# Use of Sedatives and Neuromuscular Blockers in a Cohort of Patients Receiving Mechanical Ventilation*

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***Objective:*** **To describe the use of sedatives and neuromuscular blocking agents (NMBs) and their impact in outcome in an international cohort of patients receiving mechanical ventilation.**
***Methods:*** **We analyzed the database of a prospective, multicenter cohort of 5,183 adult patients who received mechanical ventilation for > 12 h. We considered that a patient received a given agent when it was administered for at least 3 h in a 24-h period.**
***Results:*** **A total of 3,540 patients (68%; 95% confidence interval [CI], 67 to 69%) received a sedative at any time while receiving mechanical ventilation. The median number of days of use was 3 (interquartile range [IQR], 2 to 6 days). The persistent use of sedative was associated with more days of mechanical ventilation (median, 4 days [IQR, 2 to 8 days], vs 3 days [IQR, 2 to 4 days] in patients who did not receive sedatives [p < 0.001]); more weaning days (median, 2 days [IQR, 1 to 3 days], vs 2 days [IQR, 1 to 5 days] in patients who did not receive sedatives [p < 0.001]); and longer length of stay in the ICU (median, 8 days [IQR, 5 to 15 days], vs 5 days [IQR, 3 to 9 days] in patients who did not receive sedatives [p < 0.001]). Six hundred eighty-six patients (13%; 95% CI, 12 to 14%) received an NMB for at least 1 day. The median number of days of use was 2 (IQR, 1 to 4 days). The administration of an NMB was independently related with age, a normal previous functional status, main reason of mechanical ventilation (patients with ARDS received more NMBs), and with patient management (patients requiring permissive hypercapnia, prone position, high level of positive end-expiratory pressure, and high airways pressure).**
***Conclusions:*** **The use of sedatives is very common, and their use is associated with a longer duration of mechanical ventilation, weaning time, and stay in the ICU. NMBs are used in 13% of the patients and are associated with longer duration of mechanical ventilation, weaning time, stay in the ICU, and higher mortality.** ***(CHEST 2005; 128:496–506)***

**Key words:** ICU; mechanical ventilation; neuromuscular blocking agents; sedatives

**Abbreviations:** CI = confidence interval; IQR = interquartile range; NMB = neuromuscular blocking agent; OR = odds ratio; PEEP = positive end-expiratory pressure; SAPS = simplified acute physiology score

Sedatives, analgesics, and neuromuscular blocking agents (NMBs) are drugs commonly used in the ICU, mainly in patients requiring mechanical ventilation.[1] Sedatives and analgesics are often used to facilitate patient tolerance of invasive mechanical ventilation. The goals of sedation/analgesia in this context include decreasing pain and anxiety, reducing the stress response, and facilitating nursing care.[2,3] Studies[4–7] have suggested that we need to pay attention to the way we provide sedation/analgesia because of the potential impact on patient outcomes such as length of stay in the ICU, days of mechanical ventilation, and rate of self-extubation.

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Furthermore, the use of sedatives and NMBs have being shown to correlate with the subsequent presence of depression and posttraumatic stress disorder symptoms[8,9] and protracted neuromuscular weakness syndromes.[10]

The current data related to the pattern of use of sedatives, analgesics, and NMBs during mechanical ventilation are limited and derived largely from mail survey reports.[11–16] Only a few studies[17–19] have tracked drug use over time, and then for brief intervals. Recently, Bertolini et al[18] reported on 2,932 patients enrolled in a multicentric study in Italy, and noted that 60% received at least one sedative during the first week in the ICU. Although 51% of the patients in the study were receiving mechanical ventilation at the time of admission to the ICU and 71% received mechanical ventilation at any time during the ICU stay, it is unclear of the type of drugs and pattern of administration in patients receiving mechanical ventilation.

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The main objective of this study is to describe the use of sedatives and NMBs in an international cohort of patients receiving mechanical ventilation. Furthermore, we want to study their impact on patient outcomes such as duration of mechanical ventilation, length of ICU stay, and length of hospital stay. We analyzed the factors associated with their use and the association with selected outcomes, such as duration of mechanical ventilation, weaning, ICU stay, and mortality.

