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Impact et faisabilité d'un protocole d'analgésie-sédation, dirigé par les infirmières et basé sur les échelles RASS et BPS, chez les patients brûlés graves de réanimation sous ventilation mécanique. Une étude bi-centrique, de type avant/après.
L'étude SEDABURN

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Feasibility and impact of a scale-based, nursing-driven, analgesia-sedation protocol in severe burn patients undergoing mechanical ventilation : a before-after, bi-center study.

The SEDABURN Trial

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ABSTRACT

Background. No evidence-based practices exist to guide the management of sedation in mechanically ventilated burn patient. Although international guidelines suggest the use of protocols targeting a light level of sedation, the feasibility and benefits of these goal-directed sedation protocols in mechanically ventilated burn patient remain unclear.

Purpose. To determine whether the implementation of a scale-based, nurse-driven analgesia-sedation protocol, targeting light sedation was associated with a decrease in the duration of mechanical ventilation in critically burn patients.

Methods. We performed a before-after, 2-center study in burn patients requiring ≥ 24 hours of invasive mechanical ventilation. During the control phase, sedatives and analgesics were adjusted according to the physician's decision. During the protocol phase, a RASS and BPS scales-based protocol guided nurses in the titration of intravenous analgesics and sedatives. During both study phases, painful burn cares were controlled by short half-life opioid.

Measurements and Main Results. A total of 188 patients were included (control group, n = 87 (46.2%), intervention group, n = 101 (53.7%)). Baseline characteristics were comparable between the two groups. Protocol implementation was not associated with a statistically significant decrease in the duration of mechanical ventilation (control group, 14 [3; 29], intervention group, 7 [2; 24], p = 0.4). When considering the competition between mortality and weaning from mechanical ventilation, there was no significant difference between the two phases (Gray test, p = 0.4). The time series analysis revealed a non-significant trend toward a decrease in the duration of mechanical ventilation in favor of the interventional group (p = 0.6). Secondary outcomes, including duration of analgesics and sedatives drugs, were not statistically different between both phases.

Conclusion. In critically burn patients undergoing mechanical ventilation, implementation of a scale-based, nursing-driven analgesia-sedation protocol was feasible but didn't significantly decrease the duration of mechanical ventilation and offered no additional benefits for patients

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KEY WORDS : Burn patients ; intensive care ; mechanical ventilation ; sedation ; clinical protocol

1. INTRODUCTION

Continuous infusions of sedatives and analgesics are commonly used in intensive care unit (ICU) patients undergoing mechanical ventilation (MV) to relieve anxiety, reduce pain and facilitate patient care (1). However, sedative prescription and in particular deep sedation have been associated with a prolonged duration of MV and ICU length of stay as well as a higher mortality rate (2,3). Consequently, recent international guidelines recommend a light level of sedation for all ICU patients (except for intra-cranial hypertension, status epilepticus or Acute Respiratory Distress Syndrome) and suggest the use of nursing-driven protocols to achieve this goal (4). Since Brook et *al.*(5), numerous studies have demonstrated their efficacy in decreasing the duration of MV, the incidence of ventilator-associated pneumonia, the ICU and hospital length of stay (6–8). These protocols use a stepwise approach for pain and sedation management, based on regular assessment via validated tools such the BPS (Behavioral Pain Scale) and the RASS (Richmond Agitation-Sedation Scale) scores [5,6].

However, data come predominantly from medical ICU patients and to date, few studies suggest a positive impact on a surgical ICU population (8). Among surgical ICU patients, one particularly challenging subset of patients is severe burns. First, the nature of burn injury as well as the requirements for operative interventions and regular burn care leads to increased sedative and analgesic use. Second, the high incidence of aspiration (up to 30% of burn ICU admission (11)) and ventilator-associated pneumonia (12) increase the duration of MV and, by extend, the need for continuous sedative drugs. Consequently, there is paucity of data regarding the feasibility and the impact of protocols targeting a light level of sedation in mechanically ventilated burn patients.

Therefore, we conducted a bi-center, before-after study to evaluate the feasibility and the effects of a scale-based, nursing-driven analgesia-sedation protocol on the duration of mechanical ventilation in severe burn patients.

2. MATERIALS AND METHODS

2.1.Ethic and approvals

The protocol was approved by the Société Française d'Anesthésie-Réanimation institutional review board (CERAR, IRB IRB 00010254-2016-040). Since this study evaluated the effects of the implementation of a standard of care, consent was waived. Oral and written information were nonetheless delivered to patients and next-of-kin.

2.2.Population

This before-after study took place in the ICU of the university hospital of Nantes and Montpellier. These two large academic centers are specialized in burn patients care.

All critically burn patients ≥ 15 years old who were expected to receive MV for ≥ 24h were eligible. Patients were excluded for any of the following (1) moribund state, (2) early life-sustaining treatment restriction (≤ 48h), (3) brain injury (traumatic and/or anoxic), (4) pregnancy.

2.3.Study design

This study was conducted to compare the duration of MV before and after implementation of a nursing-driven analgesia and sedation protocol. Study design and protocol were elaborated by the hospital of Nantes.

Prior to protocol implementation, the "control group" was defined as all consecutive patients enrolled from January 1st 2014 to January 1st 2016 in the hospital of Nantes, and from May 1st 2015 to May 1st 2016 in the hospital of Montpellier. During this period, analgesia and sedation associated a continuous infusion of Midazolam (0.1-0.2 $mg.kg^{-1}.h^{-1}$) and Oxycodone (0.05-0.1 $mg.kg^{-1}.h^{-1}$). In the hospital of Montpellier, RASS and BPS scores were already routinely performed by nurses every 4h. However, the pursuit and the daily doses of Midazolam and Sufentanil continuous infusions were left at the attending physician's discretion in both centers. Procedural pain was controlled by additional bolus of Oxycodone and a continuous infusion of Remifentanil during wound cleansing (13).

Interphase: During this period, a nurse-controlled scale-based analgesia and sedation protocol was implemented in both units during a 3-months period. The aim of the training was to explain to nurses how to adapt the infusion of hypnotics and analgesic drugs, according to validated scales (RASS and BPS).

During the protocol phase ("protocol group"), patients were prospectively enrolled during a 2-year period following the implementation. At admission, the nurse started Midazolam (0.05 $mg.kg^{-1}.h^{-1}$) and Oxycodone (0.1 $mg.kg^{-1}.h^{-1}$) infusions, and RASS and BPS targets were defined by physicians (BPS score < 5 or < 4 if assessment of facial expression was impossible and RASS score of -1 to +1). Then, nurses titrated analgesic and sedative medication to achieve adequate pain control and light level of sedation. Patients were assessed for level of pain and sedation at minimum every 4 h with closer reassessment after any bolus or infusion rate change. More details on protocol algorithm are displayed in Fig. 1. RASS and BPS targets were revised at least daily by physicians, depending on the clinical evolution. To prevent hyperalgesia (14), Pregabalin (75mg, twice a day) was added at patient admission (15) as well as a continuous infusion of Ketamine ($0,5mg.kg^{-1}.h^{-1}$) which was discontinued after 5 days or when arbitrary predefined doses of Midazolam ($5mg.h^{-1}$) and/or Oxycodone ($3mg.h^{-1}$) were achieved. During painful burn cares and dressing changes, the targets of RASS and BPS were punctually set at -5/-4 and < 4 respectively, along with (1) a bolus of $1mg.kg^{-1}$ and $1mg.kg^{-1}.h^{-1}$ infusion of ketamine, (2) a continuous infusion of remifentanil and propofol if required. When burn care and dressing were resolved, ketamine and remifentanil were stopped and RASS/BPS were set at their previous targets.

