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Sedation in pediatric intensive care unit and its impact on outcomes of ventilated children: a prospective observational study

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Abstract

Background Sedation is an integral part in the management of critical patients in the pediatric intensive care unit (PICU). Optimum sedation is when the child is asleep but easily arousable. The patient should be able to breathe synergistically with the ventilator and should tolerate or be compliant with other therapeutic procedures. Undersedation can make the children hypertensive, tachycardic, and agitated. Conversely, oversedation can cause increased tolerance and prolonged ventilation. Both undersedation and oversedation have negative impacts on patient outcomes such as prolonged mechanical ventilation and ICU stay and increased risk of contracting ventilator-associated pneumonia, thus contributing to significant morbidity and mortality. This study aims to assess sedation levels in ventilated children using RASS in the first 48hrs of ventilation and study their correlation with patient outcomes.

Results Of the 111 children enrolled in the study, 2 were excluded because the sedation was discontinued before 48 h, and 9 were excluded because they were ventilated for more than 7 days. Majority of the children receiving ventilation in PICU were oversedated (40%). Adequately sedated children were observed to have significantly lesser duration of mechanical ventilation (*p*-value: 0.022) and PICU stay (*p*-value: 0.01). Undersedated children were noted to have significantly higher incidence of self extubation (*p*-value: < 0.001), reintubation (*p*-value: < 0.001), and higher requirement of restraints (*p*-value: < 0.001). Oversedated had a higher incidence of VAP and mortality (*p*-value: < 0.001).

Conclusion The findings of this study highlight the importance of achieving adequate sedation in PICU which is associated with better outcomes with respect to duration of ventilation, PICU stay, hospital stay, and mortality. This study also reflects the impact of absence of sedation protocols and emphasizes the need for monitoring of sedation and having protocols to guide clinical practice in order to improve patient outcome.

Keywords Sedation, Ventilation, RASS, Mortality, Ventilator-associated pneumonia

Background

Sedation is an integral part of management of critical patients in the pediatric intensive care unit (PICU). Underlying medical conditions and several "routine" aspects of critical care such as mechanical ventilation, indwelling tubes and catheters, nursing interventions, and excessive intensive care unit (ICU) noise and light amplify the fear and anxiety [1]. Pain and anxiety accentuate the sympathetic stress response which results in increased oxygen consumption, hypercoagulability, hyper-metabolism, and immunosuppression [2]. Hence, it is necessary to minimize anxiety and pain by maximizing the quality and length of sleep with minimal or no pain and anxiety [3].

Optimum sedation is when the child is asleep but easily arousable. The patient should breathe synergistically with

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the ventilator and should be able to tolerate or be compliant with other therapeutic procedures [4]. An ideal sedative agent would possess several characteristics such as rapid onset of action, allow prompt recovery after discontinuation, ease of administration, minimal drug accumulation with limited adverse effects, and interact minimally with other drugs [5].

Adequate sedation is important because undersedation can make the children hypertensive, tachycardic, and agitated. Conversely, oversedation can cause increased tolerance and prolonged ventilation [6]. Excessive sedation also has a negative impact on patient outcomes such as prolonged mechanical ventilation and ICU stay and increased risk of contracting ventilator-associated pneumonia, thereby causing significant morbidity and mortality [4, 7].

A systematic review by Vet et al. in 2013 showed that only 60% of children in PICU are optimally sedated and oversedation is much more common than undersedation. This disproportion puts the child at risk to develop post-traumatic stress disorder, with potential for future adverse neurodevelopmental outcomes, delirium, tolerance, and withdrawal [8]. The 2018 guidelines for prevention of pain, agitation, and sedation in adult patients included an ungraded statement that daily sedation interruption (DSI) protocols and nurse-protocolized targeted sedation can achieve and maintain a lower level of sedation [9]. The 2013 guidelines suggested targeting lower levels of sedation to improve outcomes such as duration of mechanical ventilation, ICU stay, and overall hospital stay. A survey from Brazil showed that 87.5% of PICUs used a validated scale of which the most commonly used scales were the Ramsay Sedation Scale (RSS) and Richmond Agitation Sedation Scale (RASS) followed by COMFORT scale and COMFORT-B scale [10]. However, a survey from Argentina showed that only 31% of PICUs used sedation tools for assessing the level of sedation which included RSS and COMFORT scale in critically ill children. The rest used the patient's physiological parameters, movement, and general wellbeing to assess the level of sedation [11]. Chawla et al. in 2014 observed that there was very low compliance with guidelines and minimal usage of recommended scales or monitoring of sedation levels despite of adequate awareness [12].

