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Conscious sedation in the critically ill ventilated patient

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Abstract

Purpose: The aim of sedation is to provide comfort and minimize anxiety. However, adverse effects are noteworthy, and the optimal end point of sedation in intensive care unit patients is still debated. We analyzed if a level 2 on the Ramsay Scale (ie, awake, cooperative, oriented, tranquil patient) is suitable for an invasive therapeutic approach.

Materials and Methods: Forty-two patients requiring respiratory support and sedation for at least 4 days were enrolled in a prospective interventional cohort study aiming at maintaining patients awake and collaborative. The Ramsay score was recorded 3 times a day. Once a day, the nurse in charge evaluated adequacy of sedation according to the compliance with nursing care and therapeutic maneuvers in the previous 24 hours. Data were collected until patients were ventilated.

Results: Overall, 264 of 582 days were classified as conscious. Sedation was adequate in 93.9% of them. In conscious days, a higher Simplified Acute Physiology Score II score and male sex significantly correlated with inadequate sedation.

Conclusions: In a population of severe intensive care unit patients, conscious sedation was achieved in almost half of the days spent on ventilation. The positive implications (eg, on length of weaning and cost of sedation) of a conservative sedation strategy may be highly relevant.

1. Introduction

The aim of sedation is to provide comfort and minimize anxiety and other forms of distress. In critically ill patients, failure to provide adequate analgesia and sedation has detrimental physiologic consequences [1,2]. However, the adverse effects of sedation therapy are noteworthy [3,4] of which hemodynamic instability, interference with ventilatory weaning, and prolonged stay in the intensive care unit (ICU) are the most relevant. Along with the need to optimize the use of ICU resources, "conscious" sedation is becoming increasingly attractive in the ICU [5,6,8-10]. Guidelines suggest that pharmacologic sedation should be individualized and administered for the shortest possible time at the lowest effective dose [3,5,6].

However, the optimal level of sedation is still debated, and most authors aim at a score of 3 to 4 [3] according to the

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Ramsay Scale [7]. Indeed, De Jonghe et al [11] have recently shown that the use of a sedation algorithm aiming at wakefulness and tolerance to ICU procedures significantly reduces the time spent on mechanical ventilation and length of stay without adverse events.

In a previous study, we demonstrated that after 2 days of ICU stay, enteral sedation with hydroxizine is feasible and effective in ventilated patients [12]. Remarkably, most of these patients were maintained awake despite the high severity of their disease. Because of the potential benefit of a conservative sedation strategy, we analyzed on the whole "ventilated" stay if a conscious level of sedation, defined as a score of 2 on the Ramsay Scale, is consistent with an invasive treatment in critically ill ventilated patients.

2. Methods

Between September 2000 and July 2001, critically ill patients with at least 4 days of expected ventilatory assistance were prospectively analyzed since ICU admission to evaluate the feasibility and efficacy of enteral sedation with hydroxizine (6-12 mg/(kg·d) in 3 doses) [12].

The daily end point of sedation was decided each morning by the attending physician but could be modified during the day based on clinical grounds. The suggested goal was a score of 2 or 3 according to the Ramsay Scale, although a deeper sedation level was accepted in the first 48 hours, when most of the diagnostic and therapeutic procedures are performed. In these days, intravenous propofol or midazolam was allowed. When indicated, analgesia was obtained with a continuous infusion of fentanyl (up to 2 μg/[kg·h]). The Ramsay score was recorded 3 times a day at each nursing shift (8 AM, 2 PM, and 8 PM). Once a day, the bedside nurse defined the level of sedation in the previous 24 hours as "insufficient," "adequate," or "excessive" according to presence of anxiety or agitation, compliance with nursing care and diagnostic and therapeutic maneuvers, patient-ventilator interaction, and tolerance to ICU environment. The presence of pain was quantified 3 times a day by the bedside nurse on a scale of 1 (absent) to 10 (maximal). Data were collected until ventilation was prosecuted or until pharmacologic sedation was indicated.

In the present analysis, each day was classified according to the 3 registered Ramsay scores. Despite a value of 3 on the Ramsay Scale still identifying an awake patient, we defined a day as conscious only if the 3 scores were 2-2-2 or 2-2-3. When the Ramsay score was higher than 2 in 2 or more observations, the day was classified as "sedated." Days were excluded from analysis if even a single Ramsay score was 1 because this was obviously a failure of the sedation therapy.