## Materials and Methods

We analyzed the database of a prospective, multicenter, international cohort of 5,183 adult patients who received mechanical ventilation for > 12 h at 361 ICUs in 20 countries.[20] The general physiologic and clinical characteristics of these patients were previously described and reported.[20] The institutional review board at each center approved the study protocol. For the purpose of this study, we collected the following information: demographic data (age, gender, simplified acute physiology score [SAPS] II), previous functional status, medical or surgical condition, date of admission to the ICU, date of initiation of mechanical ventilation, and primary indication for mechanical ventilation: acute on chronic respiratory disease (COPD, asthma, chronic pulmonary disease other than COPD), neurologic disease (coma, neuromuscular disease), or acute respiratory failure (ARDS, postoperative, congestive heart failure, aspiration, pneumonia, sepsis, trauma, cardiac arrest), date of starting weaning of mechanical ventilation, date of extubation, and date and status at discharge from the ICU.

After starting mechanical ventilation, every day for the first 28 days we recorded the use of sedatives, analgesics, and/or NMBs. We considered that a patient received one of these drugs when it was administered for at least 3 h in a 24-h period. The presence or absence of the following variables were evaluated: (1) patient management, including mode or level of ventilatory support (full support defined as ventilation with controlled volume or pressure-controlled modes or when patients received synchronized intermittent mandatory ventilation but mandatory frequency was similar to the total respiratory rate; partial support defined as ventilation with pressure support or synchronized intermittent mandatory ventilation with mandatory frequency lower than total respiratory rate; noninvasive ventilation; inverse ratio ventilation; permissive hypercapnia; prone position; and administration of inhaled nitric oxide); tidal volume (categorized as < 6 mL/kg, from 6 to 10 mL/kg, and > 10 mL/kg); applied positive end-expiratory pressure (PEEP), categorized as < 5 cm $H_2O$, from 5 to 10 cm $H_2O$, and > 10 cm $H_2O$; peak pressure > 50 cm $H_2O$; and plateau pressure > 35 cm $H_2O$; and (2) complications that developed over the course of the mechanical ventilation: ARDS, ventilator-associated pneumonia, sepsis, shock, acute renal failure, hepatic failure, coagulopathy, metabolic acidosis, respiratory acidosis and hypoxemia defined as a ratio of $PaO_2$ to fraction of inspired oxygen < 200 mm Hg. The ARDS, ventilator-associated pneumonia, and sepsis were considered as events only if they appeared > 48 h after mechanical ventilation was started. Each of these conditions has been previously defined.[20] The arterial blood gases corresponded to the values obtained once daily at approximately 8 AM. The ventilator variables corresponded to the time that the arterial blood gases were obtained.

### *Statistical Analysis*

Data are expressed as mean (SD), median (interquartile range [IQR]), or proportions as appropriate. Continuous variables were compared with Student *t* test or Mann-Whitney *U* test if the distribution was nonparametric. Categorical variables were compared using $\chi^2$ test or Fisher Exact Test; all p values are two-sided.

Primary outcome were use of sedatives or NMBs. To estimate the effects of multiple factors on these outcomes, a logistic regression analysis was performed using a backward stepwise selection method. The criterion for entering variables tested in the model were selected at $p < 0.10$. All variables were analyzed separately in three groups: variables previous to start mechanical ventilation (age and SAPS II were dichotomized taking as cut-off point the value that best correlated with the use of sedatives and NMBs), variables related with patient management, and complications appearing during mechanical ventilation. Significant variables ($p < 0.05$) from each group were entered to construct the final model.

Linear regression analysis was used to estimate the adjusted relation between the use of sedatives and NMBs with days of mechanical ventilation, days of weaning, and length of stay in the ICU. Similar methods were used to determine the variables associated to the use of benzodiazepines compared with propofol, taking as cohorts the patients who only received benzodiazepines or only propofol.

## Results

### *Use of Sedatives*

Of the 5,183 ICU patients admitted during the study period, 3,540 patients (68%; 95% confidence interval [CI], 67 to 69%) received a sedative at any time while receiving mechanical ventilation. For these patients, the median number of days receiving a sedative was 3 days (IQR, 2 to 6 days). Figure 1 shows the daily percentage of patients who received

