

**PHARMACY-LED CONTINUOUS SEDATION STOP PROCEDURE AFFECT ON VENTILATION DAYS**

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**Abstract**

**Introduction**

The use of sedation medications in intensive care units (ICUs) has been common practice to alleviate patient stress and prevent agitation-related harm. Current guidelines prioritize pain management before sedation and recommend light sedation levels, spontaneous awakening trials (SATs), and limited use of benzodiazepines for better outcomes. This study aims to assess the impact of reinforcing SATs and utilizing a multifaceted approach involving analgesic and anxiolytic medications on mechanical ventilation duration in the ICU.

**Methodology**

This study is a retrospective chart review comparing two different groups from January 2019 to December 2019 and from January 2022 to November 2022. The primary outcome is the duration of mechanical ventilation. Secondary outcomes assessed include: all-cause mortality, Confusion Assessment Method (CAM) positive days, continuous sedation duration, ICU length of stay, proportion of patients achieving desired sedation (RASS -1 to +1), and number of patients requiring restart of continuous sedation. Patients were eligible for inclusion if they were mechanically ventilated and on continuous sedation medication for > 48 hours, while exclusion criteria covered various factors.

**Results**

The study included 326 patients in the final analysis. No statistically significant difference was found for the primary outcome of mechanical ventilation days after the initiation of the procedure (5.60 vs. 5.37, p = 0.498). For secondary outcomes we found a significant difference in the number of patients achieving RASS off continuous sedation (8% vs. 40%, p = < 0.001), continuous sedation days (4.96 vs. 3.70, p = < 0.001), and total sedation hours (121.79 vs. 95.47, p = 0.002). Additionally, our study also found a lower rate of propofol use (78.5% vs. 63.8%, p = 0.05) after the initiation of our stop procedure.

**Conclusion**

The duration of mechanical ventilation days was no different between the pre- and post-procedure groups. A significant difference was found in select secondary outcomes. We were able to detect a difference in RASS achieved off continuous sedation, continuous sedation days, total sedation hours, and propofol use. The results of this study show that with this pharmacy-led procedure, there is significantly less continuous sedation medication use.

**Introduction**

The use of sedation medications in an intensive care unit (ICU) setting has been common practice for years. Sedatives have frequently been used to help alleviate a patient’s stress and anxiety from being mechanically ventilated while helping to prevent patient harm from agitation. Current Critical Care Medicine: Pain, Agitation/Sedation, Delirium, Immobility, and Sleep Disruption (PADIS) guidelines recommend that pain be managed first prior to the use of a sedative agent to reach sedation goals. Additionally, PADIS guidelines suggest using light levels of sedation, spontaneous awakening trials (SAT), and limiting the use of benzodiazepines to improve short-term outcomes such as ICU length of stay and mechanical ventilation duration.1

The Richmond Agitation-Sedation Scale (RASS) is used to assess the level of sedation/agitation of a patient with a goal of -1 to +1 being targeted for “light sedation”. Common sedation practice generally utilizes the use of multiple medications with different mechanisms of action to achieve this endpoint. These medications may include propofol, dexmedetomidine, midazolam, lorazepam, and ketamine. In general, these drugs are titrated and adjusted to meet the sedation goals set forth by the care team. Prolonged use of continuous sedation is associated with an increase in time spent on mechanical ventilation, which extends ICU length of stay.2 Daily sedation interruption or SAT is defined as a period of time in which a patient's continuous sedation is paused and the patient can be woken up. It has been found that when a SAT was performed it led to a shorter duration of continuous sedation and a decrease in mechanical ventilation duration.3

In a study done in 2010 by Strøm, T., et al it was found that a protocol of no sedation for critically ill patients receiving mechanical ventilation had positive outcomes.4 Results from the 2010 trial included a decreased length of stay in the ICU as well as a decrease in days spent mechanically ventilated. However, in a more recent study, a plan of no sedation was found to show no difference in outcome results.5

The aim of this project was to examine the impact of reinforcing the use of SATs and implementing a multifaceted approach, which includes IV push and oral analgesic and anxiolytic medication, on the duration of mechanical ventilation in the ICU.