The objective of this study was to assess the sedation levels of children ventilated in our pediatric intensive care unit and its impact on patient outcomes and comorbidities.

Methods

This is a prospective observational study conducted in the pediatric intensive care unit (PICU) over a period of 1 year and 2 months from January 2018 to March 2019. The study protocol was approved by the institutional ethics committee (vide letter ref no: 201801–013-IEC/CMCL-APPRVL-PG.THESIS/Peds), and the children were enrolled after taking written informed consent from parents or legal guardians.

Inclusion criteria

All children between 3 months and 18 years of age who were on mechanical ventilation (MV) and were sedated for at least 48 h were included.

Exclusion criteria

Children who had their ventilation discontinued or had died within 48 h of ventilation were excluded from the study. Additionally, postoperatively ventilated children, children ventilated after cardiac arrest, and children with global developmental delay or head injury were also excluded. No clinical scoring was done to assess the sickness severity of the ventilated children.

The children included in the study were initiated with an infusion of midazolam at the rate of 1 mcg/kg/min and fentanyl at the rate of 1mcg/kg/h. These initial doses were titrated within the acceptable dose range according to judgment of the treating physician. The sedation levels were assessed by the Richmond Agitation and Sedation Scale (RASS) every 4 h for the first 48 h. RASS is a 10-point scoring system ranging from $+4$ to -5 where 0 to -2 was considered as an optimal sedation score. Therefore, based on the scores calculated at the end of every 4 h, the children were categorized in 4 groups (undersedated, oversedated, adequately sedated, and improperly sedated). The overall level of sedation of the child over 48 h was categorized on the basis of 4-hourly scores (6 scores in 24 h).

- A child was considered as appropriately sedated if ≥ 4 scores were between -2 to 0 in the 24 h observation period.
- A child was considered as undersedated if ≥ 4 scores were $\geq +1$ during the 24 h observation period.
- A child was considered as over-sedated if ≥ 4 scores were ≤ -3 during the 24 h observation period.
- Children with lesser than 4 scores in one category was categorized as "improper sedation."

Different outcomes such as duration of ventilation, total PICU stay and total hospital stay, ventilator-associated pneumonia, spontaneous extubation, reintubation, and the need for restraints were documented.

Considering the number of pediatric ICU admissions in our institution over a period of 2 years, which is approximately around 500, and taking into account that nearly 50% required MV, a sample size of 100 children

were planned, with an alpha error of 5% and precision of 10%.

Data analysis was done using SPSS version 26.0. For cases where the expected count of cell was less than 5, Fisher's exact test was used. One-way ANOVA or Kruskal–Wallis test was used to compare the hospital stay, PICU stay, and duration of mechanical ventilation with levels of sedation. The p value < 0.05 was considered statistically significant.

Results

A total of 111 children who met the inclusion criteria were enrolled for the study. However, two children had to be excluded from the study because the sedation was stopped prior to 48 h; 9 were excluded because the duration of mechanical ventilation extended beyond 7 days (Fig. 1). The baseline characteristics of included children are given in Table 1.

Upon analyzing the average of the 4-hourly RASS scores calculated during the first 48 h, it was observed that 40% of patients were oversedated, 31% were

Table 1 Baseline characteristics of PICU

Median age in years (range)	2.9 (0.25–17)
Males (%)	64
Females (%)	36
Diagnosis at PICU admission (%)	
Respiratory system (RS)	42
Cardiovascular system (CVS)	9
Renal system (ReS)	3
Central nervous system (CNS)	10
Miscellaneous (M)	36
Total	100
Indication for mechanical ventilation (%)	
Respiratory failure	56
Shock	6
Low GCS	3
Respiratory failure with shock	35
Total	100