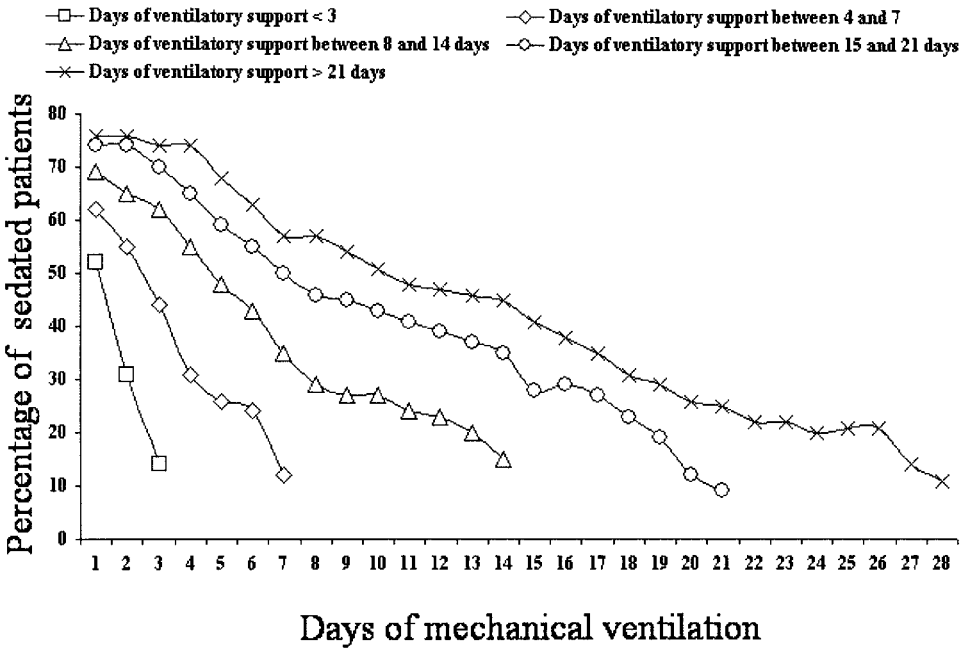


FIGURE 1. Daily use of sedatives drugs according to duration of mechanical ventilation.

a sedative according to the duration of ventilatory support. Since we registered information on sedation for 28 days, we were able to monitor 28,954 patient-days of ICU stay (96% of total). In 16,681 days of mechanical ventilation support, or 58% of the days for all patients, at least one sedative drug was administered. Benzodiazepines were administered for a total of 11,445 patients-days of ventilatory support, propofol for 3,485 patients-days of ventilatory support, and opiates for 10,491 patients-days of ventilatory support.

Most of the patients who did receive sedatives or analgesics (67.2%) received a combination of drugs. The most commonly used combinations were benzodiazepines and opiates (25%), followed by propofol and opiates (6%). Figure 2 shows the daily use of sedatives based on the duration of mechanical ventilation.

*Factors Associated With the Use of Sedatives*

The factors associated with sedative use are shown in Table 1. By multivariate analysis, sedatives were more likely to be administered to Europeans, men, patients aged $< 50$ years, and those in whom the main reason for mechanical ventilation was multiple trauma. Sedation was also independently related with the need of full ventilatory support, ventilation with a tidal volume $< 6$ mL/kg or $> 10$ mL/kg, an applied PEEP $< 5$ cm $H_2O$ or $> 10$ cm $H_2O$, and the administration of an NMB. Finally, sedation was more likely to be used in patients in whom acute sepsis and shock developed over the course of mechanical ventilation.

*Outcomes Associates With the Use of Sedatives*

The use of sedative drugs was associated with more days receiving mechanical ventilation (median, 4 days [IQR, 2 to 8 days], vs 3 days [IQR, 2 to 4 days] in patients who did not receive sedatives [$p < 0.001$]); more weaning days (median, 2 days [IQR, 1 to 5 days], vs 2 days [IQR, 1 to 3 days] in patients who did not receive sedatives [$p < 0.001$]); and longer length of stay in the ICU (median, 8 days [IQR, 5 to 15 days], vs 5 days [IQR, 3 to 9 days] in patients who did not receive sedatives [$p < 0.001$]). After adjusting for other variables, the use of sedatives was independently related with these outcomes ($p < 0.001$). Sedated patients had a higher mortality (33% vs 26.5%), however, the use of sedatives was not independently associated with mortality (odds ratio [OR], 0.89; 95% CI, 0.75 to 1.05; $p = 0.17$)

*Use of NMBs*

Six hundred eighty-six patients (13%; 95% CI, 12 to 14%) received an NMB during the study period for at least 1 day. The median number of days of use of an NMB was 2 (IQR, 1 to 4 days). An NMB was administered in 2,271 days of mechanical ventilation (8% of total days of ventilatory support). Figure 3 shows the