Baseline characteristics (age, sex, Simplified Acute Physiology Score [SAPS] II, medical or surgical type of admission, presence of infection, or trauma at admission), presence and timing of a tracheostomy (as an alternative to nasotracheal intubation), shock, open abdominal treatment, daily lowest oxygen saturation by pulse oximetry (Sp_{O_2}), and day since ICU admission were analyzed to identify factors that may influence the observed level of sedation and the adequacy of conscious sedation.

A general linear mixed model for repeated measures based on a single patient was used [13,14]. To enhance stability, we used a "building-up" approach, evaluating the impact of each variable on statistical significance ($P < .05$). Because the day of ICU stay was used as a continuous variable to create the model, we analyzed its effect after dichotomization at the lowest value significantly and independently affecting the presence of conscious sedation or adequacy. Pearson χ^2 test was used to compare categorical variables. STATA 9 (STATA, College Station, Tex) statistical package was used.

3. Results

Among the 238 patients admitted to our ICU during the study period, 66 patients received at least 4 days of ventilation. Twenty-four of them were not considered for the study: 10, because the expected period of ventilation was underestimated at ICU admission and the remaining, because of exclusion criteria (<18 years old, neurologic impairment, need for neuromuscular blockade) [12]. Demographic and clinical characteristics of the 42 enrolled patients are illustrated in Table 1. Median ICU length of stay was 14.5 days (interquartile [IQ] range, 9-25 days). All patients were initially ventilated through a nasotracheal tube, and mechanical ventilation lasted 9.5 days (IQ range, 5-21 days). Twenty-three of them were tracheostomized during ICU stay (median, 5 days; IQ range, 3-10 days). Intensive care unit mortality was 23.8%.

A total of 661 days of ventilation were evaluated. In 61 of them, at least 1 observed Ramsay score was 1. In 18 further

Table 1 Demographic and clinical characteristics of the 42 enrolled patients

Age (y)	60 (52-71)
Male sex	30 (71.4)
SAPS II	32 (23-45)
Type of admission	
Medical	21 (50.0)
Unscheduled surgery (no trauma)	10 (23.8)
Trauma with surgery	5 (11.9)
Trauma without surgery	6 (14.3)
Reasons for ICU admission	
Acute respiratory failure	
In pneumonia	13 (31.0)
In trauma	8 (19.0)
Abdominal septic shock	9 (21.4)
Hemorrhagic/hypovolemic shock	6 (14.3)
Cardiogenic shock	5 (11.9)
Pulmonary embolism	1 (2.4)

Values are mean (IQ range) or absolute number (percentage).

Table 2 Observed sedation level

	Conscious days (264)	Sedated days (318)
SAPS II	32.5 ± 11.1 (25-39)	31.9 ± 11.1 (25-33)
Age	60.4 ± 11.5 (55-69)	57.9 ± 14.5 (55-67)
Male sex	144 (54.5)	216 (67.9)
Medical admission	132 (50.0)	111 (34.9)
Infection at admission	124 (47.0)	182 (57.2)
Trauma at admission	74 (28.0)	53 (16.7)
Open abdominal treatment	40 (15.2)	133 (41.8)
>2 d since ICU admission	254 (96.2)	260 (81.8)
>8 d since ICU admission	169 (64.0)	155 (48.7)
Lowest Spo_2 >94%	204 (77.3)	192 (60.4)
Presence of shock	73 (27.7)	134 (42.1)
Presence of a tracheostomy	154 (58.3)	150 (47.2)

Values are days (percentage) or mean ± SD (IQ range). Raw data according to sedation level are reported.

days, Ramsay or adequacy data were missing. Finally, 582 days were analyzed.

Raw data are reported in Table 2. A total of 264 days were classified as conscious (45.4%). Moreover, a further 22% (128/582) of the days had observed scores of 2-3-3 or 3-3-3, a level still defined as "awake" on the Ramsay Scale.

The effects of the single variables on the observed sedation level are reported in Table 3. Multivariate analysis indicated that conscious sedation was significantly related to ICU day of stay after the second, presence of a tracheostomy, daily lowest Spo_2 of more than 94%, absence of shock, or open abdominal treatment (Table 4). Conscious days were also more frequently observed in survivors (85.2%) than in patients who finally died (58.7%, $P < .0001$).

Sedation was judged as adequate in 92.8% of conscious days (in the remaining days, insufficient sedation was always reported) compared with 81.7% of the sedated days ($P < .0001$), where 89.7% of inadequate cases were due to excessive sedation. Of note, conscious sedation itself was a strong independent determinant of adequacy on the whole 582 days, together with a lower SAPS II score, absence of hypoxemic episodes, and more than 8 days of ICU stay, at multivariate analysis (Table 4).

