Toward less sedation in the intensive care unit: A prospective observational study

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Keywords: Sedation; Mechanical ventilation; Intensive care; Length of stay

Abstract

Purpose: Excessive sedation is associated with prolonged mechanical ventilation and longer intensive care unit (ICU) and hospital stays. We evaluated the feasibility of using minimal sedation in the ICU.

Methods: Prospective observational study in a university hospital 34-bed medico-surgical department of intensive care. All adult patients who stayed in the ICU for more than 12 hours over a 2-month period were included. Intensive care unit admission diagnoses, severity scores, use of sedatives and/or opiates, duration of mechanical ventilation, length of ICU stay, and 28-day mortality were recorded for each patient.

Results: Of the 335 patients (median age, 61 years) admitted during the study period, 142 (42%) received some sedation, most commonly with midazolam and propofol. Sedative agents were administered predominantly for short periods of time (only 10% of patients received sedation for longer than 24 hours). One hundred fifty-five patients (46%) received mechanical ventilation, generating 15,240 hours of mechanical ventilation, of these, only 2,993 (20%) hours were accompanied by a continuous sedative infusion. Self-extubation occurred in 6 patients, but only 1 needed reintubation.

Conclusions: In a mixed medical-surgical ICU, minimal use of continuous sedation seems feasible without apparent adverse effects.

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1. Introduction

Administration of sedative drugs is often considered to be a standard part of the routine care of critically ill patients, primarily to improve comfort, to facilitate mechanical ventilation, and to minimize physical and psychological stress [1,2]. Benzodiazepines and propofol are the most frequently used sedative agents, especially in Europe [1,3].

Oversedation is associated with detrimental effects, including prolonged mechanical ventilation, longer intensive care unit (ICU) and hospital stays, and the need for unnecessary neurological imaging to investigate supposed coma [4,5]. To minimize problems of oversedation, recent strategies have included daily sedation interruption, use of sedation scales, and nurse-implemented algorithms [5-8]. Nevertheless, surveys still report that a considerable number of critically ill patients are deeply sedated [9], and the frequency of sedative use in mechanically ventilated patients has increased in the last few years [10].

We challenge the routine use of sedative agents in acutely ill patients. A minimal sedation strategy could reduce neuromuscular weakness, facilitate early mobilization, and
ameliorate long-term psychological outcomes [11]. We, therefore, conducted an observational study to report on the feasibility and safety of limiting sedation throughout the ICU stay.

2. Patients and methods

All patients older than 18 years who stayed for more than 12 hours in the 34-bed mixed ICU of our tertiary university hospital during a 2-month period (December 1, 2008–January 31, 2009) were included in this prospective, observational study. The study was approved by the institutional review board, and because of its purely observational nature, the need for informed consent was waived.

Current sedation and analgesia practice in our unit involves a continuous infusion of midazolam or propofol as the most commonly used sedative agents, but diazepam is used in alcohol withdrawal syndromes. Morphine is the standard drug for analgesia. Wherever possible, patients receive a trial of acetaminophen or nonsteroidal anti-inflammatory drugs to control pain before opiate administration. Remifentanil is preferred in patients with severe renal or liver dysfunction. Although decisions concerning sedation/analgesia management are left to the discretion of the attending physician, indications for sedation in each patient are critically discussed during morning and evening rounds. Discontinuation of sedation is encouraged whenever possible, and especially in patients who are not likely to require a surgical or invasive procedure, patients not receiving neuromuscular blocking agents or therapeutic hypothermia, and patients without seizures or uncompensated intracranial pressure. Sedation scores were not computed in this study because we do not use them routinely in our department. Sedation is titrated to patient needs according to the principles included in the Feeding, Analgesia, Sedation, Thromboembolic Prophylaxis, Head of Bed Elevation, Stress Ulcer Prevention, and Glucose Control [FAST HUG] mnemonic [12], which encourages use of sedation to keep patients calm, collaborative, and comfortable. Visits by family members are allowed between 12:30 and 19:30 everyday. We have no stepdown units in our hospital and no significant limitations for ward discharge.