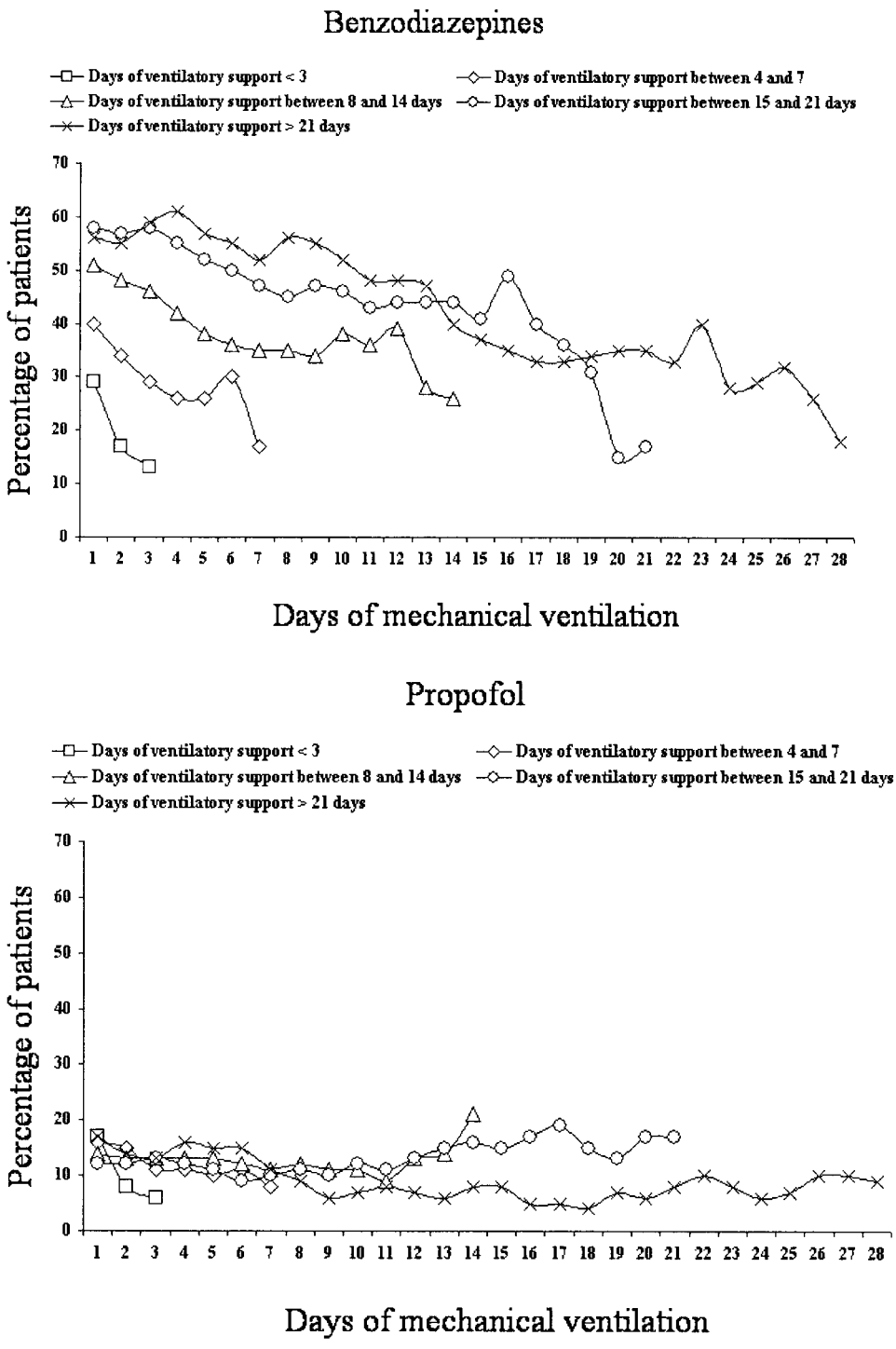


FIGURE 2. Daily use of benzodiacepines and propofol according to duration of mechanical ventilation.

daily percentage of patients receiving an NMB grouped according to the duration of mechanical ventilation.

*Factors Associated With the Use of NMBs*

Table 2 shows the variables associated with the daily use of NMBs. The administration of an NMB was independently related to age (more likely to be used in patients < 50 years old); gender (more common in males); a normal previous functional status; main reason of mechanical ventilation (patients with ARDS received more NMBs, while patients with coma, neuromuscular disease, and postoperative respiratory failure were less likely to receive these agents); with management strategy (patients requiring full ventila-

