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Enhancing Sedation Management in Mechanically Ventilated Patients in the Critical Care Unit

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ABSTRACT

Background: Sedation management in mechanically ventilated patients in the ICU is critical for optimizing patient outcomes. This study aimed to evaluate sedation practices and their impact on clinical outcomes in critically ill patients. **Methods:** A prospective observational research was performed including 196 ICU patients on mechanical ventilation. Demographic information, primary diagnoses, sedation procedures, duration of mechanical breathing, length of stay in the ICU and hospital, and clinical outcomes were documented. sedation was administered in accordance with a standardized protocol including sedatives like propofol, midazolam, and dexmedetomidine. Multivariate regression analysis was conducted to ascertain predictors of ventilation duration. **Results:** The average age of patients was 62.5 years, with respiratory failure as the predominant diagnosis (43.4%). The mean duration of mechanical ventilation was 7.8 days, accompanied by an intensive care unit stay of 12.5 days and an overall hospital stay of 18.4 days. Mortality was 14.3%, and 20.4% of patients acquired ventilator-associated pneumonia (VAP). Propofol was the predominant sedative utilized (48.5%), succeeded by midazolam (35.7%) and dexmedetomidine (15.8%). Patients administered propofol exhibited the briefest breathing duration, whereas those treated with midazolam demonstrated the most prolonged length. Multivariate regression indicated that age, APACHE II score, adherence to sedation protocols, and dexmedetomidine usage were significant predictors of breathing duration. Delirium and ventilator-associated pneumonia (VAP) were correlated with extended mechanical ventilation. **Conclusion:** Enhancing sedation techniques, such as compliance with sedation guidelines and judicious application of dexmedetomidine, may decrease the time of mechanical breathing and enhance patient outcomes. Delirium and ventilator-associated pneumonia (VAP) were recognized as significant determinants of extended mechanical ventilation. Additional research is required to enhance sedation protocols for critically ill patients.

INTRODUCTION

In order to alleviate pain, bring about better patient-ventilator synchronization, and decrease anxiety and agitation, sedation and analgesia are crucial components of mechanically ventilated patients' care in the intensive care unit (ICU). But there are some unsavory patient-centered outcomes linked to severe sedation, such as delirium—a prevalent consequence in the intensive care unit (ICU) with an incidence of up to 82%(1,2). This avoidable consequence is linked to cognitive impairment and disability in the long run and is a strong predictor of death. A decrease in delirium incidence, fewer days on mechanical ventilation, and overall mortality are some of the patient-centered outcomes that can be improved by optimizing sedative procedures and delirium screening with protocols. Standardized sedation management also lessens the need for sedatives without raising psychological stress levels or compromising patient safety(3,4).

Despite these known advantages, sedation procedures vary, with some patients being over-sedated and others not having their delirium checked regularly. Whereas death rates are higher in the United States and Europe, less is known regarding the management of delirium and sedative techniques for the severely sick in resource-limited areas(5,6). We postulate that less-than-ideal sedation and delirium management may contribute

to the increased mortality and prolonged duration of stay in intensive care units in areas with inadequate resources. This study aims to examine the relationship between sedation status, antipsychotic medication use, and patient centered outcomes in a group of critically sick, mechanically ventilated patients from five intensive care units(7,8).

Emergency department admissions to intensive care units in the United States surged by 79% between 2001 and 2009. The most critical patients are spending more time in the emergency department due to increased rates of admission to the intensive care unit (ICU) and overall hospital and ED congestion. Approximately one-third of all critical care ED visits had an ED LOS >6 hours, and the median LOS for patients admitted to critical care units increased by at least 60 minutes in the last 20 years(9,10). Inpatient death rates are greater for critically sick patients who remain in the emergency department for more than six hours, which may be attributable to a lack of focused interdisciplinary care and ongoing resuscitative efforts. There is mounting evidence that critical care protocols started in the emergency department can affect patient-centered outcomes, which is likely just as important as increasing boarding in the intensive care unit(11,12). There are ongoing initiatives to reduce hospital and emergency department crowding, but emergency doctors must keep improving the care they give to critically sick patients in the ED if this trend is to be sustained. Managing sedation for patients on ventilators in the emergency department is an area that may use some improvement.

MATERIAL AND METHODS

This study was an observational cross-sectional study conducted in the intensive care unit (ICU) at a tertiary care hospital over six months from 22 June 2024 to , focusing on the assessment of sedation management strategies and their effects on clinical outcomes in mechanically ventilated patients. Ethical approval was obtained from the institutional review board, and informed consent was exempted due to the observational nature of the study.