2.4. Common burn patients' care in both periods.

2.4.1. Surgical treatment

Initial surgical treatment included early debridement of non-viable tissue and wound covering with paraffin gauze dressing (16). In case of circumferential burn eschar (limb, hand, chest or abdomen), escharotomy could be performed if ischemia and/or necrosis was detected. Until skin graft, burned area was covered daily by silver-sulfadiazine-impregnated wound dressings. After initial care, permanent wound coverage was realized with a split-thickness skin graft from an uninjured donor site (autograft). Skin grafting could be realized several times in case of high burned surface area or graft failure (hematoma, infection, necrosis) until the entire burned area were healed. In case of extensive burns with little donor zone, a temporary wound coverage could be performed with allograft or xenograft. Graft and wound care require daily para-medical cleaning and dressing, until healing of the grafted area (usually within two weeks after surgery (17)).

2.4.2. Critical care management

When burn involved a body surface area ≥ 20%, initial fluid resuscitation was based on the Parkland formula and relied mostly on crystalloid administration (18). As recommended by the American Burn Association, a urine output of 0,5 to 1ml.kg^{-1}.h^{-1} was targeted whilst monitoring blood pressure, pulse and oxygen saturation (19). Transfusion strategy (20), ventilatory support, weaning procedure and airway management were unchanged between both periods. Notably, endo-tracheal intubation was indicated for any of the following (1) total burned surface area ≥ 20%; (2) airway burn injury; (3) respiratory, hemodynamic or neurological instability. Early tracheostomy (in the first week following admission) was performed in case of (1) total burned surface area ≥ 20%; (2) smoke inhalation injury; (3) severe face/neck burn injury with difficult access to airway; (4) severe face burn injury with significant airway impairment (assessed with a

fiberoptic evaluation and cuff-leak test 24 hours after admission). Although its positive effects are debated, early tracheostomy is medically justified in case of airway burn injury in our experience, and is likely to benefit most those with major burns because they require numerous surgical procedures with prolonged mechanical ventilation (21).

2.5. Baseline assessment and data collection

At admission, baseline demographics (age, sex, weight, comorbidities and chronic treatments (with special attention to cardiac, respiratory and psychiatric anteriority)), burn injury characteristics (mechanism of burn injury, total burn surface area (TBSA), airway burn injury, smoke inhalation) and severity of illness (Simply Acute Physiology II (SAPS II), and Abbreviated Burn Severity Index (ABSI) (22,23)) were collected.

During the ICU stay, the following respiratory events were registered: tracheostomy, Ventilator Associated Pneumonia (VAP), ARDS (Acute Respiratory Distress Syndrome), duration of MV, extubation failure. The following ICU events were also collected: duration of catecholamine, duration of sedatives and analgesics continuous infusions; number of surgery procedures; withdrawal of life-sustaining therapy; ICU LOS; ICU, hospital and 90-day mortality.

To assess protocol adherence, we recorded in the first 48h after admission (1) medical prescription of a targeted analgesia and sedation using the RASS and BPS scales; (2) number of nurse-reported RASS and BPS scores; (3) number of sedative and analgesic dose modifications according to the protocol.

2.6. Study outcomes

The primary outcome was the in-ICU duration of MV before and after the implementation of the sedation protocol. Duration of mechanical ventilation was defined as cumulative days of

ventilatory support. Punctual ventilator assistance used exclusively during dressing changes in tracheostomized patients was not upheld in the definition.

Secondary outcomes included protocol adherence in the first 48h after admission, duration of sedative and analgesic continuous infusion; incidence of VAP and ARDS; extubation failure rate (defined as the need for ventilatory support reinstitution within 48h of planned extubation (24)); ICU length of stay; in-ICU mortality.

2.7.Statistics

Continuous data are expressed as mean (±standard deviation) or median [quantile] and compared with the Student t-test or Mann-Whitney test whenever appropriate. Nominal data are expressed as N (%) and compared with the Chi2 or Fisher test whenever appropriate.

Because of the before-after design of the study, we elaborated an interrupted time-series analysis. We studied the segmented linear regression in the control and the intervention period and compared the regression coefficient of the linear trend between both periods. The aggregated value was the mean of the duration of MV per each semester. First, we looked for auto-correlated errors of the aggregated duration of MV score in the overall cohort with an ARIMA model. Auto-correlated errors were checked with a graphical analysis and the Ljung-Box test. Second, we analyzed the effect of time on the aggregated value with an ARIMA model. We then elaborated a segmented linear regression in the Control and the Intervention phase and compared the β regression coefficient of the linear regression between the control and the intervention phase (25).

Given the competition between mortality and the duration of MV, we studied the duration of mechanical ventilation with an Aalen-Johanssen estimator between the 2 periods (26).

Finally, using a standard Cox regression model with mortality as a competitive event in the overall cohort (Control and Intervention phase), we calculated the odds ratio of spontaneous breathing in various subgroups (patients with a burned surface area ≥ 20%, patients with tracheostomy, patients ≥ 65 years old) between both phases.

All statistical tests were two-sided. A p value <0.05 was considered statistically significant. Statistical analyses were performed with R Studio® version 1.0.136, with the *nlme* package (The "R" Foundation for Statistical Computing, Vienna, Austria).

3. RESULTS

3.1.Population

We included 188 patients in the overall population, 87 (46.3%) in the Control phase and 101 (53.7%) in the Intervention phase. The hospital of Nantes was the main center, providing 83.9% (n=73) and 72,3% (n=73) of the included patients in the control and the protocol phase respectively (Fig 2). Patients were mostly middle-aged men (49 [33-61] years). A psychiatric anteriority and a chronic medication by benzodiazepine were reported for 34.6% and 30.3% of them, respectively. The median TBSA (Total burn Surface Area) was 22 [12.5-40], included the airway in 80.5% of cases, and was associated with smoke inhalation in 19.7% of patients. The median ABSI score was 7 [5-8.8]. The two groups were similar regarding demographic aspects, medical history, substance abuse, burn injury characteristics, severity of illness and burn patients' general care (Table 1).

3.2.Main outcome: Duration of Mechanical Ventilation.