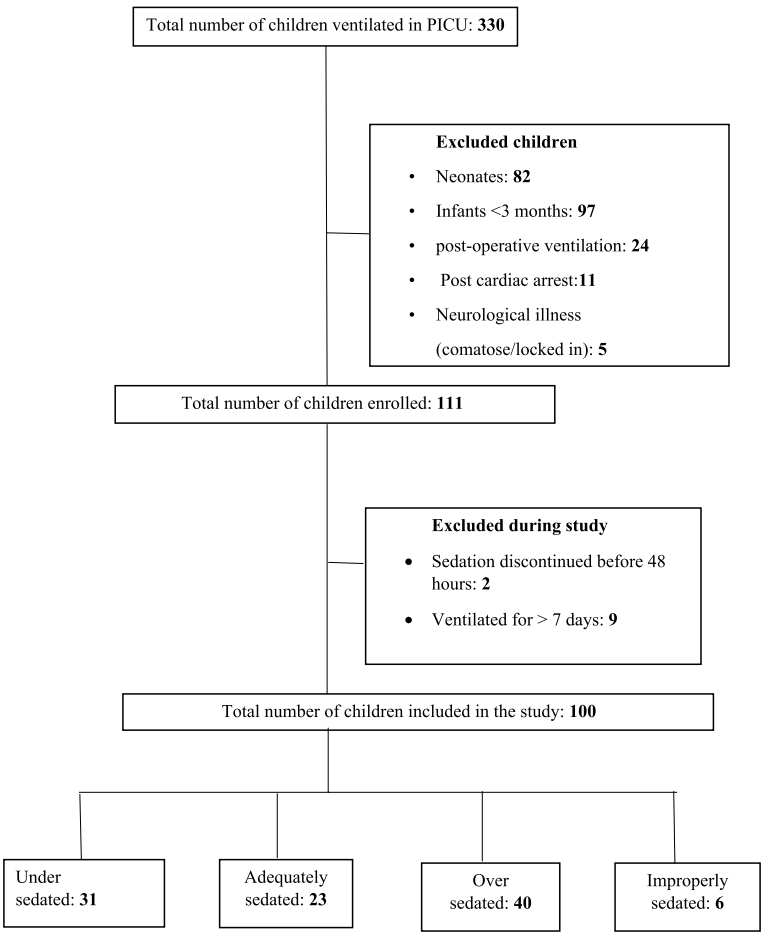

Fig. 1 Flow chart

undersedated, 23% were adequately sedated, and 6% were improperly sedated (Fig. 1). The most common diagnosis was respiratory illnesses, and there was no statistically significant correlation between the levels of sedation observed and primary illness (p-value: 0.760).

Among the different sedation levels, adequately sedated children had shortest duration of mechanical ventilation (p-value: 0.022). The mean (SD) and duration of mechanical ventilation among the adequately sedated children, undersedated children, oversedated children, and improperly sedated children were 3.6 (1.2) days, 4.9 (1.32) days, 4.5 (1.9) days, and 4.3 (1.2) days respectively. During the course of the study, 28 children expired, of which 71.4% were oversedated, 21.4% were undersedated, 3.6% were adequately sedated, and 3.6% were improperly sedated. The incidence of mortality was significantly higher in the oversedated children (p-value: 0.001).

The duration of PICU and hospital stay was calculated among 72 surviving children. The average duration of PICU stay was 5.7 (2.9) days, 6.9 (3.1) days, 6.9 (3.2) days, and 5.8 (1.1) days in the adequately sedated, undersedated, oversedated, and improperly sedated children respectively. However, this difference was not statistically significant (p-value: 0.402). A statistically significant proportion of adequately sedated children had less than 7 days of PICU stay (p-value: 0.01). Also, the adequately sedated children had a shorter hospital stay although the values were not statistically significant (p-value: 0.215).

The occurrence of spontaneous extubation and reintubations was significantly more in undersedated and improperly sedated children (p-value: < 0.001). Among children who received adequate and oversedation, there was no incidence of reintubation or spontaneous extubation. The incidence of ventilator associated pneumonia was highest among the over-sedated children (41.8%) followed by 34.8% in under-sedated, 16.27% in adequately sedated, and 6.9% in improperly sedated. However, there was no statistically significant correlation (p-value: 0.565).