Volume-controlled ventilation and pressure support are the preferred modes in patients receiving invasive mechanical ventilation in our department. Patients are considered for weaning from invasive mechanical ventilation whenever they meet all the following criteria: control of the disease process that necessitated mechanical ventilation; conscious and able to protect the upper airway; PaO2/FiO2 ratio greater than 200 mm Hg; positive end-expiratory pressure less than 5 cm H2O; normal pH; and hemodynamic stability. Patients are then submitted to a spontaneous breathing trial using a T-piece for 30 minutes (FiO2, 0.5) and extubated immediately if there are no signs of intolerance as suggested by a respiratory rate greater than 35 breath/min, SpO2 greater than 90%, respiratory acidosis, tachycardia, severe arterial hypertension, or physical signs of respiratory distress [13].

Use of sedatives and/or opiates was recorded everyday for each patient. When sedatives were used, the type, dose (total and maximum daily dose), duration, and predominant mode of administration (continuous or intermittent bolus) were recorded. The number of hours during which a patient received mechanical ventilation but did not have continuous sedation was called “time free of sedation.” Indications for sedation were classified and recorded as early postoperative period, severe respiratory failure (PaO2/FiO2 <200 in the presence of FiO2 >0.5), hemodynamic instability, high intracranial pressure, seizures, therapeutic hypothermia, uncontrolled psychomotor agitation, withdrawal syndrome (defined as the acute onset of symptoms including dysphoria, insomnia, anxiety, irritability, nausea, agitation, tachycardia, hypertension, in patients with abusive use of alcohol, sedatives, opiates or stimulants [14]), end-of-life care, invasive procedures, and others. The use of a single bolus dose of sedative (usually etomidate) to facilitate endotracheal intubation was not considered as sedation for the purposes of this study. Administration of opiate analgesic agents was recorded with information on type, duration, dose (total and maximum daily dose), and mode of administration.

The main ICU admission category was recorded as medical, surgical, or nonsurgical trauma. Patient disease severity was defined by the Acute Physiology and Chronic Health Evaluation (APACHE) II score [15] and the Sequential Organ Failure Assessment (SOFA) score [16] from the first 24 hours of ICU stay. Duration of invasive mechanical ventilation, vasoactive drug administration, and renal replacement therapy were recorded for the first 28 days of the ICU stay. Total length of stay and 28-day ICU mortality were recorded. Unplanned self-extubation was noted.

Statistical analysis was carried out using SPSS 17.0 statistical package software (SPSS Incorporation, Chicago, Ill) and GraphPad Prism software (GraphPad Software, San Diego, Calif). Continuous variables are expressed as median and interquartile range (25%-75%) and categorical variables as n (%). After exclusion of normal distribution of the data by a Kolmogorov-Smirnov test, nonparametric tests were used (Mann-Whitney U test for 2 independent-samples and Kruskal-Wallis H test for several independent-samples with the Dunn multiple comparison post hoc test). Continuous variables with normal distribution were analyzed by the t test. For categorical variables a χ² or Fisher exact test was applied. A survival analysis was used to calculate the length of stay in patients with continuous and intermittent sedation. A Cox proportional regression analysis was performed to analyze the effect, adjusted for age, APACHE II and SOFA score on ICU admission, of sedation (continuous or intermittent) on ICU mortality. A logistic multivariate analysis was performed to define the independent variables associated with use of sedation. Variables considered for the
model were sex, APACHE II and SOFA scores, use of mechanical ventilation, use of norepinephrine, and renal replacement therapy, and they were introduced into the multivariate model if significantly associated with the use of sedation on a univariate basis at a $P$ value less than .2. Differences were considered significant if $P < .05$.