**Table 1—*Variables Associated With Sedative Use by Univariate and Multivariate Analysis***

| Variables | No. | Use of Sedatives, No. (%) | Univariate Analysis | | Multivariate Analysis | |
|---|---|---|---|---|---|---|
| | | | OR | 95% CI | OR | 95% CI |
| Geographic area | | | | | | |
| Latin America | 1,222 | 684 (56) | 1 | | 1 | |
| United States-Canada | 1,455 | 987 (68) | 1.65 | 1.42–1.94 | 3.60 | 2.77–4.67 |
| Europe | 2,506 | 1,869 (75) | 2.30 | 1.99–2.67 | 4.97 | 3.75–6.58 |
| Age, yr | | | | | | |
| ≥ 50 | 3,675 | 2,449 (66) | 1 | | 1 | |
| 50 | 1,508 | 1,085 (72) | 1.30 | 1.13–1.45 | 1.30 | 1.04–1.64 |
| SAPS II score | | | | | | |
| ≥ 50 points | 1,759 | 1,151 (65) | 1 | | | |
| 50 points | 3,424 | 2,389 (67) | 1.22 | 1.07–1.37 | | |
| Gender | | | | | | |
| Female | 1,985 | 1,267 (64) | 1 | | 1 | |
| Male | 3,198 | 2,273 (71) | 1.39 | 1.23–1.56 | 1.31 | 1.08–1.61 |
| Problem | | | | | | |
| Medical | 3,428 | 2,253 (66) | 1 | | 1 | |
| Surgical | 1,755 | 1,287 (73) | 1.43 | 1.26–1.63 | 2.02 | 1.62–2.51 |
| Previous functional status | | | | | | |
| Limited activity | 2,016 | 1,326 (66) | 1 | | | |
| Normal | 3,167 | 2,214 (70) | 1.20 | 1.07–1.37 | | |
| COPD | 522 | 336 (64) | 0.82 | 0.68–099 | | |
| Coma | 864 | 472 (55) | 0.49 | 0.42–0.57 | 0.47 | 0.36–0.62 |
| Neuromuscular disease | 94 | 48 (51) | 0.48 | 0.32–0.72 | | |
| ARDS | 231 | 201 (87) | 3.24 | 2.19–4.78 | | |
| Postoperative acute respiratory failure | 1,080 | 764 (71) | 1.16 | 1.00–1.33 | | |
| Pneumonia | 721 | 530 (73) | 1.34 | 1.12–1.60 | | |
| Sepsis | 458 | 375 (82) | 2.23 | 1.74–2.85 | | |
| Trauma | 407 | 343 (84) | 2.65 | 2.01–3.48 | 1.58 | 1.04–2.39 |
| Cardiac arrest | 100 | 54 (54) | 0.54 | 0.36–0.80 | | |
| Full ventilatory support | 4,248 | 3,113 (73) | 3.26 | 2.82–3.77 | 63.36 | 43.21–92.92 |
| Partial ventilatory support | 1,677 | 542 (32) | 0.08 | 0.07–0.09 | 0.008 | 0.006–0.012 |
| Tidal volume, mL/kg | | | | | | |
| 6–10 | 2,652 | 1,769 (67) | 1 | | 1 | |
| ≥ 10 | 1,920 | 1,323 (69) | 1.11 | 0.97–1.25 | 1.34 | 1.09–1.65 |
| ≤ 6 | 571 | 498 (71) | 1.25 | 1.02–1.52 | 1.49 | 1.07–2.08 |
| Level of applied PEEP, cm $H_2O$ | | | | | | |
| 5–10 | 1,258 | 623 (49) | 1 | | 1 | |
| ≤ 5 | 2,298 | 1,495 (65) | 1.89 | 1.65–2.18 | 2.86 | 2.27–3.60 |
| ≥ 10 | 745 | 674 (90) | 9.68 | 7.39–12.65 | 5.99 | 4.08–8.78 |
| Noninvasive ventilation | 247 | 74 (30) | 0.18 | 0.14–0.24 | 0.22 | 0.14–0.35 |
| Inverse-relation ventilation | 95 | 88 (93) | 5.96 | 2.75–12.89 | | |
| Permissive hypercapnia | 94 | 89 (95) | 8.45 | 3.43–20.84 | | |
| Prone position | 72 | 70 (97) | 16.55 | 4.05–67.58 | | |
| Nitric oxide inhaled | 54 | 54 (100) | | | | |
| Peak pressure 50 cm $H_2O$ | 207 | 172 (83) | 2.35 | 1.62–3.39 | | |
| Plateau pressure 35 cm of water | 143 | 128 (89) | 4.07 | 2.38–6.97 | | |
| Use of NMBs | 686 | 670 (98) | 23.74 | 14.40–39.12 | 17.81 | 9.23–34.35 |
| Barotrauma | 140 | 116 (83) | 2.28 | 1.47–3.56 | | |
| ARDS during mechanical ventilation | 375 | 345 (92) | 5.81 | 3.40–8.47 | 2.86 | 1.64–4.98 |
| Ventilator-associated pneumonia | 814 | 641 (79) | 1.88 | 1.57–2.25 | | |
| Sepsis during mechanical ventilation | 724 | 626 (86) | 3.39 | 2.71–4.23 | 2.47 | 1.74–3.52 |
| Shock | 1,204 | 980 (81) | 2.42 | 2.07–2.84 | 1.36 | 1.03–1.79 |
| Acute renal failure | 1,029 | 819 (80) | 2.05 | 1.74–2.42 | | |
| Hepatic failure | 340 | 268 (79) | 1.79 | 1.37–2.33 | | |
| Coagulopathy | 580 | 482 (83) | 2.48 | 1.98–3.11 | | |
| Metabolic acidosis | 428 | 330 (77) | 1.62 | 1.28–2.05 | | |
| Respiratory acidosis | 545 | 429 (79) | 1.81 | 1.46–2.25 | | |