In conscious days (Table 4), only SAPS II score and male sex independently predicted inadequacy of sedation (sedation was defined as insufficient in 17/144 days in males vs 1/120 days in females, $P < .0001$).

Fentanyl was used in 10.6% of conscious days (28/264), at a mean dose of 0.72 ± 0.41 μg/(kg·h). The presence of a pain level higher than 3 in at least 1 of the 3 daily evaluations was reported in 7 of 264 conscious days.

4. Discussion

Sedation is mandatory in critically ill patients because outcome is negatively affected by anxiety and agitation. The stress response causes increased oxygen consumption, hypercoagulability, immunosuppression, dyssynchronous mechanical ventilation, and inadvertent self-removal of invasive devices [1,2]. On the other hand, excessive sedation can also lead to dangerous adverse effects (hemodynamic impairment, tachyphylaxis and drug dependence, hepatic and renal damage, etc) and can prolong mechanical ventilation and ICU length of stay [3,4].

In the last 10 years, clinical research has focused on finding the "optimal" sedative drug, on protocols for drug

Table 3 Univariate analysis for observing a day of conscious sedation and for being adequately sedated in overall days or only in conscious sedation days

	Conscious sedation	Adequacy (in overall days)	Adequacy (in conscious days)
SAPS II	−0.01 (−0.04 to 0.02)	**−0.05 (−0.08 to −0.01)**	**−0.08 (−0.14 to −0.03)**
Age	0.02 (−0.01 to 0.05)	−0.01 (−0.05 to 0.03)	−0.01 (−0.09 to 0.07)
Male sex	−0.65 (−1.42 to 0.11)	**−1.53 (−2.49 to −0.58)**	**−2.90 (−5.22 to −0.58)**
Medical admission	−0.32 (−1.15 to 0.52)	0.31 (−0.87 to 1.49)	0.14 (−1.58 to 1.87)
Infection at admission	0.41 (−0.44 to 1.25)	−0.07 (−0.96 to 0.83)	0.21 (−1.53 to 1.95)
Trauma at admission	[a]	−0.02 (−1.00 to 0.97)	−0.73 (−2.94 to 1.49)
Open abdominal treatment	**−1.63 (−2.09 to −1.17)**	0.16 (−0.71 to 1.03)	0.13 (−2.11 to 2.37)
>8 d since ICU admission	–	**−0.99 (0.39 to 1.58)**	**1.36 (0.15 to 2.57)**
>2 d since ICU admission	**2.37 (1.51 to 3.24)**	–	−0.98 (−1.00 to 2.96)
Daily lowest Spo_2 >94%	**1.15 (0.53 to 1.76)**	**0.84 (0.21 to 1.47)**	−0.19 (−1.51 to 1.13)
Presence of shock	**−1.00 (−1.59 to −0.42)**	−0.53 (−1.15 to 0.09)	−0.67 (−1.86 to 0.53)
Presence of a tracheostomy	**0.98 (0.29 to 1.67)**	0.70 (−0.03 to 1.42)	1.46 (−0.26 to 3.17)

Values are correlation coefficients (95% confidence interval). Variables included in the multilevel analysis are in bold.

[a] Two trauma patients were always awake during ICU stay.

Table 4 Multilevel analysis for observing a day of conscious sedation and for being adequately sedated in overall days or only in conscious sedation days

	Conscious sedation	Adequacy (in overall days)	Adequacy (in conscious days)
SAPS II	–	**−0.05 (−0.09 to −0.01)**	**−0.06 (−0.11 to −0.02)**
Male sex	–	−0.98 (−2.03 to 0.07)	**−21.24 (−23.38 to −19.10)**
Open abdominal treatment	**−2.10 (−3.48 to −0.73)**	–	–
>8 d since ICU admission	–	**0.73 (0.06 to 1.40)**	0.68 (−0.52 to 1.88)
>2 d since ICU admission	**2.21 (1.26 to 3.16)**	–	–
Lowest Spo_2 >94%	**1.14 (0.49 to 1.79)**	**0.79 (0.08 to 1.50)**	–
Presence of shock	**−0.76 (−1.37 to −0.14)**	–	–
Presence of a tracheostomy	0.23 (−0.61 to 1.07)	–	–
Conscious sedation	–	**0.87 (0.17 to 1.58)**	–
Constant	−2.05	3.46	25.36

Numbers are correlation coefficients (95% confidence interval). Significant values are in bold.

administration, and on improvement of sedation monitoring. This has resulted in a significant impact on the duration of weaning and ICU length of stay. More recently, increased attention has been posed on redefining goals, aiming at lighter levels of sedation [5,6,8-11], to minimize adverse effects without affecting the quality of care. De Jonghe et al [11] have reported that the implementation of a sedation algorithm that preserves consciousness resulted in a 57% reduction of the time spent on ventilation.