3. Results

3.1. In the whole cohort

A total of 512 patients were admitted to the ICU during the study period; 177 were excluded because of age greater than 18 years ($n = 28$) or ICU stay shorter than 12 hours ($n = 149$). The clinical data of the 335 patients studied are presented in Table 1. One hundred fifty-five (46%) patients were treated with mechanical ventilation during their ICU stay. One hundred forty-two patients (42%) received some sedation at some time during their ICU stay, predominantly patients who were treated with mechanical ventilation ($131/155$ [85%]). Sedative drugs were predominantly administered by continuous infusion (continuous in 122 [86%] patients and intermittent in 20 [14%]). Use of continuous sedation was more frequent in mechanically ventilated patients than in patients not receiving mechanical ventilation ($92\%$ vs $18\%$, $P < .001$) and in patients with than without acute respiratory distress syndrome ($19\%$ vs $0\%$, $P = .04$). Intermittent sedation (exclusively with benzodiazepines) was used for the treatment of withdrawal syndrome (7), control of severe agitation (2), to perform short-term procedures (8), and briefly in the postoperative period (3).

Using a survival analysis, the median ICU length of stay was longer in patients who received continuous sedation than in those who received intermittent sedation (24 [95% confidence interval (CI), 12-36] days vs 16 [95% CI, 8-24] days, log rank $P < .01$). In the Cox regression analysis, when adjusted for age, SOFA, and APACHE II scores on admission, patients who received continuous sedation had a greater risk of death than those who received intermittent sedation (hazard ratio, 2.82 [95% CI, 0.66-12]; $P = .16$).

Midazolam and propofol were used in 53% and 49% of patients, respectively. Propofol was preferred in surgical

### Table 1  Characteristics of the study population

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total population</th>
<th>No sedatives during ICU stay (n = 193)</th>
<th>Sedatives during ICU stay (n = 142)</th>
<th>$P$ value (sedatives vs no sedatives)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male, n (%)</td>
<td>191 (57)</td>
<td>104 (54)</td>
<td>87 (61)</td>
<td>.18</td>
</tr>
<tr>
<td>Age (y)</td>
<td>61 (48-73)</td>
<td>61 (47-72)</td>
<td>61 (51-73)</td>
<td>.39</td>
</tr>
<tr>
<td>Body mass index</td>
<td>25 (23-29)</td>
<td>24 (22-29)</td>
<td>26 (23-29)</td>
<td>.04</td>
</tr>
<tr>
<td>Type of admission, n (%)</td>
<td></td>
<td></td>
<td></td>
<td>.23</td>
</tr>
<tr>
<td>Medical</td>
<td>128 (38)</td>
<td>77 (40)</td>
<td>51 (36)</td>
<td></td>
</tr>
<tr>
<td>Surgical</td>
<td>183 (55)</td>
<td>99 (51)</td>
<td>84 (59)</td>
<td></td>
</tr>
<tr>
<td>Trauma (nonsurgical)</td>
<td>24 (7)</td>
<td>17 (9)</td>
<td>7 (5)</td>
<td></td>
</tr>
<tr>
<td>Morbid conditions</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systemic arterial hypertension, n (%)</td>
<td>115 (34)</td>
<td>67 (35)</td>
<td>48 (34)</td>
<td>.86</td>
</tr>
<tr>
<td>Diabetes mellitus, n (%)</td>
<td>63 (19)</td>
<td>34 (18)</td>
<td>29 (20)</td>
<td>.52</td>
</tr>
<tr>
<td>Coronary artery disease/heart failure, n (%)</td>
<td>69 (21)</td>
<td>29 (15)</td>
<td>40 (28)</td>
<td>.003</td>
</tr>
<tr>
<td>Chronic renal failure, n (%)</td>
<td>35 (10)</td>
<td>24 (12)</td>
<td>11 (08)</td>
<td>.17</td>
</tr>
<tr>
<td>Chronic obstructive lung disease, n (%)</td>
<td>50 (15)</td>
<td>27 (14)</td>
<td>23 (16)</td>
<td>.58</td>
</tr>
<tr>
<td>Immunosuppression, n (%)</td>
<td>73 (22)</td>
<td>45 (23)</td>
<td>28 (20)</td>
<td>.43</td>
</tr>
<tr>
<td>Cirrhosis, n (%)</td>
<td>39 (12)</td>
<td>23 (12)</td>
<td>16 (11)</td>
<td>.86</td>
</tr>
<tr>
<td>Sepsis, n (%)</td>
<td>78 (23)</td>
<td>40 (21)</td>
<td>38 (27)</td>
<td>.20</td>
</tr>
<tr>
<td>Acute respiratory distress syndrome, n (%)</td>
<td>23 (7)</td>
<td>0 (0)</td>
<td>23 (16)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Altered mental status, n (%)</td>
<td>117 (35)</td>
<td>60 (31)</td>
<td>57 (40)</td>
<td>.09</td>
</tr>
<tr>
<td>Glasgow coma scale (points)</td>
<td>15 (13-15)</td>
<td>15 (14-15)</td>
<td>15 (10-15)</td>
<td>.005</td>
</tr>
<tr>
<td>Serum bilirubin (mg/dL)</td>
<td>0.8 (0.5-1.2)</td>
<td>0.8 (0.5-1.0)</td>
<td>0.9 (0.5-1.4)</td>
<td>.049</td>
</tr>
<tr>
<td>Serum creatinine (mg/dL)</td>
<td>0.8 (0.6-1.2)</td>
<td>0.8 (0.6-1.1)</td>
<td>0.9 (0.6-1.4)</td>
<td>.01</td>
</tr>
<tr>
<td>$\text{PaO}_2/\text{FiO}_2$</td>
<td>280 (180-420)</td>
<td>370 (239-430)</td>
<td>230 (147-330)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>APACHE II score</td>
<td>15 (10-22)</td>
<td>13 (9-19)</td>
<td>18 (13-25)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Length of ICU stay (d)</td>
<td>2 (1-4)</td>
<td>1 (1-3)</td>
<td>3 (1-8)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Use of mechanical ventilation, n (%)</td>
<td>155 (46)</td>
<td>24 (12)</td>
<td>131 (92)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Duration of mechanical ventilation (d)</td>
<td>0 (0-2)</td>
<td>0 (0-0)</td>
<td>2 (1-4)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Use of norepinephrine, n (%)</td>
<td>67 (20)</td>
<td>11 (0.6)</td>
<td>56 (39)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Use of renal replacement therapy, n (%)</td>
<td>19 (6)</td>
<td>8 (4)</td>
<td>11 (8)</td>
<td>.16</td>
</tr>
<tr>
<td>ICU mortality, n (%)</td>
<td>32 (10)</td>
<td>4 (2)</td>
<td>28 (20)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