tory support, permissive hypercapnia, prone position, high level of PEEP, and high airways pressure were more likely to receive an NMB); and complications during mechanical ventilation (ventilator-associated pneumonia and respiratory acidosis) were the events related with the use of NMBs.

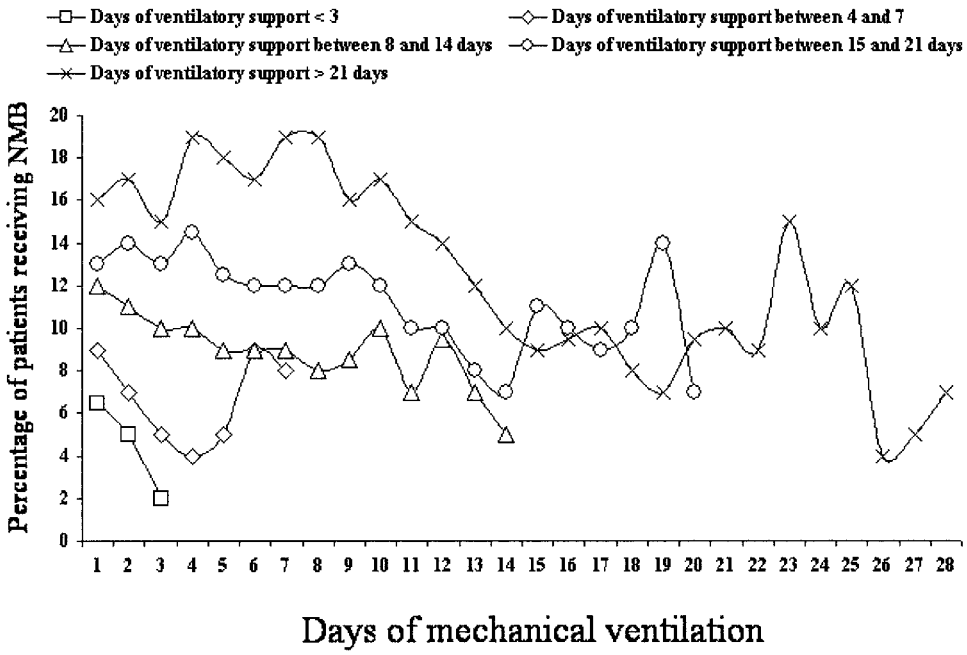


FIGURE 3. Daily use of NMBs according to duration of mechanical ventilation.

*Outcomes Associated With the Use of NMBs*

The use of NMBs was associated with a longer duration of mechanical ventilation (median, 7 days [IQR, 4 to 13 days], vs 3 days [IQR, 2 to 6; $p < 0.001$]); duration of weaning (median, 3 days [IQR, 1 to 6 days], vs 3 days [IQR, 1 to 4; $p < 0,001$]; and stay in the ICU (median, 10 days [IQR, 6 to 19 days], vs 7 days [IQR, 4 to 12 days; $p < 0.001$]). The mortality of patients who received NMBs was 50% (95% CI, 46 to 55%), and the use was independently related with mortality in the ICU (OR, 1.39; 95% CI, 1.08 to 1.79) [$p < 0.001$].