In the overall population, the median duration of MV was 14 [2,5;29] days in the control phase and 7 [2;24] in the protocol phase (p = 0,4). Because of the competitive risk between mortality and the duration of MV, we took into consideration the competitive risk between death and weaning from invasive MV with Aalen-Johanssen model. The duration of invasive ventilation was not significantly different between the two periods (p=0.4) (Fig 3).

Given the study design, and to investigate a potential secular trend in the evolution of the duration of invasive MV, we performed a time-interrupted time-series analysis. There were no errors of the aggregated duration of MV score in the overall cohort with an ARIMA model or and the Ljung-Box test, implying the lack of seasonal trend. In the Control phase, an upward trend was revealed (β coefficient 1.25 CI_{95} [-2.3;4.8]), whereas the intervention phase revealed a downward trend (β coefficient -0.5 CI_{95} [-2.1;1.1]). The difference between the two β coefficients was not statistically different (p=0.6) (Fig 4).

3.3.Compliance with protocol elements in the first 48h.

At admission, RASS and BPS targets were prescribed for 101 (100%) and 97 (96%) patients, respectively. In the first 48h, RASS and BPS scores were reported 11.7 (±5.7) times by nurses. After RASS and BPS assessment, nurses adapted continuous infusion rate 3.7 (±2.8) times for sedative drugs and 2.6 (±2.5) times for analgesic drugs.

3.4.Secondary outcomes

The intervention period was associated with a non-significant decrease in the duration of analgesic and sedative drugs. Duration of hypnotic infusion was 8 [2-24] days in the Control phase and 6 [2-17] days in the Intervention phase (p=0.3). The duration of opioid infusion was 17 [4-32] days before vs. 8 [3-23] days after the intervention (p=0.06). There was no difference regarding respiratory events, in-ICU LOS or in-ICU mortality (Table 2).

3.5.Subgroup analysis

We separately analyzed protocol impact in each center (Table 3). In the hospital of Nantes, we observed a shorter use of opioid (17 [4-32] vs 5 [3-15] ; p=0.002) and hypnotic (6 [2-23] vs 4 [2-10] ; p=0.05), and the time series analysis revealed a significant difference in the mean duration of MV between the two period (β coefficient before 1,23 CI_{95} [-2,4;4,9] before ; β coefficient after -0,9 CI_{95} [-2,5;0,5]; p=0.03) (Fig 5.). In the small subgroup of Montpellier, the protocol implementation had no statistically significant impact. We compared protocol adherence between both centers during the intervention phase. Medical prescription and nurse report of RASS/BPS scores were more frequent in the hospital of Montpellier than in the hospital of Nantes (Table 4).

As exploratory analyses, we investigated the effects of the intervention in pre-specified subgroups. The odd ratio of spontaneous breathing during the intervention phase was 1.1 IC_{95} [0.7-

1.8] in severe burn patients (burned cutaneous surface ≥ 20%) and 0.9 IC_{95} [0.5-1.5] in patients with tracheostomy (Figure 6).

4. DISCUSSION

In this before-after, bi-center study of mechanically ventilated burn patients, implementation of a scale-based, nursing-driven analgesia and sedation protocol did not significantly decrease the duration of mechanical ventilation. When considering secondary outcomes, protocol implementation didn't reduce the duration of opioids and hypnotic continuous infusion, neither the VAP incidence rate nor the ICU length of stay

Unique aspects of burn injury and burn care were points of resistance to implementation of protocolized ICU care applied to medical and general surgical ICU populations. As a consequence, very few evidence-based data exist to guide critical care of severe burn patients (27) and practices vary widely between centers and countries (28,29). A European survey conducted in 2011, reported that among responding burn ICUs, only 60% used standard operating procedures for sedation and analgesia and two third perceived the need for a change in their concepts (29). Recently, a retrospective before-after single center study of 307 severe burn patients undergoing MV reported the beneficial impact of a paired spontaneous awakening and spontaneous breathing protocol on duration of MV, ICU length of stay, pneumonia incidence (30). However, this study bears significative limitations (retrospective, single center) and didn't evaluate safety aspects such as unplanned extubation or aspiration.

Our study is the first to report the feasibility and the impact of a nursing-driven analgesia and sedation protocol in ventilated burn patients. Our protocol is in line with the current Society of Critical Care Medicine Pain, Agitation/ Sedation, Delirium, Immobility, and Sleep Disruption Guidelines which recommends (1) the use of validated tools for monitoring depth of sedation and analgesia; (2) an analgesia-first approach to sedation; and (3) a targeted light sedation. To achieve and maintain a light level of sedation, we chose a nurse-protocolized sedation rather than a daily sedative interruption. Both protocols are considered as efficient in a medical ICU setting (4,31), but daily sedative interruption may be less tolerated and more dangerous in the specific burn population who experiences high level of pain. An original feature of our protocol was the

adjunction of a temporary low-dose ketamine infusion in order to reduce opioid consumption and hyperalgesia. If no study has evaluated the effects of ketamine in ICU burn patients, its positive effects are documented in post-surgical ICU patients and in burn patients outside the ICU (4,14,32).

Safety is paramount when considering changes to medical practice; a natural concern then is whether implementation of such a protocol had deleterious effects. Indeed, an increase in rate of unplanned extubation was seen with implementation of a combined sedation and weaning protocol in a medical ICU setting, although this did not contribute to higher re-intubation rates (33). In our study, extubation failure rate didn't change with protocol implementation, suggesting no increase in harmful unplanned extubation. When considering other safety aspects, protocol implementation was associated with a decreasing trend in duration of MV, ventilator associated pneumonia rate, ICU length of stay or ICU mortality.

Limitations

A two-phased intervention was chosen to avoid cross-contamination which could have occurred in a randomized-controlled trial. Two major pitfalls are associated with this setting (1) the lack of randomization precludes the control of independent factors that might differ between both groups. However, patient baseline characteristics were similar between both periods when considering demographic characteristics, medical co-morbidities, substance abuse, burn injury characteristics or severity of illness at admission; (2) secular trends unrelated to our intervention can influence study results. We therefore performed a time series analysis that did not demonstrate a secular time trend.

We didn't collect patients' RASS scores during the intervention phase. Consequently, we cannot ascertain that a light level of sedation was effectively achieved with the protocol implementation. Inability to obtain and maintain a targeted light level of sedation might be due to inappropriate protocol design or low protocol adherence. This last aspect was only evaluated in

the first 48h after ICU admission and didn't consider the rate of correct drug adaptation according to BPS and RASS scores. Reluctance to decrease sedative drug is underpinned by common clinical concerns, such as additional workload or patient discomfort (31), that weren't investigated in the present study. Prospective studies would permit a better evaluation of these feasibility aspects.

Last, given the large dispersion in the duration of MV in our ventilated burn patients population, our study is probably underpowered to demonstrate statistically a significant effect of the protocol implementation.

This advocates for the urgent development of large multi-centric, potentially international, research networks in critically burn patients.