*Data are presented as number (%) or median (25%-75% interquartile range).*
patients (96%), whereas midazolam was more frequently used in medical patients (63%). The most common indications for sedation were during early postoperative surveillance (50%), for severe respiratory failure (20%), during short-term procedures (20%), and for withdrawal syndrome (10%) (Table 2). Patients with severe respiratory failure received sedatives for the longest duration, followed by postoperative patients and patients who were hemodynamically unstable (Fig. 1). In the group of patients who received some sedation, the median duration of sedation was 8 (2-23) hours, and only 34 (10%) patients received continuous sedation for more than 24 hours. Despite a greater severity of disease on admission, patients admitted for medical diagnoses did not receive more sedative drugs than those admitted postoperatively or after trauma. More opiates were administered in surgical than in medical patients (Table 3).

### 3.2. In mechanically ventilated patients

The main differences in sedation and analgesia practices in ventilated and nonventilated patients are presented in Table 4. As expected, patients receiving invasive mechanical ventilation were sicker on ICU admission (APACHE II 18 [13-26] vs 12 [8-18] points, \( P < .001 \) and SOFA 6 [4-9] vs 3 [1-5] points, \( P < .001 \)), stayed longer in the ICU (3 [1-7] vs 1 [1-2] days, \( P < .001 \)), and had higher mortality rates (19% vs 2%, \( P < .001 \)) than nonmechanically ventilated patients.