In a population of critically ill patients requiring prolonged (>96 hours) ventilatory assistance, we analyzed if conscious sedation, defined as a score of 2 on the Ramsay Scale throughout the day, may be maintained without interference with the provided care.

Adequacy of sedation was assessed by the nursing staff in a subjective way. Nurses spend most of their time at the bedside, and we deemed their opinion on patients' needs as the best way to evaluate this factor. The definition of adequacy does not duplicate the definition of the Ramsay Scale but represents a global view of patients' tolerance to the ICU environment as a whole.

A value of this study is the selection of a severe ICU population, that is, with at least 4 days of ventilatory assistance, in which an improved sedation strategy may offer relevant advantages. No limits of severity were posed. We included patients with adult respiratory distress syndrome, septic or cardiogenic shock, or open abdominal treatment because of abdominal sepsis. Nevertheless, conscious sedation accounted for almost half of the examined days, and more than 90% of them were judged as adequate by the nursing staff. If we expand our definition criteria for consciousness, 67.4% of the days had observed scores always equal to or lower than 3 (ie, awake according to Ramsay), demonstrating how deep sedation (ie, a score of 4 or more) was needed in less than 1/3 of the days.

The main limitation of the present study is the lack of a randomization procedure because the sedation level was chosen each morning by the attending physician on a clinical basis. However, our intention was to evaluate and suggest the feasibility of a highly conservative sedation strategy. We are absolutely aware that conscious sedation cannot be generalized and that it may be unsuitable in many situations. In our study, deeper sedation levels were observed in the first 2 days of ICU stay (when patients are more invasively treated and most of the diagnostic and therapeutic procedures are performed), in patients receiving open abdominal treatment (with intraperitoneal surgical medications performed daily, at least in the first period), and in the days when shock or a low Spo_2 was present. All these conditions require a more aggressive ICU treatment and, hence, a deeper level of sedation. Indeed, conscious days were significantly less frequently observed in patients with an adverse outcome.

Although expressing severity, SAPS II did not correlate with the observation of conscious sedation. Of note, in our clinical practice we do not base our therapeutic strategies on SAPS II value. Indeed, it was a significant predictor of inadequacy of sedation in conscious days. The lack of influence of other day-by-day criteria of severity (mainly shock and open abdominal treatment) may be the result of the preemptive choice of a deeper sedation levels in these days.

Because of the lack of a control group, we cannot evaluate the positive implications of lighter sedation levels, although most of them are well established [3]. Besides a shorter weaning period and ICU length of stay, a further possible advantage is the likelihood of using a less invasive ventilatory strategy, such as pressure support ventilation, which is implemented as early as possible in our protocols. Although not defined, a decrease in intrathoracic pressures, with reduced pulmonary injury, and maintenance of respiratory muscle endurance, with a favorable impact on weaning, may be speculated. A further advantage to be stressed is the economic impact: enteral hydroxyzine was quite effective in obtaining awake, calm, and cooperative patients; and the total daily cost of this sedative protocol is less than 4 US dollars [12].

A drawback of lighter sedation is a higher workload for nursing staff because it requires a closer surveillance of the patient, but the high rate of perceived adequacy of sedation reinforces the feasibility of this sedation strategy. Finally, we did not analyze recall and posttraumatic stress disorders; the former correlated to factual memory, which could be higher in the awake patient. However, it has been hypothesized that recall is higher in deeply sedated patients because of a distorted perception of reality during ICU stay [15].

Despite the limits of this investigation, we believe that conscious sedation, defined as a score of 2 on the Ramsay Scale, is a highly cost-effective strategy in the ICU. The reported efficacy of protocols aiming at reducing adverse effects of sedation through close monitoring, daily interruption of therapy, and choice of drugs with lower accumulative potential [3] may be overcome by this sedation strategy, which proved successful in most critically ill patients requiring prolonged ventilatory support.

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