A significant proportion of undersedated (71.4%) children required restraints (p-value: < 0.001). About 11.4% of adequately sedated and 8.6% each of oversedated and improperly sedated children needed restraints. These outcomes are summarized in Table 2.

Discussion

Ensuring patient comfort and promoting tolerance to the PICU environment are crucial goals in the care of the critically ill. It is important to strike a balance since excessive sedation can have a negative impact on patient outcomes including duration of mechanical ventilation, ICU stay, and risk of contracting ventilator-associated pneumonia, ultimately leading to significant morbidity and mortality [4, 7]. In spite of these risks, not all PICUs have implemented a sedation monitoring protocol.

In a survey conducted by Blackwood et al. in 23 PICUs in UK from June to November 2014, it was found that majority of the PICUs utilized a validated scale for assessing sedation levels [13]. Another survey from Brazil showed that 87.5% of PICUs employed sedation scales of which the most commonly used scales were the RSS and RASS followed by COMFORT scale and COMFORT-B scale [10].

In contrast, a survey from Argentina showed that only 31% of PICUs used sedation tools for assessing the level of sedation which included RSS and COMFORT scale in critically ill children, and the rest used the patient's physiological parameters, movement, and wellbeing to assess the level of sedation [11]. A survey done by Liu and Gi in China in 2019 which included 14 PICUs revealed that RSS is the most frequently used scale followed by COMFORT scale and RASS [14].

Before conducting this research, our PICU did not follow a sedation protocol. A significant proportion of the

Table 2 Correlation of levels of sedation with outcome

Outcomes	Adequately sedated	Undersedated	Oversedated	Improperly sedated	Total no. of patients (*n*)	*p*-value
Mean duration of MV in days (SD)	3.6 (1.2)	4.9 (1.32)	4.5 (1.9)	4.3 (.21)	100	**0.02***
Mean duration of PICU stay in days (SD)	5.7 (2.9)	6.9 (3.1)	6.9 (3.2)	5.8 (1.1)	72	0.402
PICU stay < 7 days	18 (81.8)	12 (48)	9 (45)	5 (100)	72	**0.01***
Mean duration of Hospital stay (SD)	10.1 (6.1)	12.3 (5.3)	13.8 (6.5)	10.2 (5.1)	72	0.21
Spontaneous extubation (%)	0 (0)	5 (62.5)	0 (0)	3 (37.5)	8	**< 0.00***
Reintubation (%)	0 (0)	5 (55.6)	1 (11.1)	3 (33.3)	9	**< 0.00***
Restraints (%)	4 (11.4)	25 (71.4)	3 (8.6)	3 (8.6)	35	**< 0.00***
VAP (%)	7 (16.27)	15 (34.8)	18 (41.8)	3 (6.9)	43	0.56
Mortality (%)	1 (3.6)	6 (21.4)	20 (71.4)	1 (3.6)	28	**0.00***

* p-value < 0.05: statistically significant

children were observed to be oversedated (40%). In a systematic review about optimum sedation levels in PICU by Vet et al., it was concluded that the primary reason for oversedation was to prevent adverse events like accidental extubation, pulling out intravenous, and urinary catheters [8]. Additionally, it has been noted that, as preverbal infants cannot communicate their wellbeing and anxiety, PICU workers prefer to keep them oversedated. Vet et al. noted that the nursing personnel assumed that oversedation helped the discomfort of mechanical ventilation besides nothing; poor adherence to sedation protocols is another reason [8]. These factors could be the reason for the high prevalence of oversedation in our PICU. The sedatives were given as a continuous combined infusion of midazolam and fentanyl. Da Silva et al. in their study in 2015 concluded that children receiving a combined infusion of midazolam and fentanyl were given a significantly higher total cumulative dose when compared with the children who received separate infusions of midazolam and fentanyl [15].