5. CONCLUSION

In critically burn patients undergoing mechanical ventilation, implementation of a scale-based, nursing-driven, analgesia-sedation protocol targeting a light level of sedation was feasible but didn’t significantly decrease the duration of mechanical ventilation and offered no additional benefits for patients.

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7. TABLES AND FIGURES

Fig. 1. Sedation and Analgesia protocol for mechanically ventilated burn patients in the intensive care unit of the hospital of Nantes and Montpellier.

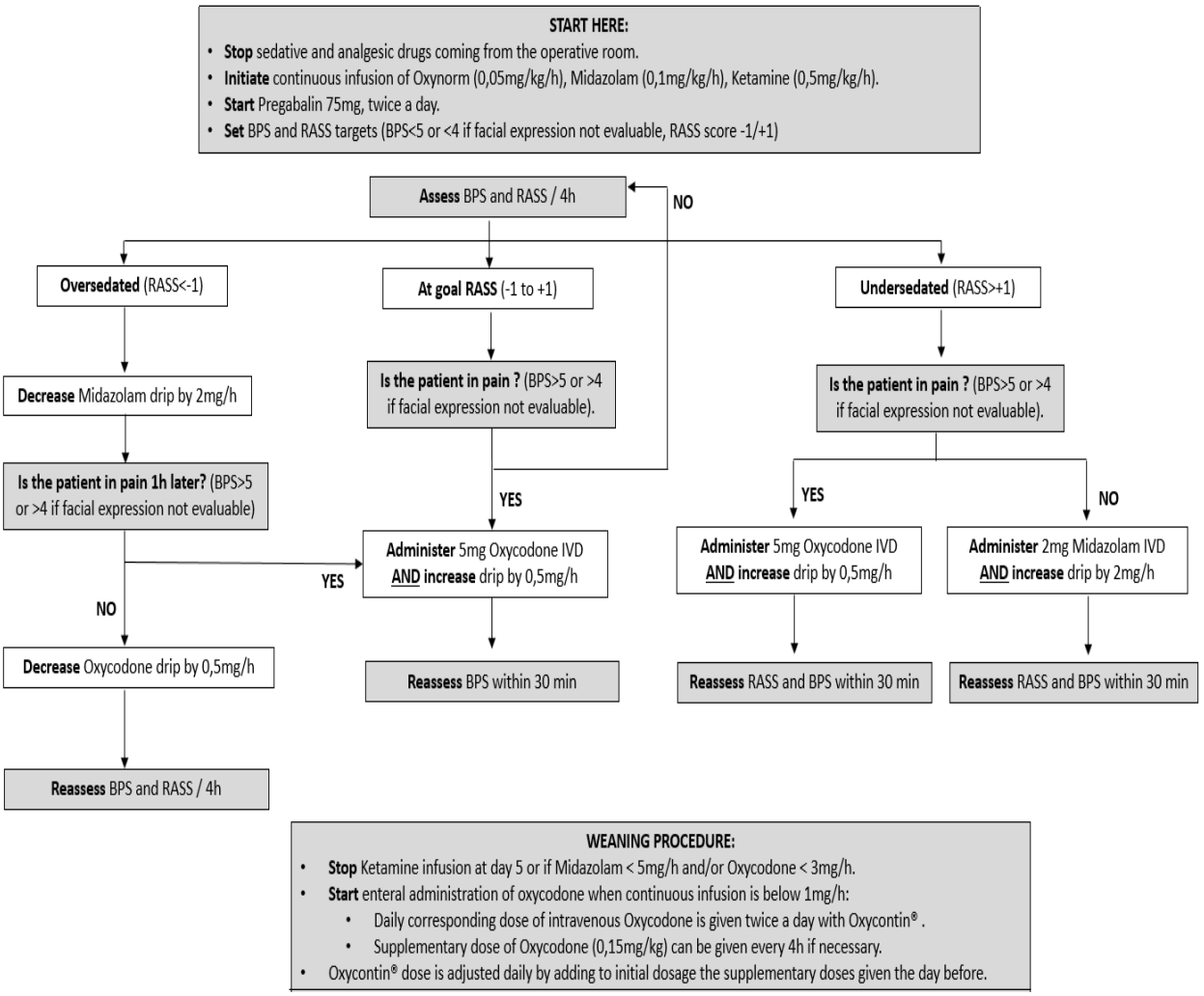
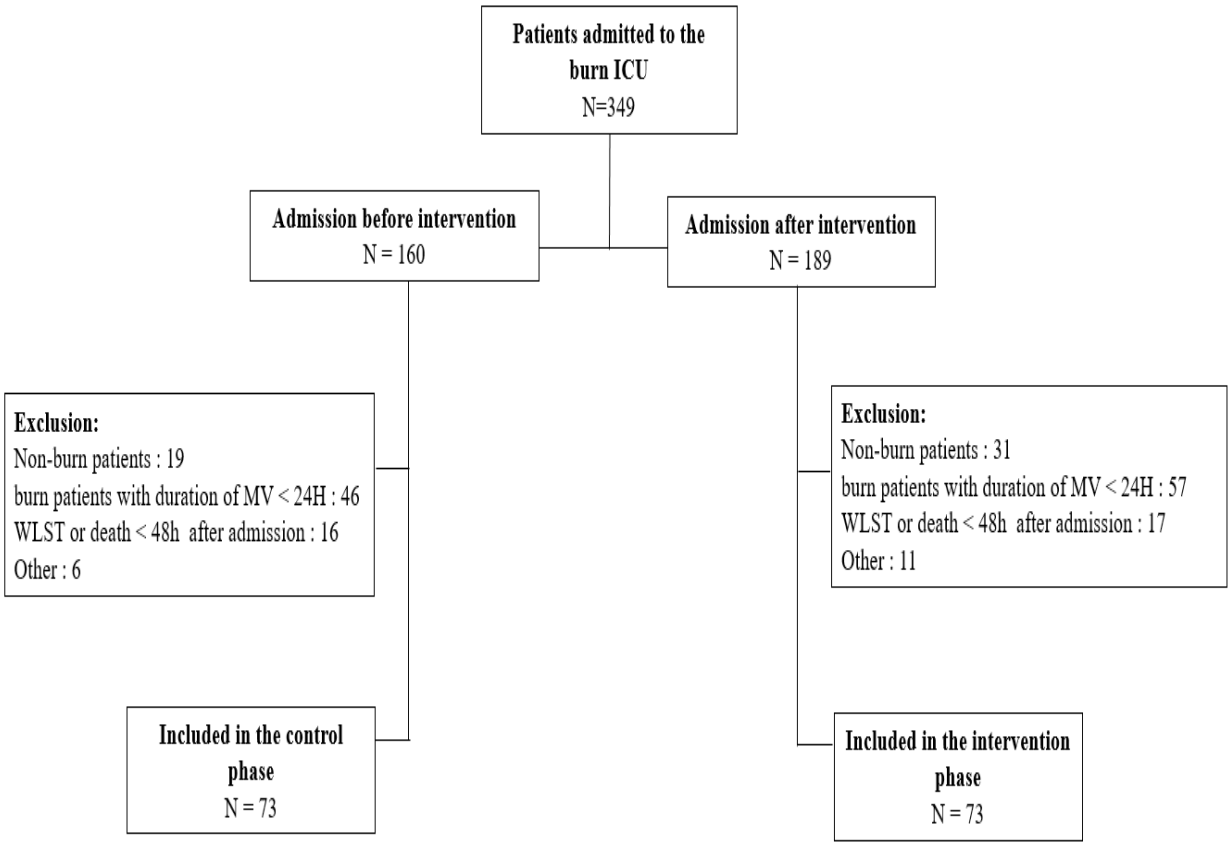
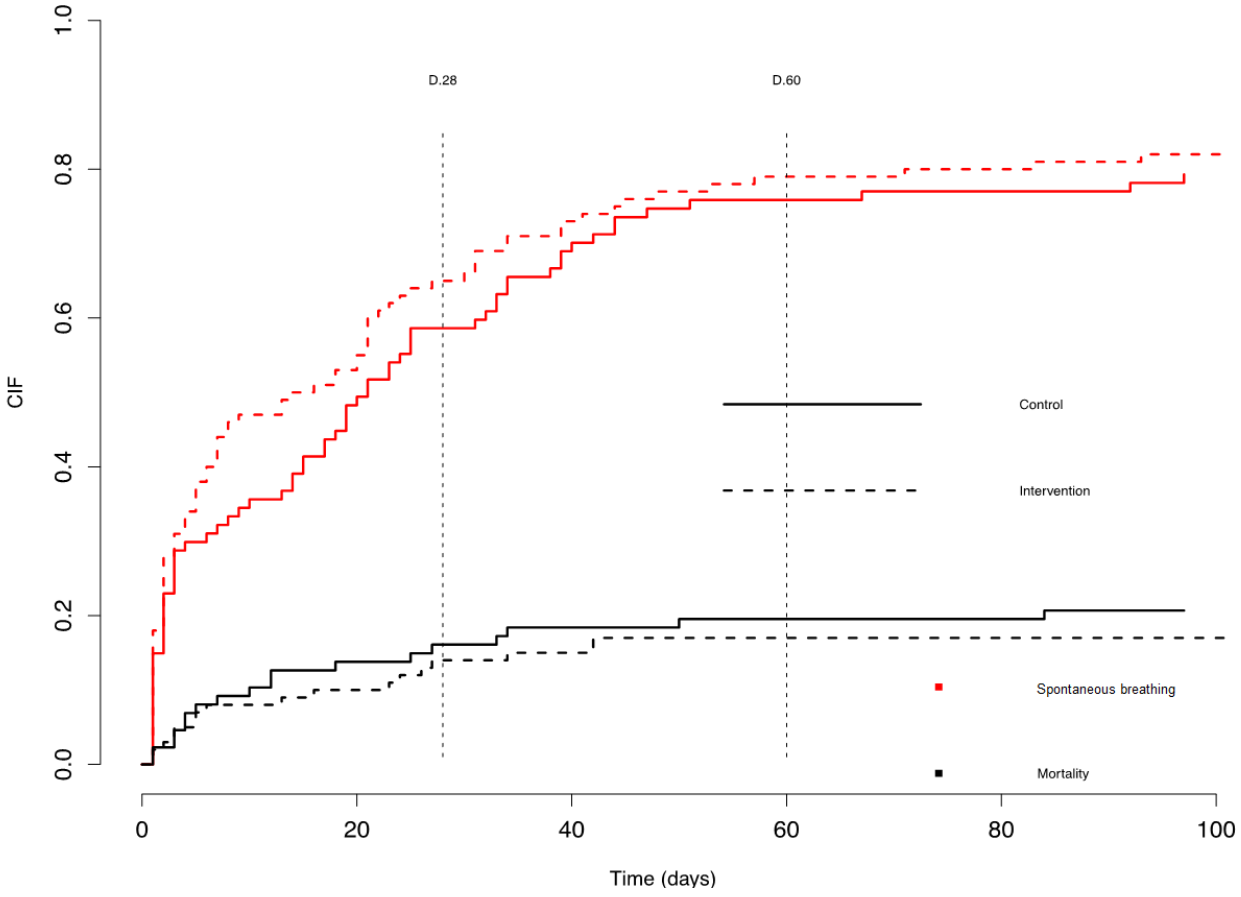