## DISCUSSION

The main findings of this prospective, international, multicentric, observational study are as follows: (1) 68% (3,540 of 5183 patients receiving mechanical ventilation) received a sedative at any time while receiving mechanical ventilation; (2) the persistent use of sedatives was associated with more days of mechanical ventilation, more weaning days, and longer length of stay in the ICU; (3) NMBs were used in 13% (686 of 5,183 patients); and (4) patients requiring NMB has a longer duration of mechanical ventilation, weaning time, ICU stay, and higher mortality.

The use of sedatives and analgesics are very common in the ICU; however, the frequency of use of these medications is not well known. Bertolini et al[18] found that 60% of 2,932 patients admitted to 128 adult, general ICUs received a sedative or analgesic. The most common sedatives were propofol (40%) and diazepam (34%); the most common analgesics were fentanyl (36%) and morphine (22%). In their patients, the prevalence of sedation tends to decrease linearly overtime. Unfortunately no data of outcomes were described in this study. Similarly to Bertolini et al,[18] we found that 68% of our patients received a sedative at any moment during the ICU stay. Most of the patients received the sedative for a short period of time, and two thirds (67%) received a combination of drugs, more commonly benzodiazepines and opiates. Patients who received sedatives had longer time on mechanical ventilation, a longer weaning period, and a longer ICU stay.

The usage of NMBs is less known than the use of sedatives.[11,12,21–23] Small, single-institution, prospective studies[1,22,23] suggest that the rates vary between 3.4% and 15.5%. Watling et al[17] reported a survey of the use of sedatives, analgesics, and NMB in the United States. After the survey was completed, the study participants were asked to collect drug administration information for 5 consecutive days on all patients in the ICUs during the study period. Nine percent of their patients received an NMB. Unfortunately, the authors[17] did not offer information regarding the patient characteristics or concomitant therapy. Murray et al[24] did a retrospective audit of the use of NMBs in a tertiary care medical center for a 3-month period, showing that NMB use in the ICU

**Table 2—*Variables Associated With NMB Use by Univariate and Multivariate Analysis***

| Variables | No. | Use of NMBs, No. (%) | Univariate Analysis | | Multivariate Analysis | |
|---|---|---|---|---|---|---|
| | | | OR | 95% CI | OR | 95% CI |
| Geographic area | | | | | | |
| United States-Canada | 1,455 | 167 (11.5) | 1 | | | |
| Europe | 2,506 | 319 (13) | 1.12 | 0.92–1.37 | | |
| Latin-America | 1,222 | 200 (16) | 1.51 | 1.21–1.88 | | |
| Age, yr | | | | | | |
| ≥ 50 | 3,675 | 372 (10) | 1 | | 1 | |
| 50 | 1,508 | 313 (21) | 2.32 | 1.98–2.74 | 2.28 | 1.85–2.80 |
| Gender | | | | | | |
| Female | 1,985 | 203 (10) | 1 | | 1 | |
| Male | 3,198 | 483 (15) | 1.56 | 1.31–1.86 | 1.57 | 1.27–1.94 |
| Previous functional status | | | | | | |
| Limited activity | 2,016 | 202 (10) | 1 | | 1 | |
| Normal | 3,167 | 484 (15) | 1.62 | 1.36–1.93 | 1.53 | 1.23–1.92 |
| COPD | 522 | 40 (8) | 0.51 | 0.37–0.72 | | |
| Asthma | 79 | 19 (24) | 2.10 | 1.01–3.55 | | |
| Coma | 864 | 87 (10) | 0.69 | 0.54–0.88 | 0.61 | 0.45–0.83 |
| Neuromuscular disease | 94 | 4 (4) | 0.29 | 0.10–0.78 | 0.22 | 0.06–0.87 |
| ARDS | 231 | 87 (38) | 4.39 | 3.32–5.80 | 2.01 | 1.43–2.83 |
| Postoperative acute respiratory failure | 1,080 | 98 (9) | 0.60 | 0.58–0.75 | 0.65 | 0.49–0.86 |
| Congestive heart failure | 539 | 47 (9) | 0.60 | 0.44–0.82 | | |
| Aspiration | 129 | 27 (21) | 1.76 | 1.14–2.72 | | |
| Pneumonia | 721 | 144 (20) | 1.80 | 1.47–2.21 | | |
| Sepsis | 458 | 83 (18) | 1.51 | 1.17–1.95 | | |
| Trauma | 407 | 94 (23) | 2.12 | 1.66–2.71 | | |
| Full ventilatory support | 4,338 | 662 (15) | 6.16 | 4.07–9.32 | 3.68 | 2.38–5.70 |
| Inverse-relation ventilation | 89 | 43 (48) | 6.47 | 4.23–9.88 | | |
| Permissive hypercapnia | 88 | 54 (61) | 11.22 | 7.24–17.36 | 4.49 | 2.53–7.95 |
| Prone position | 66 | 42 (64) | 12.15 | 7.31–20.20 | 4.36 | 2.33–8.12 |
| Nitric oxide inhaled | 47 | 32 (68) | 14.62 | 7.87–27.14 | | |
| Level of applied PEEP, cm $H_2O$ | | | | | | |
| ≤ 5 | 3,112 | 218 (7) | 1 | | 1 | |
| 5–10 | 757 | 125 (16) | 2.62 | 2.07–3.32 | 1.94 | 1.50–2.50 |
| ≥ 10 | 737 | 239 (32) | 6.37 | 5.18–7.83 | 3.06 | 2.39–5.70 |
| Tidal volume, mL/kg | | | | | | |
| 6–10 | 2,466 | 272 (11) | 1 | | | |
| ≥ 10 | 2,076 | 307 (15) | 1.40 | 1.17–1.67 | | |
| ≤ 6 | 641 | 107 (17) | 1.61 | 1.27–2.06 | | |
| Peak pressure > 50 cm $H_2O$ | 291 | 93 (32) | 3.40 | 2.62–4.42 | 1.46 | 1.04–2.06 |
| Plateau pressure > 35 cm $H_2O$ | 186 | 78 (42) | 5.21 | 3.85–7.06 | 2.19 | 1.45–3.22 |
| Barotrauma | 143 | 31 (22) | 1.85 | 1.23–2.78 | | |
| ARDS during mechanical ventilation | 413 | 123 (30) | 3.17 | 2.52–3.98 | | |
| Ventilator-associated pneumonia | 855 | 131 (15) | 1.23 | 1.00–1.51 | 1.48 | 1.14–1.91 |
| Sepsis during mechanical ventilation | 742 | 154 (21) | 1.92 | 1.58–2.35 | | |
| Shock | 1,211 | 224 (18) | 1.72 | 1.45–2.05 | | |
| Acute renal failure | 1,022 | 176 (17) | 1.49 | 1.23–1.79 | | |
| Coagulopathy | 581 | 107 (18) | 1.57 | 1.25–1.97 | | |
| Metabolic acidosis | 448 | 76 (17) | 1.38 | 1.06–1.79 | | |
| Respiratory acidosis | 554 | 144 (26) | 2.65 | 2.15–3.26 | 1.40 | 1.06–1.87 |