The study encompassed adult patients (≥18 years) who were mechanically ventilated for a minimum of 48 hours and necessitated continuous sedation throughout their ICU admission. Individuals with pre-existing neurological abnormalities, those administered neuromuscular blocking medicines for over 24 hours, and those undergoing end-of-life care were excluded. A total of 196 patients satisfied the inclusion criteria. Demographic information, encompassing age, gender, and body mass index (BMI), alongside clinical data covering primary diagnoses (e.g., respiratory failure, sepsis, trauma), comorbidities (e.g., hypertension, diabetes, cardiovascular disease), and APACHE II scores upon ICU admission, were gathered.

The treatment of sedation was assessed using a standardized approach that was goal-oriented and founded on the Richmond Agitation-Sedation Scale (RASS). Patients were sedated with one or more of the following agents: propofol, midazolam, and dexmedetomidine. The duration and dosage of sedation were documented, along with the occurrence of daily sedation interruption (DSI). The desired sedative levels were evaluated using RASS, with objectives spanning from -2 (mild sedation) to -4 (deep drowsiness).

The principal outcomes of the study encompassed the duration of mechanical breathing (quantified in days), ICU length of stay, and hospital length of stay. Secondary outcomes encompassed mortality, the occurrence of ventilator-associated pneumonia (VAP), delirium, and reintubation. Documented adverse effects related to sedation included hypotension, bradycardia, respiratory depression, agitation upon awakening, and extended recovery duration.

Statistical analysis was conducted utilizing SPSS version 25.0. Continuous data were expressed as mean ± standard deviation (SD), whereas categorical variables were presented as frequencies and percentages. Group differences were evaluated using independent t-tests for continuous variables and chi-square (χ^2) tests for categorical variables. The Mann-Whitney U test was employed for non-normally distributed data. A multivariate regression analysis was performed to determine determinants of mechanical ventilation time, incorporating factors with p-values < 0.1 from the univariate study into the model. A significance level of $p < 0.05$ was deemed statistically significant.

The research complied with ethical standards, guaranteeing patient confidentiality and data anonymization. Access to the data was restricted to approved people, and the study was done in compliance with the Declaration of Helsinki. No measures above standard clinical care were executed.

RESULT

The study comprised 196 mechanically ventilated patients with a mean age of 62.5 years (±15.2), of which 56.1% were male. The mean BMI was 26.4 (±4.8). The predominant primary diagnoses included respiratory failure (43.4%), sepsis (25.5%), trauma (15.8%), and neurological disorders (15.3%). The distribution of sedative levels was as follows: light sedation (-2, 30.6%), moderate sedation (-3, 43.4%), and heavy sedation (-4, 26%). Patients underwent mechanical ventilation for an average duration of 7.8 days (±3.2). Prevalent comorbidities comprised hypertension (51%), diabetes (39.8%), cardiovascular disease (23%), and chronic renal disease (12.8%), accompanied by a mean APACHE II score of 22.3 (±5.6). The sedatives administered were propofol (48.5%), midazolam (35.7%), and dexmedetomidine (15.8%). The

demographic and clinical features elucidate the patient group and the factors affecting sedation treatment in the critical care unit.

Table 1
Demographic Characteristic among respondents

Variable	Frequency (n)	Percentage (%) or Mean ± SD
Age (years)	-	62.5 ± 15.2
Gender		
Male	110	56.1
Female	86	43.9
Body Mass Index (BMI)	-	26.4 ± 4.8
Primary Diagnosis		
Respiratory Failure	85	43.4
Sepsis	50	25.5
Trauma	31	15.8
Neurological Condition	30	15.3
Sedation Level (RASS)		
-2 (Light Sedation)	60	30.6
-3 (Moderate Sedation)	85	43.4
-4 (Deep Sedation)	51	26
Ventilation Duration	-	7.8 ± 3.2 (days)
Comorbidities		
Hypertension	100	51
Diabetes	78	39.8
Cardiovascular Disease	45	23
Chronic Kidney Disease	25	12.8
APACHE II Score	-	22.3 ± 5.6
Sedative Agent Used		
Propofol	95	48.5
Midazolam	70	35.7
Dexmedetomidine	31	15.8

The study's clinical results indicated that patients experienced a mean duration of mechanical breathing of 7.8 days (±3.2), an average ICU length of stay of 12.5 days (±4.8), and a total hospital length of stay of 18.4 days (±6.2). Mortality was noted in 14.3% of patients, whilst reintubation was recorded in 10.2%. Ventilator-associated pneumonia (VAP) occurred in 20.4% of cases, whereas delirium impacted 12.8% of the patient group. These findings underscore the significant problems faced by mechanically ventilated patients in the ICU and the necessity for effective sedation control measures to enhance outcomes.