Fig 2. Flow chart in the hospital of Nantes.



Legend. ICU: Intensive Care Unit. MV: Mechanical Ventilation. WLST: Withdrawal or Withholding of Life Sustaining Therapy.

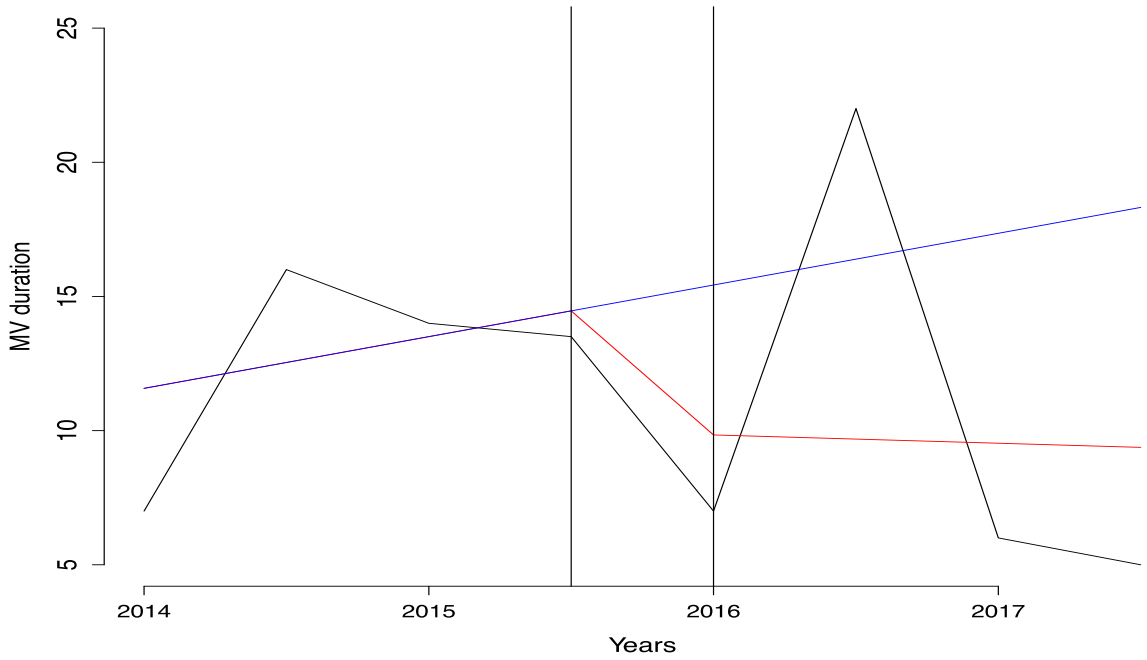
Fig 3. Aalen-Johanssen estimator regarding the competition between mortality and the duration of mechanical ventilation.