The total cumulative time on invasive mechanical ventilation for all patients was 15 240 hours; only 2993 (20%) hours were associated with administration of a continuous infusion of a sedative agent, and patients spent a median of 88% (68%-98%) of their time on mechanical ventilation without continuous sedation. Patients ventilated for a period longer than 6 hours spent 76% of their time on mechanical ventilation without continuous sedation. Patients who received mechanical ventilation for between 24 and 72 hours (the period of the ICU stay when patients are most critically ill) spent about 75% of the time without sedation (Fig. 2A). The percentage of time on mechanical ventilation without continuous sedation was independent of the length of ICU stay (varying from 73% to 80% (\( P = .99 \)) (Fig. 2B). There was no difference in the duration of mechanical ventilation without continuous sedation according to admission category (medical 74% vs surgical 77%, \( P > .27 \)). There was also no correlation between the time on mechanical ventilation without continuous sedation and the severity of disease on admission as assessed by the APACHE II (Spearman \( \rho = 0.032, P = .70 \)) or the total SOFA (Spearman \( \rho = -0.035, P = .67 \)) scores. When only patients who received continuous sedation for more than 3 hours (excluding the time spent on sedation for end-of-life support) were considered, the total cumulative time spent on mechanical ventilation with sedation was 2819 (19%) hours, corresponding to a median of 94% (71%-100%) of hours on mechanical ventilation without sedation for each patient.

In multivariate regression analysis, in addition to invasive mechanical ventilation (odds ratio, 70.2 [95% CI, 30.8-160]), only the use of norepinephrine (odds ratio, 6.3 [95% CI, 1.8-22.2]) was independently associated with use of sedation.

### 3.3. Safety, analgesia, and neuroleptics

Self-extubation occurred in 6 patients, but only 1 was reintubated within the subsequent 48 hours. Haloperidol was administered in only 14 subjects of the whole cohort, more frequently in the group who received sedatives than in those who did not receive sedatives (7% vs 2%, \( P = .03 \)). Morphine was used in 54% of patients and remifentanil in 13%. Significantly more opiates were administered in surgical than in medical patients (Table 3). Analgesic opiates were more commonly used in sedated patients (83% vs 52%, \( P < .001 \)), in whom they were predominantly given by continuous infusion, whereas in nonsedated patients analgesics were predominantly given as intermittent bolus doses (81% vs 19%, \( P < .001 \)). Combined infusion of opiates and sedatives was administered in 69% of mechanically ventilated patients (Table 4).

### 4. Discussion

In the present observational study in a mixed medical-surgical critically ill population, about 80% of the time on mechanical ventilation was achieved without continuous sedative administration regardless of the severity of illness. Even for patients receiving mechanical ventilation for between 24 and 72 hours, when they are most critically ill, about 75% of the time on mechanical ventilation was without
Less sedation in the ICU

sedation. These findings speak against a dilutional effect caused by the presence of “short- or long-stayers” on mechanical ventilation, which could potentially skew the results. Our results contrast with those of Weinert and Calvin [17], who reported that sedatives were used in 85% of hours of mechanical ventilation in their mixed medical-surgical ICU population.

Heavy sedation remains common practice in the ICU [9] despite increasing evidence of potentially hazardous consequences [5,18]. Sedative use has consistently been associated with increased lengths of ICU stay and duration of mechanical ventilation, risks of delirium, and unnecessary scans to investigate persistent coma [5,18,19]. In addition, sedation increases the risks of neuromyopathy and may contribute to persistence of shock [11,20]. Efforts aimed at reducing sedation load in the ICU have been proposed, such as use of sedation scales, daily interruption of sedative agents, use of sedative agents with short half-lives, intermittent administration of sedatives, and nurse/pharmacist-driven protocols [5-8,18,21]. Multidisciplinary team approaches, involving physicians, nurses, physiotherapists, and pharmacists are also recommended to optimize sedative management [6,22-24]. However, these measures have not been widely incorporated into daily practice [9], in part

Fig. 1  Cumulative time (hours) on sedation for each indication of sedation.