This could explain the higher proportion of oversedated children in this study as all the children received a combined infusion of midazolam and fentanyl for sedation. We discovered that the duration of mechanical ventilation was significantly lesser in the children who were adequately sedated when compared with children who were undersedated and oversedated. Drefus et al. in his study also observed a shorter duration of mechanical ventilation in children who are adequately sedated [16].

In another study by Vet et al., a lesser mean duration of mechanical ventilation was observed in the group of patients receiving protocolized sedation with DSI when compared to the patients receiving protocolized sedation alone. A larger number of patients were also found to be oversedated in those receiving protocolized sedation alone [17].

In our study, there was no statistically significant difference in the average duration of PICU and hospital stay. However, a significantly greater proportion of children who were adequately sedated (81.8%) had < 7 days of PICU stay when compared with patients who were oversedated and undersedated. A study by Jin et al. showed a significantly lower median length of PICU stay in the group of patients receiving protocolized sedation when compared to non-protocolized sedation group. The study also showed a lesser duration of sedation in the protocolized group as well as a significant lower total dose of fentanyl and maximum rate of continuous midazolam infusion [18].

We found that there was a significantly higher incidence of mortality observed among the oversedated children. Shehabi et al., in a multicentric study in the year 2018, observed a significantly increased influence of oversedation on the 180-day mortality, thereby suggesting to keep the sedation level equivalent to a RASS 0 as the goal [19].

Additionally, we observed a significantly higher incidence of spontaneous extubation, reintubations, and the use of restraints among undersedated children when compared with the adequately and oversedated children. Similar results were observed in the study done by Vet et al. comparing protocolized sedation with DSI and protocolized sedation alone, where only one case of unplanned spontaneous extubation in the group receiving DSI [17]. In Rose et al., in their study of prevalence, risk factors, and outcomes associated with use of physical restraints among oversedated critically ill mechanically ventilated adult patients in Canada, a significantly lower utilization of restraints were observed among oversedated patients [20].

Limitations

1 The level of sedation was limited to the first 48 h, and the subsequent duration of hospitalization was not recorded which may have also had influenced the outcomes.
2 PRISM scoring of the ventilated children to assess the severity of illness was not done which may bear an independent impact on the outcomes.

Conclusion

There is a lack of studies from Indian PICUs that highlights the importance of sedation protocols and benefits to patient outcomes. Our study reflects the impact of absence of sedation protocols and suggests that monitoring of sedation and having protocols to enhance the overall quality of care provided in PICUs.

Every pediatric ICU should adopt a sedation monitoring protocol in mechanically ventilated children and ensure optimal sedation levels to potentially reduce mechanical ventilation and duration of PICU stay as well as decrease the incidence of reintubations. This approach will indirectly reduce the incidence of ventilator-associated pneumonia and improve mortality rates.

This study also invokes the potential of RASS to be used as an interventional tool among children and titrate the sedation levels for better patient outcomes.

Abbreviations

DSI	Daily sedation interruption
ICU	Intensive care unit
MV	Mechanical ventilation
PICU	Pediatric intensive care unit
RASS	Richmond Agitation Sedation score
RSS	Ramsay Sedation Scale
SD	Standard deviation

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Authors' contributions
NS collected, compiled, and analyzed the data. The manuscript was also drafted by the same author. MS analyzed the data and revised the manuscript. GK revised the manuscript.

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Availability of data and materials
The datasets generated and/or analyzed during the current study are not publicly available due to data sharing policy of the institution and to protect the privacy of the study participants. However, it can be availed from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
The study was started after obtaining approval from the institutional (Christian Medical College, Ludhiana) research and ethics committee, reference no.-201801–013-IEC/CMCL.
Consent to participate in the study was obtained from all the subjects included in the study.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