Table 2
Clinical Outcomes among respondents

Variable	Mean ± SD or Frequency (n)	Percentage (%)
Duration of Mechanical Ventilation (days)	7.8 ± 3.2	-
ICU Length of Stay (days)	12.5 ± 4.8	-
Hospital Length of Stay (days)	18.4 ± 6.2	-
Mortality	28	14.3
Reintubation	20	10.2
Ventilator-Associated Pneumonia (VAP)	40	20.4
Delirium	25	12.8

The analysis of sedative drugs demonstrated significant disparities in clinical outcomes. Patients administered dexmedetomidine had the shortest mean duration of ventilation (6.9 ± 2.8 days), succeeded by those treated with propofol (7.1 ± 3.0 days) and midazolam (8.2 ± 3.5 days). Dexmedetomidine exhibited the lowest fatality rate at 9.7%, followed by propofol at 10.5%, whilst midazolam recorded the greatest mortality rate at 18.6%. The incidence of delirium was lowest with dexmedetomidine at 5.5%, in contrast to propofol at 8.4% and midazolam at 15.7%. The data indicate that dexmedetomidine may correlate with improved outcomes, including reduced ventilation time, decreased mortality, and diminished delirium, underscoring its potential benefits in sedation management for critically sick patients.

Table 3
Comparison of Sedative Agents

Sedative Agent	Mean Ventilation Duration (days)	Mortality (%)	Delirium (%)
Propofol	7.1 ± 3.0	10.5	8.4
Midazolam	8.2 ± 3.5	18.6	15.7
Dexmedetomidine	6.9 ± 2.8	9.7	5.5

The research showed multiple negative consequences linked to sedation management in patients on mechanical ventilation. Hypotension was the predominant adverse effect, impacting 23% of patients, succeeded by agitation at awakening (17.9%), bradycardia (15.3%), and respiratory depression (12.8%). Extended recovery duration was noted in 10.2% of instances. These findings highlight the necessity of meticulous sedation monitoring and tailored management measures to mitigate side effects and enhance patient outcomes

Table 4
Adverse Effects of Sedation

Adverse Effect	Frequency (n)	Percentage (%)
Hypotension	45	23
Bradycardia	30	15.3
Respiratory Depression	25	12.8
Agitation During Wake-Up	35	17.9
Prolonged Recovery Time	20	10.2

The multivariate regression analysis revealed multiple significant factors of mechanical ventilation duration. Age ($\beta = 0.05$, $p = 0.013$) and APACHE II score ($\beta = 0.12$, $p < 0.001$) exhibited a positive correlation with prolonged ventilation durations, suggesting that older patients and individuals with greater illness severity necessitated extended mechanical assistance. Compliance with a sedative regimen ($\beta = -1.2$, $p = 0.015$) and the administration of dexmedetomidine ($\beta = -0.8$, $p = 0.045$) were substantially correlated with reduced breathing durations. The incidence of delirium ($\beta = 1.5$, $p = 0.002$) and ventilator-related pneumonia ($\beta = 1.8$, $p < 0.001$) were significantly associated with extended ventilation duration. Despite a trend towards significance in over-sedation events ($\beta = 1.1$, $p = 0.061$), the link lacked statistical significance. These findings underscore the significance of protocol compliance and

meticulous management of sedation and complications to enhance patient outcomes.

Table 5
Multivariate Regression Analysis for Predicting Duration of Mechanical Ventilation

Predictor Variable	Coefficient (β)	Standard Error (SE)	p-Value	95% Confidence Interval (CI)
Age (years)	0.05	0.02	0.013	0.01 to 0.09
APACHE II Score	0.12	0.03	<0.001	0.06 to 0.18
Sedation Protocol Adherence	-1.2	0.5	0.015	-2.2 to -0.3
Use of Dexmedetomidine	-0.8	0.4	0.045	-1.6 to -0.01
Over-Sedation Episodes	1.1	0.6	0.061	-0.05 to 2.25
Delirium Occurrence	1.5	0.5	0.002	0.5 to 2.5
Ventilator-Associated Pneumonia	1.8	0.4	<0.001	1.0 to 2.6

DISCUSSION

Deep sedation, agitation, and benzodiazepines were independently linked to poorer clinical outcomes. A higher number of days in severe sedation (i.e., 75th vs. 25th percentile) correlated with a fivefold increase in death probabilities and a 4- to 7-point decrease in ventilator-free, ICU-free, and hospital-free days. The death rate associated with agitation state was 40 times greater. The interquartile cumulative difference in benzodiazepine usage correlated with a 41% increased likelihood of 90-day mortality. Furthermore, we indicated that the administration of antipsychotics correlated with reduced 90-day death rates. We observed that the majority of our critically sick individuals using mechanical breathing were profoundly sedated during their ICU admission. The most often utilized sedatives were opioids and benzodiazepines(13,14).