Table 3  Main differences according to admission categories

<table>
<thead>
<tr>
<th></th>
<th>Medical (n = 128)</th>
<th>Surgical (n = 183)</th>
<th>Nonsurgical trauma (n = 24)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male, n (%)</td>
<td>79 (62)</td>
<td>99 (54)</td>
<td>13 (54)</td>
<td>.39</td>
</tr>
<tr>
<td>Age (y)</td>
<td>64 (50-74)</td>
<td>59 (47-71)</td>
<td>55 (34-74)</td>
<td>.13</td>
</tr>
<tr>
<td>SOFA (first ICU day) (points)</td>
<td>6 (3-8)</td>
<td>3 (1-6)</td>
<td>3 (1-4)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>APACHE II (points)</td>
<td>21 (15-26)</td>
<td>13 (9-16)</td>
<td>13 (6-19)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Length of ICU stay (d)</td>
<td>3 (1-5)</td>
<td>1 (1-3)</td>
<td>2 (1-3)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>ICU mortality, n (%)</td>
<td>20 (16)</td>
<td>11 (6)</td>
<td>1 (4)</td>
<td>.01</td>
</tr>
<tr>
<td>Duration of mechanical ventilation (d)</td>
<td>0 (0-3)</td>
<td>1 (0-1)</td>
<td>0 (0-0)</td>
<td>.03</td>
</tr>
<tr>
<td>Use of norepinephrine, n (%)</td>
<td>31 (24)</td>
<td>35 (19)</td>
<td>1 (4)</td>
<td>.07</td>
</tr>
<tr>
<td>Use of renal replacement therapy, n (%)</td>
<td>13 (10)</td>
<td>6 (3)</td>
<td>0</td>
<td>.02</td>
</tr>
<tr>
<td>Use of opiates</td>
<td>47 (37)</td>
<td>127 (69)</td>
<td>10 (42)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Duration (h)</td>
<td>0 (0-4)</td>
<td>7 (0-24)∗</td>
<td>0 (0-7)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Use of sedative drugs</td>
<td>51 (40)</td>
<td>84 (46)</td>
<td>7 (29)</td>
<td>.23</td>
</tr>
<tr>
<td>Duration (h)</td>
<td>0 (0-8)</td>
<td>0 (0-5)</td>
<td>0 (0-2)</td>
<td>.31</td>
</tr>
</tbody>
</table>

Data presented as number (%) or median (25%-75% interquartile range).
∗ P < .05 vs medical and nonsurgical trauma (analysis by Dunn multiple comparison post hoc test).
because of the common belief that sedation can improve comfort and tolerance to mechanical ventilation.

There have been concerns related to possible long-term consequences of sedative limitation practices, for example, an increased risk of psychological distress or posttraumatic stress disorder (PTSD) [25]. We did not specifically study this question; however, PTSD has been associated more frequently with heavy sedation and lack of recall [26], and a strategy of daily interruption of sedation was associated with a lower incidence of PTSD and a better psychosocial adjustment to illness score in a long-term follow-up [27]. Treggiari et al [28] showed that light sedation tended to be less associated with PTSD and memory disturbances than a deep sedation strategy, in addition to reducing ICU days and time on invasive ventilation. A recent follow-up of part of the population included in the Awakening and Breathing Controlled trial showed that there was no greater risk for PTSD and cognitive or functional outcomes at 3 and 12 months in critically ill patients submitted to a combined protocol of daily sedation interruption and spontaneous breathing test [29]. Interestingly, this protocol resulted in greater survival rates at 1 year after ICU discharge [18]. In our study, longer ICU lengths of stay and higher mortality rates were observed in patients who received continuous sedation compared with those who received intermittent sedation. This is in agreement with results from the study by Kollef et al [4], in which the duration of mechanical ventilation and lengths of ICU and hospital stays were longer in patients who received continuous sedation compared with those who received intermittent sedation.