Legend. Non-significant trend towards a shorter duration of mechanical ventilation between the 2 phases, Gray test, p=0.4.

CIF: Cumulative Incidence Function

Fig 4. Time-interrupted time-series analysis of the aggregated mechanical ventilation duration between the Control and the Intervention Phase in the overall cohort.



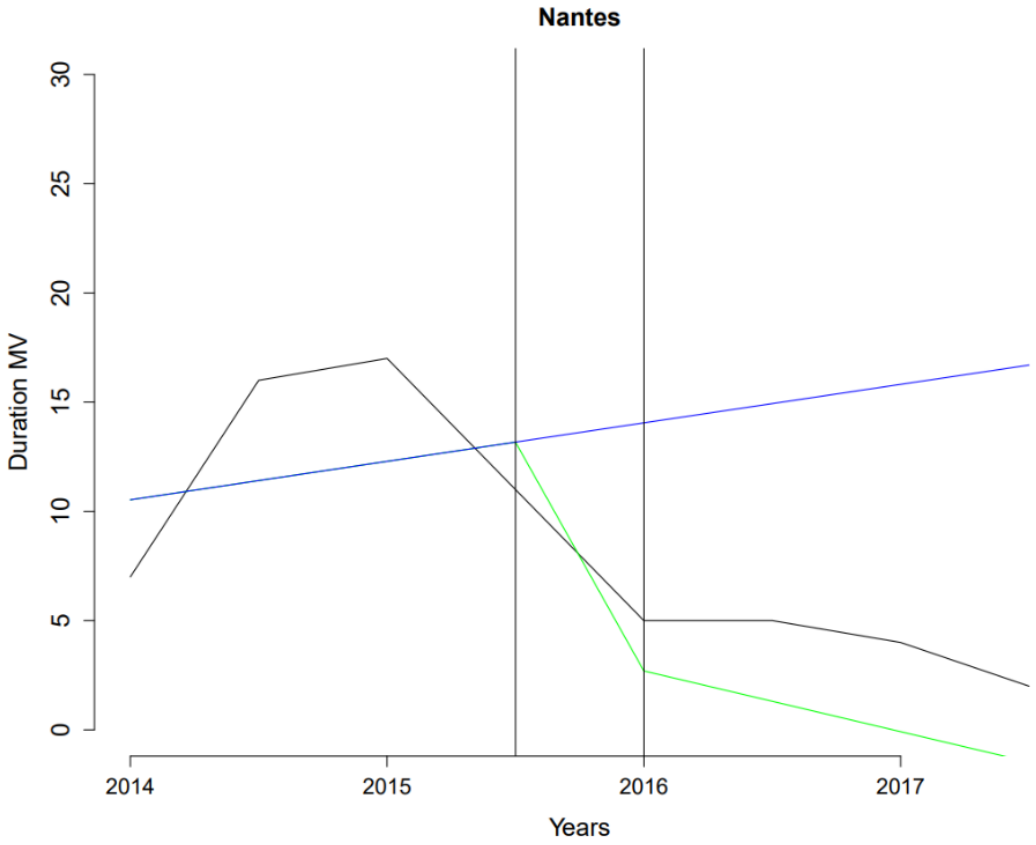
Legend. The figure displays the evolution of the aggregated value of the mechanical ventilation duration, during the study period. The aggregated value is the mean of the mechanical ventilation duration per semester. The vertical lines stand for the period of the implementation of the protocol. The lines embody the regression slope of the aggregated value.

The blue regression line during the intervention phase, embodies the estimated trend of aggregated value after 2016, if the sedation-analgesia protocol would not have been implemented.

The difference between the 2 β coefficients are not statistically different (p=0.6).

MV: mechanical ventilation

Figure 5. Time-interrupted time-series analysis of the aggregated mechanical ventilation duration between the Control and the Intervention Phase in the hospital of Nantes.

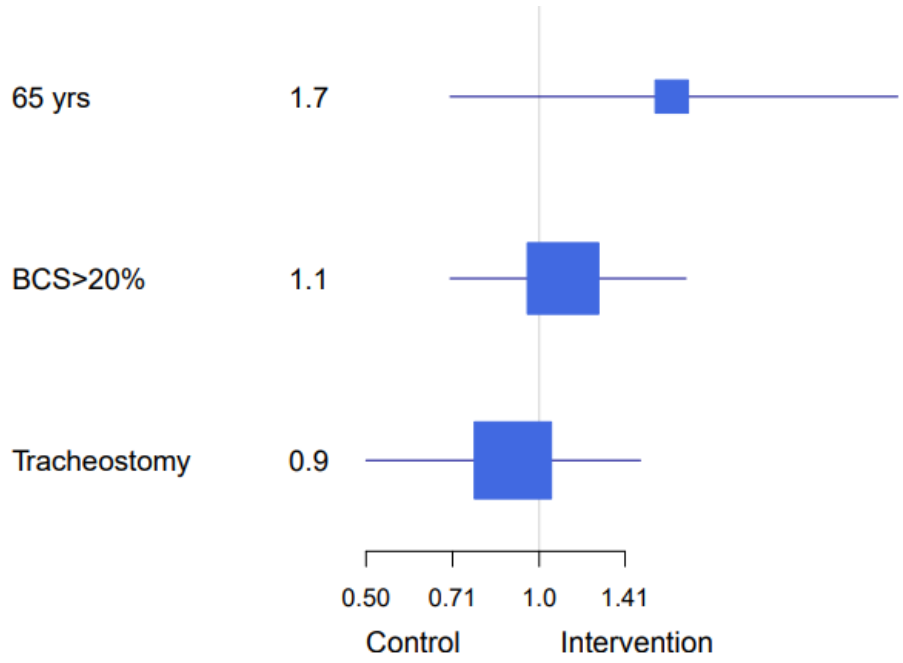


Legend. The figure displays the evolution of the aggregated value of the mechanical ventilation duration, during the study period. The aggregated value is the mean of the mechanical ventilation duration per semester. The vertical lines stand for the period of the implementation of the protocol. The lines embody the regression slope of the aggregated value. The blue regression line during the intervention phase, embodies the estimated trend of aggregated value after 2016, if the sedation-analgesia protocol would not have been implemented.

The difference between the 2 β coefficients are statistically different (p=0.03).

MV: mechanical ventilation

Figure 6. Forest plot of the odds ratio of spontaneous breathing in pre-planned subgroups.



Legend. BCS: Burn Cutaneous Surface

Table 1. Patients' baseline characteristics and burn patients' general care of study population.