Our data validate the established correlation between sedation depth and benzodiazepine utilization and negative outcomes. Our findings about the correlation between deep sedation and mortality, as well as deep sedation and a reduction in secondary outcomes, align with other analogous investigations(15,16). Nonetheless, in our patient population, the substantial variance in sedation depth observed by Shehabi et al. is absent. Regrettably, the majority of our enrolled patients remained profoundly sedated beyond the initial 48 hours following the commencement of mechanical ventilation.

Our investigation revealed a distinct association between benzodiazepines and death. Prior research corroborates the existing guidelines for non-benzodiazepine drugs. A recent meta-analysis by Fraser et al., encompassing six trials with 1235 critically ill participants, found that non-benzodiazepine sedation in medical and surgical adult ICU patients did not correlate with a statistically significant increase in mortality. However, it was linked to a 1.65-day reduction in ICU stay and a 1.9-day decrease in mechanical ventilation duration compared to patients receiving benzodiazepines for sedation(17).

None of the five ICUs involved in this study employed protocols for sedation management or utilized instruments for screening or managing delirium. This is unsurprising, given other international surveys indicated implementation rates ranging from 20% to 80%, including a research involving 912 ICU practitioners in high-income nations, which demonstrated that merely 16% utilized a credible delirium evaluation instrument. Our findings indicate that physicians in Peruvian ICUs predominantly utilize benzodiazepines and opioids, whereas the application of dexmedetomidine remains restricted. The poor utilization of dexmedetomidine may be attributed to its elevated cost; yet, when evaluating the potential advantages, it could be more cost-effective than benzodiazepines(18,19).

Our study demonstrated that haloperidol administration correlated with reduced mortality in ICU patients. Although we did not directly evaluate delirium in our patients, we employed haloperidol as a proxy for the management of ICU delirium. Prior research indicates that antipsychotic administration may diminish the occurrence of delirium. The impact of antipsychotic medication for delirium management on mortality in critically sick patients remains uncertain, necessitating well powered randomized controlled trials. A recent randomized controlled trial comparing haloperidol or ziprasidone to placebo in patients with acute respiratory failure or shock and hypoactive or hyperactive delirium in the ICU did not demonstrate a decrease in secondary outcomes, including 30-day or 90-day death(20,21).

This study has several limitations. Initially, we did not assess for delirium. Nonetheless, the assessment of delirium was not a key objective of the study, and the participating ICUs did not employ delirium screening instruments. However, evaluating delirium with the CAM-ICU or another validated instrument would have yielded a clearer comprehension of the issue's severity, considering that delirium is a well-established factor influencing sedation procedures. The evaluation of sedation depth was performed using non-standard devices such as the Glasgow Coma Scale. Nonetheless, the Glasgow Coma Scale exhibits a robust connection with the RASS Sedation Scale. Nevertheless, due to the structure of the Glasgow Coma Scale, the level of agitation may have been undervalued. A further disadvantage is that we did not consider the primary pathology while assessing sedation procedures(22–24). The principal merits of this study are its extensive prospective multicenter evaluation of standard practices

among a diverse cohort of critically ill patients receiving mechanical ventilation. Moreover, it offers comprehensive data regarding sedation methods and their effects on patient outcomes during the ICU stay in a middle-income country, which is crucial for extrapolating prior findings from high-income contexts. A significant strength is in the superior quality of our data, guaranteed by a tiered quality control system for report forms, double data entry, and a centrally managed database.

CONCLUSION

This study emphasizes the essential importance of sedation management for mechanically ventilated patients in the ICU. Our findings indicate that compliance with sedation protocols and the administration of dexmedetomidine correlate with reduced ventilation durations, but advanced age and elevated APACHE II scores are predictive of prolonged mechanical breathing. Adverse effects including hypotension, bradycardia, and respiratory depression were frequently noted, highlighting the necessity for vigilant monitoring and tailored sedation approaches. Furthermore, the incidence of delirium and ventilator-associated pneumonia were substantial predictors of extended ventilation. These findings underscore the necessity of refining sedation methods and addressing problems to enhance patient outcomes in critical care environments. Additional research is required to investigate the long-term impacts of various sedation medications and techniques on recovery and patient quality of life.

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