Limitation of sedative infusion may facilitate early mobilization and rehabilitation in mechanically ventilated patients, which can reduce neuromuscular complications related to critical illness and reduce the incidence of delirium [11,30]. Recently, Strom et al [31] reported the effects of a “no sedation” vs a daily sedation interruption routine in a prospective randomized study. These authors found that the no-sedation strategy was associated with a shorter period on mechanical ventilation and a significant reduction in ICU and hospital lengths of stay, but with a higher frequency of delirium. More patients in the no-sedation group needed extra staff to help reassure and comfort them than did patients in the control group (11 vs 3 patients, $P = .02$). Assessment of the longer-term effects of sedationless strategies is needed to fully evaluate this issue.

The primary indications for prolonged sedation remain severe hypoxemic respiratory failure and uncontrolled agitation. Sedation is also often required for induced hypothermia (for postanoxic brain damage) and some cases

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**Table 4** Sedation and analgesia data in mechanically ventilated and nonmechanically ventilated patients

<table>
<thead>
<tr>
<th></th>
<th>No mechanical ventilation (n = 180)</th>
<th>Mechanical ventilation (n = 155)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sedation</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Strategy of sedation</td>
<td>Continuous</td>
<td>2 (1)</td>
<td>120 (77)</td>
</tr>
<tr>
<td></td>
<td>Intermittent</td>
<td>9 (5)</td>
<td>11 (7)</td>
</tr>
<tr>
<td>Type of sedative drug</td>
<td>Midazolam</td>
<td>6 (3)</td>
<td>70 (45)</td>
</tr>
<tr>
<td></td>
<td>Propofol</td>
<td>1 (1)</td>
<td>68 (44)</td>
</tr>
<tr>
<td></td>
<td>Diazepam</td>
<td>9 (5)</td>
<td>7 (5)</td>
</tr>
<tr>
<td></td>
<td>Thiopental</td>
<td>0</td>
<td>2 (1)</td>
</tr>
<tr>
<td>Duration of sedation</td>
<td>0 (0-0)</td>
<td>5 (1-18)</td>
<td></td>
</tr>
<tr>
<td>Sedative max dose</td>
<td>Midazolam (mg/h)</td>
<td>2.5 (2-3)</td>
<td>5 (2.5-10)</td>
</tr>
<tr>
<td></td>
<td>Propofol (mg/h)</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td>Sedative total dose</td>
<td>Midazolam (mg)</td>
<td>3.5 (3-4)</td>
<td>74.5 (18-178)</td>
</tr>
<tr>
<td></td>
<td>Propofol (mg)</td>
<td>40</td>
<td>470 (240-1170)</td>
</tr>
<tr>
<td><strong>Analgesia</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Strategy of analgesia</td>
<td>Continuous</td>
<td>15 (8)</td>
<td>108 (70)</td>
</tr>
<tr>
<td></td>
<td>Intermittent</td>
<td>71 (39)</td>
<td>25 (16)</td>
</tr>
<tr>
<td>Type of analgesic drug</td>
<td>Morphine</td>
<td>65 (36)</td>
<td>115 (74)</td>
</tr>
<tr>
<td></td>
<td>Remifentanil</td>
<td>0</td>
<td>42 (27)</td>
</tr>
<tr>
<td></td>
<td>Fentanyl</td>
<td>0</td>
<td>1 (1)</td>
</tr>
<tr>
<td></td>
<td>Paracetamol</td>
<td>88 (49)</td>
<td>60 (39)</td>
</tr>
<tr>
<td></td>
<td>Others a</td>
<td>8 (4)</td>
<td>7 (11)</td>
</tr>
<tr>
<td>Duration of analgesia</td>
<td>0 (0-2)</td>
<td>19 (3-41)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Analgesia max dose</td>
<td>Morphine (mg/h)</td>
<td>2 (2-2)</td>
<td>2 (2-4)</td>
</tr>
<tr>
<td></td>
<td>Remifentanil (mg/h)</td>
<td>0</td>
<td>0.5 (0.2-1.1)</td>
</tr>
<tr>
<td>Analgesia total dose</td>
<td>Morphine (mg)</td>
<td>8 (3.5-17)</td>
<td>67 (25.5-162)</td>
</tr>
<tr>
<td></td>
<td>Remifentanil (mg)</td>
<td>0</td>
<td>24 (22.1-99.1)</td>
</tr>
<tr>
<td>Coinfusion of sedation and opiates</td>
<td>0 (0)</td>
<td>96 (62)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