	Control group N = 87	**Intervention group N = 101**	*P value*
Baseline characteristics			
Hospital of Nantes	73 (83.9%)	73 (72.3%)	0.06
Age (years)	48 [33-60.5]	49 [35-63]	0.9
Male sex	59 (67.8%)	70 (69.3%)	0.8
BMI	24 [22-28.5]	25.25 [23-30]	0.2
Comorbidities			
Chronic respiratory failure	3 (3.5%)	2 (2%)	0.7
Chronic cardiac failure	2 (2.3%)	0 (0%)	0.1
Psychiatric disorder	32 (36.8%)	33 (32.7%)	0.6
Medication history			
Benzodiazepine	23 (26.4%)	34 (33.6%)	0.3
Antipsychotic	16 (18.4%)	17 (16.8%)	0.8
Antidepressant	20 (23%)	19 (18.8%)	0.5
Substance abuse			
Alcohol	19 (21.8%)	20 (19.8%)	0.9
Tobacco	30 (34.5%)	36 (35.6%)	0.9
Burn injury characteristics			
Burn by fire	81 (93.1)	87 (86.1)	0.9
TBSA	18 [10-39]	20 [12-35]	0.9
Full-thickness burn	0 [0-9.3]	1 [0-15]	0.5
Airway burn injury	73 (83.9%)	79 (78.2%)	0.3
Smoke inhalation	16 (18.4%)	21 (20.8%)	0.7
Severity of illness			
ABSI	7 [5-8]	7 [5-9]	0.9
SAPS II	42 [36.5-50]	47 [40-52]	0.3
Burn patients' general care			
Tracheostomy	36 (41.4%)	42 (41.6%)	1
Surgery for burn care	2 [1-4]	2 [1-4]	0.9

Legend. ABSI: Abbreviated Burn Severity Index. BMI: Body Mass Index. TBSA: Total Burned Surface Area. SAPS II: Simplified Acute Physiology Score II.

Table 2. Secondary outcomes.

	Control group N = 87	**Intervention group N = 101**	P value
Opioid continuous infusion	17 [4-31.5]	8 [3-23]	0.06
Hypnotic continuous infusion	8 [2-23.5]	6 [2-17]	0.3
Catecholamine continuous infusion	4 [0-12]	3 [0-11]	0.8
VAP	49 (56.3%)	47 (47%)	0.2
ARDS	21 (24.1%)	21 (21%)	0.6
Extubation failure	6 (7.5%)	5 (5.3%)	0.6
WLST	9 (10.3)	12 (11.9)	0.7
ICU LOS	25 [8.5-45]	24 [10-44]	0.8
ICU mortality	18 (20.7%)	18 (18%)	0.6

Legend. ARDS: Acute Respiratory Distress Syndrome. VAP: Ventilator Associated Pneumonia. ICU: Intensive Care Unit. LOS: Length Of Stay. WLST: Withdrawal or withholding of life sustaining therapy.

Table 3. Outcomes in the center of Nantes and Montpellier.

	Control group Nantes N = 73 Montpellier N = 14	**Intervention group Nantes N = 73 Montpellier N = 28**	*P value*
Duration of mechanical ventilation			
Nantes	13 [2 -25]	5 [2-21]	0.08
Montpellier	19.5 [3.3-31.5]	19 [7-36]	0.7
Opioid continuous infusion			
Nantes	17 [4-32]	5 [3-15]	**0.002**
Montpellier	17 [4.3-30.8]	19.5 [8.8-40]	0.8
Hypnotic continuous infusion			
Nantes	6 [2-23]	4 [2-10]	**0.05**
Montpellier	17 [4.3-26.8]	13 [7-32.8]	0.4
Catecholamine continuous infusion			1
Nantes	3 [0-12]	3 [0-6]	0.9
Montpellier	9.5 [3.5-20]	8.5 [2-21.5]	0.4
VAP			
Nantes	38 (52%)	27 (37%)	0.08
Montpellier	11 (78%)	20 (71%)	0.7
ARDS			
Nantes	14 (19%)	11 (15%)	0.5
Montpellier	7 (50%)	10 (36%)	0.4
Extubation failure			
Nantes	5 (7.4%)	3 (4.5%)	0.5
Montpellier	1 (12%)	2 (7%)	0.6
ICU LOS			
Nantes	25 [9-42]	23 [9-39]	0.9
Montpellier	25.5 [6.3-69]	28.5 [13.75-54.5]	0.9
ICU mortality			
Nantes	12 (16.4%)	12 (16.4%)	1
Montpellier	6 (42.9%)	6 (22.1%)	0.3

Legend. ARDS: Acute Respiratory Distress Syndrome. VAP: Ventilator Associated Pneumonia. ICU: Intensive Care Unit. LOS: Length Of Stay. WLST: Withdrawal or withholding of life sustaining therapy.

Table 4. Comparison of protocol adherence between both centers in the intervention phase.

	Nantes (n=73)	**Montpellier (n=28)**	*P Value*
Medical prescription of a targeted analgesia and sedation			
RASS	73 (100%)	28 (100%)	> 0,99
BPS	71 (97%)	26 (93%)	> 0,99
Nurse-assessment of analgesia and sedation			
RASS	10,7 (6)	14,4 (3,8)	**0,003**
BPS	10,9 (6)	14 (3,8)	**0,01**
Change in continuous infusion rate after analgesia and sedation assessment			
Hypnotics	3,2 (2,9)	5,2 (2,1)	**0,001**
Opioids	2,4 (2,6)	3,3 (2,2)	0,09

8. SUPPLEMENTAL DATA

8.1 Richmond Agitation Sedation Scale (RASS score)

Score	Term	Description
+4	Combative	Overtly combative or violent; immediate danger to staff
+3	Very agitation	Pulls on or removes tube(s) or catheter(s) or has aggressive behavior toward staff
+2	Agitated	Frequent nonpurposeful movement or patient–ventilator dyssynchrony
+1	Restless	Anxious or apprehensive but movements not aggressive or vigorous
0	Alert and calm	
−1	Drowsy	Not fully alert, but has sustained (more than 10 seconds) awakening, with eye contact, to voice
−2	Light sedation	Briefly (less than 10 seconds) awakens with eye contact to voice
−3	Moderate sedation	Any movement (but no eye contact) to voice
−4	Deep sedation	No response to voice, but any movement to physical stimulation
−5	Unarousable	No response to voice or physical stimulation

