a “sedation vacation” strategy in the ICUs may be beneficial in countering the adverse effects associated with indiscriminate sedative usage.[6,7] Similar strategy employed at our institution showed an improvement in the overall RASS scores. As we did not have drug dispensing data we cannot attribute the RASS improvement to a decrease in sedative exposure, but based on prior literature,[6,7] this seems to be the most plausible explanation. The RASS scores though improved after the QI project, still remained in the deeply sedated range. This is a cause for concern as there is data reflecting the impact of deeper sedation on patient outcomes.[11] This prompted the implementation team to start a

checklist project to impress upon the ICU multidisciplinary team the importance of adhering to national sedation guidelines. In order to achieve the desired RASS targets, more frequent monitoring of RASS levels (every 4 hours) by the nursing personnel have been introduced in the local ICU. Our project was not able to decrease the hospital length of stay as seen in the original ABC trial[7] and on the contrary increased the duration of mechanical ventilation. The reasons behind the increased mechanical ventilation duration are unclear and could reflect conservative practice pattern at our institute. Instead of our daily awakening approach, utilizing a protocolized analgesia, sedation, and delirium approach may have produced different results as shown in the studies by Skrobik[12] and Mehta et al.[13] The other potential explanations include the differences between a real life implementation as compared to a rigorous clinical trial, and differences in patient populations. No hospital mortality benefit was observed which was consistent with the ABC trial results.[7]

Our QI project has several limitations. 1) Due to the pre-post design, we could not definitively attribute the improvement in the sedation scores and acute brain dysfunction to our implementation project. An inherent risk in conducting time-dependent studies is that the changes observed are a function of time and are not related to the intervention. Analysis of our data did not show a simple linear time-trend, making it more likely that our positive findings were attributable to our intervention. 2) We did not have the drug dispensing data, necessary to show that the protocol actually reduced the drug exposure. 3) Our study was conducted at a single site, so the results may not be generalizable. 4) We did not collect data on failed spontaneous awakening and spontaneous breathing attempts; therefore adherence to the intervention could not be reported.

The strengths of the project include: 1) We were able to implement a research protocol in a real world setting thus demonstrating the feasibility. 2) We had a robust data collection by utilizing an ongoing clinical study. 3) RASS and CAM-ICU were administered twice daily. 4) We enrolled a diverse patient population including females and African American patients.

Conclusion

Implementing a “Wake-up and Breathe Program” resulted in less sedation but was not able to reduce incident or prevalent delirium.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Appendix 1: Wake-Up and Breathe Protocol

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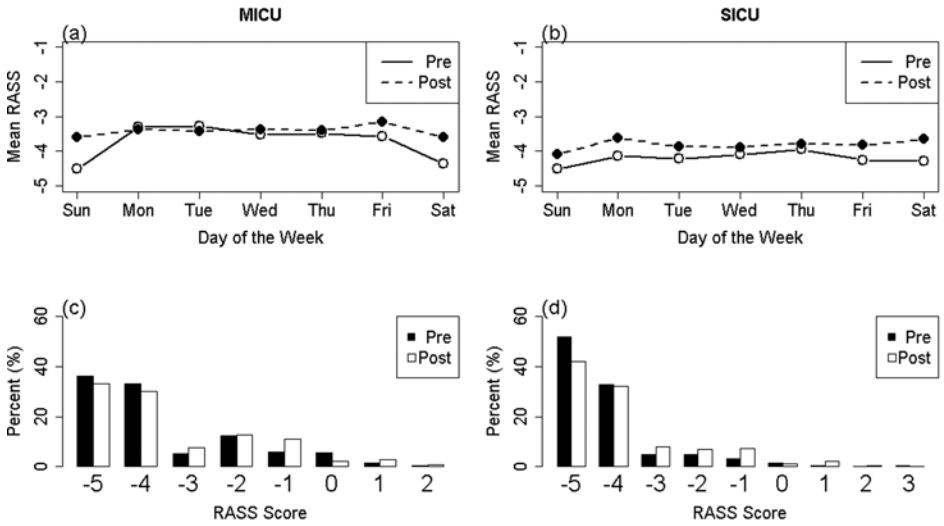

Figure 1.

Mean daily RASS scores (1a, b), and their frequencies (1c, d) pre and post implementation of wake up and breathe protocol in MICU and SICU.

Table 1

Baseline Patient Characteristics

Patient Characteristics	Overall	Pre-protocol Implementation (Control group)	Post-protocol Implementation (Intervention group)	*p* value
Admissions (n)	702	262	440	--
Age[1](years)	55.7 (15.4)	55.4 (14.9)	55.9 (15.8)	0.711
Females[2]	343 (48.9%)	123 (47.0%)	220 (50.0%)	0.434
African Americans[2]	307 (43.7%)	109 (41.6%)	198 (45.0%)	0.380
APS[1*]	10.7 (5.3)	10.6 (5.2)	10.7 (5.3)	0.797
MICU[2#]	484	177 (67.6%)	307 (69.8%)	--
SICU[2+]	218	85 (32.4%)	133 (30.2%)	--
RASS[†] screens	3902	1262	2640	--
RASS screens per admission[3]	4 (2-8)	3 (2-7)	4 (2-9)	0.010
Principal Diagnoses[2]				0.022
Sepsis/Septic shock	186 (26.5%)	58 (22.1%)	128 (29.1%)	
Acute Respiratory Failure	156 (22.2%)	52 (19.9%)	104 (23.6%)	
Trauma	93 (13.3%)	31 (11.8%)	62 (14.1%)	
Neurologic[±]	80 (11.4%)	29 (11.1%)	51 (11.6%)	
Surgery[a]	42 (6%)	21 (8%)	21 (4.8%)	
Congestive heart failure/myocardial infarction	33 (4.7%)	18 (6.9%)	15 (3.4%)	
Gastrointestinal[€]	23 (3.3%)	11 (4.2%)	12 (2.7%)	
Malignancy	19 (2.7%)	10 (3.8%)	9 (2.1%)	
Substance abuse	18 (2.6%)	11 (4.2%)	7 (1.6%)	
Other[£]	52 (7.4%)	21 (8%)	31 (7.1%)	

[1] Reported as Mean (standard deviation), *p*-value from 2-sample *t*-test

[2] Reported as Count (percent), *p*-value from Chi-square test

[3] Reported as Median (IQR), *p*-value from Wilcoxon Rank Sum test

[*] APS: Acute Physiology Score derived from Acute Physiology and Chronic Health Evaluation Score (APACHE)-III

[#] MICU: Medical Intensive Care Unit

[+] SICU: Surgical Intensive Care Unit

[†] RASS: Richmond Agitation Sedation Scale

[±] Includes seizures, ischemic cerebrovascular accident, altered mental status, subarachnoid, subdural, epidural and intracerebral hemorrhages

[a] Includes abdominal, thoracic, and vascular procedures

[€] Includes hepatitis, gastric ulcer, gastrointestinal hemorrhage

[£] Includes burns, diabetic ketoacidosis, renal failure, angioedema