was 1.4%, mainly in patients admitted with acute respiratory failure as a reason for mechanical ventilation (9%). In our study, 13% of the patients received an NMB during the ICU stay. The use was short (median of 2 days) and was likely to be associated with severe respiratory failure, as suggested by the factors associated with their use. Contrary to the use of sedatives, there was an association with a higher mortality on univariate and multivariate analysis. We speculate that the use of an NMB is usually a final option in the management of severely ill patients, and the frequency of use is reduced when patients are treated following clinical practice guidelines.[25]

The major limitation of our study is that it is an observational study related to the use of mechanical ventilation and was not specifically design to study the usage of sedatives or NMBs. Therefore, there is

relevant information that we do not have available, such as the indications for sedation and/or NMBs, or the use of protocols for sedation and/or NMB in the participating ICUs. There are data in the literature that suggest that sedation protocols can have a significant impact on outcome.[20] However, in a survey by Rhoney and Murry,[26] only 33% of the 474 respondent reported the use of protocols for sedation in their ICUs, and 47% reported the use of protocols for NMBs.

Another limitation is that we do not have any information concerning the route of drug administration (*ie*, continuous IV infusion or intermittent bolus), doses, ways to monitor the depth of sedation, or level of neuromuscular blockade. Finally, we did not obtain information related to specific drugs sedatives and/or NMBs. Despite these limitations, the data presented in this article provide a significant insight into the patterns of usage of these drugs and their potential impact on patient outcome.

In conclusion, this study advances the knowledge of this important aspect of the care of the critically ill by describing patient characteristics and outcomes in those who receive sedatives and NMBs. This study has shown that the persistent use of sedatives is associated with longer duration of mechanical ventilation, more weaning days and, consequently, a longer length of stay in the ICU. Furthermore, patients who receive NMBs not only have a longer duration of ICU stay, but also increased mortality. We need to recognize that in order to provide patient comfort and facilitate the tolerability of mechanical ventilation, these medications need to be used, and in many circumstances the clinician has no alternatives. We believe that a prospective study specifically designed to address the issues identified in this study should be conducted in order to prospective verify our findings.

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