**Methods**

A continuous sedation stop procedure was implemented at St. Rose Dominican Hospital - Siena Campus ICU in June 2021. The procedure involved the active involvement of a pharmacist who identified patients receiving continuous sedation and reviewed critical care pain observation (CPOT) scores, Richmond Agitation-Sedation Scale (RASS) assessments, sedation drip rates, use of as-needed pain/anxiety medications, and exclusion criteria. Eligible patients were then discussed with the licensed independent provider for a decision regarding the suspension of continuous sedation. If approved, the continuous infusion was discontinued, and the nursing team was encouraged to achieve RASS goals using as-needed pain and anxiety medications.

For this retrospective chart review study, patient records from two different time periods were compared: January 2019 to December 2019 and January 2022 to November 2022. Patient records were identified using a Cerner report. The inclusion criteria encompassed patients who were mechanically ventilated and had received continuous sedation medication for a duration exceeding 48 hours. The continuous sedation agents utilized in this study consisted of dexmedetomidine, fentanyl, hydromorphone, ketamine, midazolam, and propofol. Patients were excluded if they had a chronic ventilation status with a tracheostomy, expired before day 3, had high ventilator settings (FiO2 > 80%, PEEP > 10) on day 3, underwent induced hypothermia, received a neuromuscular blockade infusion, were pending comfort care, underwent prone positioning, were admitted for seizures, or were admitted for substance withdrawal.

The primary outcome of interest in this study was the duration of mechanical ventilation days. Additionally, several secondary outcomes were assessed, including all-cause mortality, the number of days with positive Confusion Assessment Method (CAM) scores, the number of days under continuous sedation, the total number of days spent in the ICU, the proportion of patients who achieved the desired level of sedation (RASS -1 to +1), and the number of patients who required the restarting of continuous sedation.

**Statistical Analysis**

Statistical analyses were performed using appropriate methods for parametric and nonparametric values. Parametric values were compared using two-sided t-tests, while nonparametric values were compared using Fisher's exact or chi-square tests, as deemed appropriate.

To determine the required sample size for adequate statistical power, power calculations were conducted. Based on assumptions of an 80% power level and a significance threshold of p < 0.05, it was estimated that a sample size of 456 patients would

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|  | **Pre-Procedure****(n = 163)** | **Post-Procedure****(n = 163)** | **P Value** |
| **Characteristics** |  |  |  |
| Age – years, mean (SD) | 69 (14.5) | 70 (14.9) | 0.746 |
| Male – sex, n (%) | 87 (53.4) | 84 (51.5) | 0.739 |
| BMI – kg/m2, mean (SD) | 27.8 (7.7) | 28.9 (8.1) | 0.225 |
| APACHE II score, mean (SD) | 21.8 (6.8) | 23.2 (7.3) | 0.81 |
| COVID positive, n (%) | 0 (0) | 38 (23.3) | < 0.001 |
| **Table 1: Baseline characteristics on admission to the ICU** |
|  |
|  | **Pre-Procedure****(n = 163)** | **Post-Procedure****(n = 163)** |
| **Type of Admission, n (%)** |  |  |
| MedicalAcute surgicalElective surgical | 147 (90.1)12 (7.4)4 (2.5) | 153 (93.9)9 (5.5)1 (0.6) |
| **Admitting Diagnosis, n (%)** |  |  |
| RespiratorySepsisCardiovascularNeurologicGastrointestinalMetabolic/EndocrineTraumaOther | 58 (35.6)40 (24.5)23 (14.1)19 (11.7)12 (7.4)4 (2.5)0 (0)5 (3.1) | 66 (40.5)25 (15.3)30 (18.4)21 (12.9)8 (4.9)6 (3.9)1 (0.6)5 (3.1) |
| **Table 2: Baseline ICU admission type and admitting diagnosis**  |

**Results**

A total of 326 patients were included in the final analysis of this study. Baseline characteristics, as presented in Table 1, were well balanced between the study groups, except for the identification of COVID-positive patients, which differed significantly (0% vs. 23.3%, p < 0.001). The majority of ICU admissions were medical (90.1% vs. 93.9%), with respiratory causes being the most common (35.6% vs. 40.5%), as shown in Table 2. Regarding the primary outcome of mechanical ventilation days, no statistically significant difference was found between the two groups after the initiation of the continuous sedation stop procedure (5.60 vs. 5.37, p = 0.498).

However, notable differences were observed in several secondary outcomes. Specifically, there was a significant difference in the proportion of patients achieving the desired Richmond Agitation-Sedation Scale (RASS) scores after discontinuation of continuous sedation (8% vs. 40%, p < 0.001). Furthermore, the intervention group had significantly fewer continuous sedation days (4.96 vs. 3.70, p < 0.001) and lower total sedation hours (121.79 vs. 95.47, p = 0.002) compared to the pre-procedure group (Table 3).