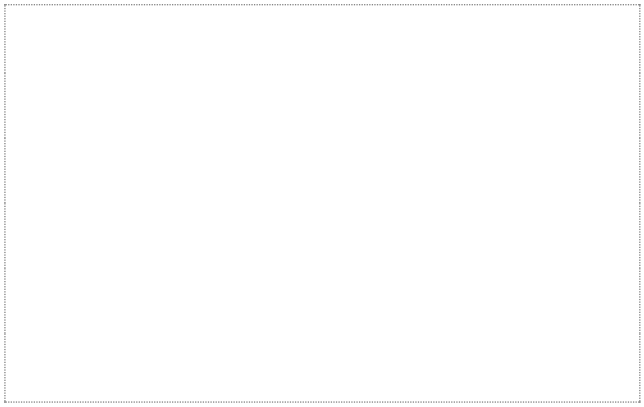
Procedure

1. Observe patient. Is patient alert and calm (score 0)?
   Does patient have behavior that is consistent with restlessness or agitation (score +1 to +4 using the criteria listed above, under DESCRIPTION)?
2. If patient is not alert, in a loud speaking voice state patient's name and direct patient to open eyes and look at speaker. Repeat once if necessary. Can prompt patient to continue looking at speaker.
   Patient has eye opening and eye contact, which is sustained for more than 10 seconds (score −1).
   Patient has eye opening and eye contact, but this is not sustained for 10 seconds (score −2).
   Patient has any movement in response to voice, excluding eye contact (score −3).
3. If patient does not respond to voice, physically stimulate patient by shaking shoulder and then rubbing sternum if there is no response to shaking shoulder.
   Patient has any movement to physical stimulation (score −4).
   Patient has no response to voice or physical stimulation (score −5).

8.2 Behavioral Pain Scale (BPS score)

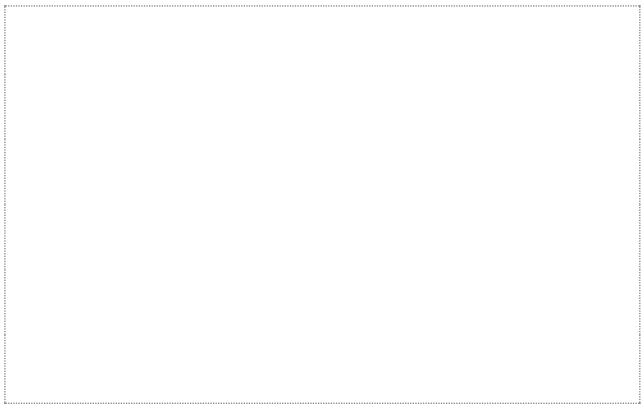
Item	Description	Score
Facial expression	Relaxed	1
	Partially tightened (e.g., brow lowering)	2
	Fully tightened (e.g., eyelid closing)	3
	Grimacing	4
Upper limbs	No movement	1
	Partially bent	2
	Fully bent with finger flexion	3
	Permanently retracted	4
Compliance with ventilation	Tolerating movement	1
	Coughing but tolerating ventilation for most of the time	2
	Fighting ventilator	3
	Unable to control ventilation	4

Vu, le Président du Jury,



Professeur Antoine ROQUILLY

Vu, le Directeur de Thèse,



Dr Raphael CINOTTI

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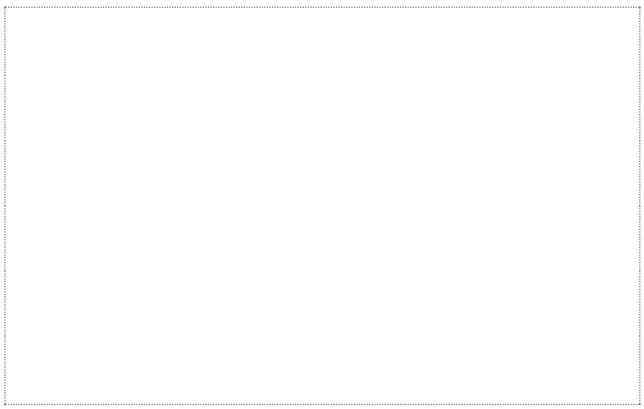

Professeur Pascale JOLLIET

DESMEDT Luc

Impact et faisabilité d'un protocole d'analgésie-sédation, dirigé par les infirmières et basé sur les échelles RASS et BPS, chez les patients brûlés graves de réanimation sous ventilation mécanique. Une étude bi-centrique, de type avant/après. L'étude SEDABURN

RESUME

Contexte. La gestion de l'analgésie-sédation est l'une des pierres angulaires de la prise en charge des patients sous ventilation mécanique en réanimation. Elle doit permettre le confort du patient, tout en évitant les effets adverses reconnus d'une sédation profonde et prolongée. Pour ce faire, les recommandations internationales préconisent l'utilisation de protocoles visant l'obtention d'une sédation légère à l'aide d'échelles d'évaluation clinique. A ce jour, aucune étude n'a évalué la faisabilité et l'intérêt de tels protocoles chez les patients brûlés graves de réanimation.

Objectif. Déterminer si la mise en place d'un protocole d'analgésie-sédation, dirigé par les infirmières et visant l'obtention d'une sédation légère à l'aide des échelles RASS et BPS, était associée à une diminution de la durée de ventilation mécanique des patients brûlés graves de réanimation.

Méthode. Nous avons réalisé une étude de type avant/après chez les patients brûlés de réanimation dont la durée de ventilation mécanique était estimée supérieure à 24 heures, dans les hôpitaux universitaires de Nantes et Montpellier. Durant la période « avant », la gestion des sédatifs et antalgiques intraveineux était laissée à l'appréciation du prescripteur. Durant la période « après », un protocole guidait les infirmières dans la titration des morphiniques et des sédatifs intraveineux à partir des échelles RASS et BPS, avec comme cible l'absence de douleur (BPS<5) et l'obtention d'une sédation légère (RASS+1/-1). Durant ces deux phases, la douleur liée aux soins était contrôlée par l'administration protocolisée de morphinique à durée de vie courte et les pratiques courantes de réanimation étaient inchangées.

Résultats. Au total, 188 patients ont été inclus (groupe contrôle, n = 87 (46.2%) ; groupe intervention, n = 101 (53.7%)). Les données démographiques, les caractéristiques des brûlures et la gravité des patients à l'admission étaient comparables entre les deux groupes. La mise en place du protocole n'était pas associée à une diminution significative de la durée de ventilation mécanique des patients (groupe contrôle, 14 [3 ;29] ; groupe intervention, 7 [2 ;24] ; p=0.4). La prise en compte de la compétition entre mortalité et sevrage de la ventilation mécanique ne mettait pas en évidence de différence significative entre les deux phases (Gray test, p=0.4). L'analyse de série chronologique dégageait une tendance non significative vers une diminution de la durée de ventilation mécanique en faveur du groupe interventionnel (p=0.6). La mise en place du protocole n'apportait pas d'autres bénéfices, que cela soit sur la durée d'administration des hypnotiques et morphiniques intraveineux, l'incidence des pneumonies acquises sous ventilation mécanique, la durée de séjour ou la mortalité en réanimation.

Conclusion. La mise en place d'un protocole d'analgésie-sédation dirigé par les infirmières et visant l'obtention d'une sédation légère était réalisable mais ne permettait pas de diminuer la durée de ventilation mécanique chez les patients brûlés graves de réanimation.

MOTS-CLES : Patients brûlés ; soins intensifs ; ventilation mécanique ; protocole clinique ; sédation