Data are presented as n (%) or median (25%-75% interquartile range). NA indicates not applicable; max: maximum.

a Nonsteroidal anti-inflammatory drugs, tramadol.
of intracranial hypertension. Although a less common indication, uncontrolled agitation in the absence of withdrawal syndromes may be even less common with more personalized care, reassurance, implementation of nonverbal communication tools, early recognition and effective delirium treatment, and optimization of analgesia [6,24].

Adequate pain management remains of paramount importance in all critically ill patients, and one must...
recognize that analgesic agents including morphine and remifentanil also have some sedative properties. Morphine was the preferred opiate agent in our population followed by remifentanil, and these agents were used mostly in surgical patients. Sixty-two percent of patients received combined sedation and opiate infusion during their time on mechanical ventilation, and this may have contributed to the low use of sedatives we observed, because opiates have recognized sedative properties.

For a strategy of less or no sedation to be effective, patient-focused, personalized care is required [6]. A strategy of sedative limitation may increase the risk of undersedation, and clinicians need to be aware of the early signs of inadequate sedation. Nonpharmacological approaches that can be used to maximize patient comfort include appropriate lighting, noise reduction, and provision of music, television, or light reading (Fig. 3) [32]. Good communication between the patient and staff is essential to address any concerns the patient may have and to provide reassurance. Extended visiting hours may decrease delirium and help in a patient’s sense of well-being [33]. Importantly, few spontaneous extubation events were observed and only 1 patient needed to be reintubated. Although the number of reintubations was less than expected, we can hypothesize that the low sedation rate may have contributed to a greater preservation of respiratory muscle strength and to better conscious levels, contributing to the low rate of self-extubations.

Our study has several limitations, including its observational nature. This obviously resulted in some imbalances in the baseline characteristics of patients who received sedatives and those who did not. However, it was a prospective analysis, and such observational data are important in informing about current practice and in generating hypotheses for future studies. Second, we analyzed a heterogeneous population of patients, rather than any specific subgroup, because we wanted to represent as closely as possible the situation on a “real-life” general ICU. Third, we recognize that the lack of a validated sedation scale to quantitate the level of sedation was a limitation, especially as a substantial proportion of patients received opiates, which have sedative properties. In addition, some of the sedative agents used may have prolonged effects after infusions are stopped because of slow metabolism in critically ill patients [34]. However, in our department, a deliberate decision was made not to adopt sedation scales because we prefer to encourage frequent discussions about the adequacy of sedation among staff using the FAST HUG approach [12] rather than rely on scales. Fourth, a no-sedation strategy requires a dedicated multidisciplinary team with a high staff/patient ratio, as demonstrated in the study by Strom et al [31], and this may not be achievable in sites with very high workloads. Finally, we did not report the evolution of disease severity during the ICU stay for our population, which could have influenced sedation use. However, this was not the purpose of our study, which was simply to observe whether minimal sedation is feasible and without major adverse effects. Moreover, delayed extubation was not a problem in our study or at least was similar to other reports in the literature. We noted a median duration of 2 days of invasive mechanical ventilation in the sedated group, which is lower than the duration of 3.5 days (median) reported by Riker et al [19] in their dexmedetomidine group and the 4.9 days reported by Kress et al [5] in their intervention group, although their patients did have a slightly higher APACHE II score (20 vs 18 in our group).

5. Conclusions

In this observational study in a mixed medical-surgical population of critically ill patients, only 10% of patients received sedation for more than 24 hours and more than 80% of the time on mechanical ventilation was without continuous sedation; a minimal sedation strategy, therefore, appears feasible and without major adverse effects. The potential benefits of such an approach include a reduction in the length of ICU stay, reduced duration of mechanical ventilation, less delirium and neuromuscular dysfunction, and improved outcomes, although these factors need to be assessed in future prospective studies.

Acknowledgment

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References