In terms of other secondary outcomes, as shown in Table 3, no significant differences were observed between the pre- and post-procedure groups. Additionally, our study revealed a lower rate of propofol use after the initiation of the continuous sedation stop procedure (78.5% vs. 63.8%, p = 0.005), as presented in Table 4.

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| --- | --- | --- | --- |
|  | **Pre-Procedure****(n = 163)** | **Post-Procedure****(n = 163)** | **P Value** |
| **Primary Outcome** |  |  |  |
| Mechanical ventilation days, mean (SD) |  5.60 (3.2) |  5.37 (3.1) |  0.498 |
| **Secondary Outcomes**  |  |  |  |
| All-cause mortality, n (%) | 23 (14) | 21 (13) | 0.871 |
| CAM positive days, mean (SD) | 6.82 (4.2) | 6.85 (3.8) | 0.953 |
| ICU days, mean (SD) | 8.52 (4.1) | 8.07 (4) | 0.322 |
| RASS achieved off continuous sedation, n (%) | 13 (8) | 65 (40) | < 0.001 |
| Continuous sedation days, mean (SD) | 4.96 (3.4) | 3.70 (2.9) | < 0.001 |
| Continuous sedation restarted, n (%) | 6 (3.7) | 12 (7.4) | 0.145 |
| Total sedation hours, mean (SD) | 121.79 (81.9) | 95.47 (72) | 0.002 |
| **Table 3: Outcomes** |
|  | **Pre-Procedure****(n = 163)** | **Post-Procedure****(n = 163)** | **P Value** |
| **Continuous Sedation Medication Used, n (%)** |
| Fentanyl | 163 (100) | 163 (100) | 1.00 |
| Dexmedetomidine | 116 (71.2) | 100 (61.3) | 0.079 |
| Propofol | 128 (78.5) | 104 (63.8) | 0.005 |
| Benzodiazepine | 23 (14.1) | 19 (11.7) | 0.620 |
| Ketamine | 2 (1.2) | 5 (3.1) | 0.448 |
| **Table 4: Medication use** |

**Discussion**

The findings of this project indicate that the pharmacist-led continuous sedation stop procedure had limited effects on mechanical ventilation days. Similarly, all-cause mortality, CAM positive days, ICU days, and the number of patients restarted on continuous sedation did not differ significantly between the groups. However, positive outcomes were observed in terms of achieving a desired RASS score off continuous sedation, reduced continuous sedation days, and decreased total sedation hours. These results suggest that a procedure emphasizing the use of spontaneous awakening trials (SATs) may have beneficial effects on sedation medication use. Interestingly, a decrease in the use of propofol was incidentally discovered following the initiation of the stop procedure. However, it is important to note that sedation selections are based on provider preference rather than being procedure-driven, which could have influenced this finding.

One notable difference in baseline characteristics was the incidence of COVID-19. Although this was an expected difference between the two study groups, it is believe that patients identified with COVID-19 did not significantly contribute to the differences in mechanical ventilation days due to the defined exclusion criteria.

 It is crucial to acknowledge the limitations of this study. Firstly, the desired statistical power could not be achieved after screening for exclusion criteria, which restricts the ability to draw definitive conclusions regarding the significant impact of the procedure on mechanical ventilation duration in critically ill patients. Secondly, the results hindered on the accuracy and consistency of start times for sedation and mechanical ventilation were dependent on the documentation entered by the nursing staff. Thirdly, data on total amounts of each medication was not collected, which may have been a miss opportunity to further assess the impact of this pharmacist-led procedure. Finally, documentation of SATs was inconsistent between the two study groups, which might have affected the interpretation of our findings. Before the initiation of the procedure, there was no standardized SAT time, and documentation of SATs was not consistently performed.

In conclusion, this study provides insights into the effects of a continuous sedation stop procedure on various outcomes in critically ill patients receiving mechanical ventilation. While there was no significant difference observed in mechanical ventilation days or other major outcomes, positive outcomes were evident in terms of achieving desired RASS scores off continuous sedation and reducing sedation medication use. Further studies with larger sample sizes are warranted to validate these findings and overcome the limitations identified in this study.

**Conflicts of Interest**

The author has no conflicts of interest to declare.

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