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References

1. Parthasarathy, S. and Tobin, M. J. (2009). Sleep in the intensive care unit. Applied Physiology in Intensive Care Medicine, 191–200.https://doi.org/10.1007/s00134-003-2030-6
2. Jacobi J, Fraser GL, Coursin DB, Riker RR, Fontaine D, Wittbrodt ET et al (2002) Clinical practice guidelines for the sustained use of sedatives and analgesics in the critically ill adult. Crit Care Med 30(1):119–141. https://doi.org/10.1097/00003246-200201000-00020
3. Ely EW, Truman B, Shintani A, Thomason JW, Wheeler AP, Gordon S et al (2003) Monitoring sedation status over time in ICU patients: reliability and validity of the Richmond Agitation-Sedation Scale (RASS). JAMA 289(22):2983–2991. https://doi.org/10.1001/jama.289.22.2983
4. Vet NJ, Kleiber N, Ista E, De Hoog M, De Wildt SN (2016) Sedation in critically ill children with respiratory failure. Front Pediatr 4:89. https://doi.org/10.3389/fped.2016.00089
5. Ostermann ME, Keenan SP, Seiferling RA, Sibbald WJ (2000) Sedation in the intensive care unit: a systematic review. JAMA 283(11):1451–1459. https://doi.org/10.1001/jama.283.11.1451
6. Riker RR, Fraser GL (2009) Altering intensive care sedation paradigms to improve patient outcomes. Crit Care Clin 25(3):527–538. https://doi.org/10.1016/j.ccc.2009.05.004
7. Sessler, C. N., Grap, M. J. and Ramsay, M. A. (2008). Evaluating and monitoring analgesia and sedation in the intensive care unit. Critical care, 12(3):1–13. https://doi.org/10.1186/cc6148.
8. Vet NJ, Ista E, de Wildt SN, van Dijk M, Tibboel D, de Hoog M (2013) Optimal sedation in pediatric intensive care patients: a systematic review. Intensive Care Med 39:1524–1534. https://doi.org/10.1007/s00134-013-2971-3
9. Devlin JW, Skrobik Y, Gélinas C, Needham DM, Slooter AJ, Pandharipande PP et al (2018) Clinical practice guidelines for the prevention and management of pain, agitation/sedation, delirium, immobility, and sleep disruption in adult patients in the ICU. Crit Care Med 46(9):e825–e873. https://doi.org/10.1097/CCM.0000000000003299
10. Oliveira FRCD, Araujo ORD, Garros D, Colleti Junior J, Carvalho WBD, Lequier L (2022) Extracorporeal membrane oxygenation for respiratory failure in children: the years before and after the 2009 H1N1 pandemic. Rev Bras Terapia Intens 33:544–548. https://doi.org/10.5935/0103-507X.20210082
11. Taffarel P, Bonetto G, Jorro Barón F, Meregalli C (2018) Sedation and analgesia in patients on mechanical ventilation in pediatric intensive care units in Argentina. Arch Argent Pediatr 116(2):e196–203. https://doi.org/10.5546/aap.2018.eng.e196
12. Chawla R, Myatra SN, Ramakrishnan N, Todi S, Kansal S, Dash SK (2014) Current practices of mobilization, analgesia, relaxants and sedation in Indian ICUs: a survey conducted by the Indian Society of Critical Care Medicine. Indian J Crit Care Med 18(9):575. https://doi.org/10.4103/0972-5229.140146
13. Blackwood B, Tume L (2015) The implausibility of 'usual care' in an open system: sedation and weaning practices in Paediatric Intensive Care Units (PICUs) in the United Kingdom (UK). Trials 16(1):1–9. https://doi.org/10.1186/s13063-015-0846-3
14. Liu Z, Ge X (2019) The sedation practices of paediatric intensive care unit nurses and the influencing factors in China. Nurs Crit Care 24(5):306–312. https://doi.org/10.1111/nicc.12426
15. da Silva PSL, Reis ME, de Aguiar VE, Fonseca MCM (2016) Use of fentanyl and midazolam in mechanically ventilated children—Does the method of infusion matter? J Crit Care 32:108–113. https://doi.org/10.1016/j.jcrc.2015.12.003
16. Dreyfus L, Javouhey E, Denis A, Touzet S, Bordet F (2017) Implementation and evaluation of a paediatric nurse-driven sedation protocol in a paediatric intensive care unit. Ann Intensive Care 7(1):1–13. https://doi.org/10.1186/s13613-017-0256-7
17. Vet NJ, de Wildt SN, Verlaat CW, Knibbe CA, Mooij MG, van Woensel JB et al (2016) A randomized controlled trial of daily sedation interruption in critically ill children. Intensive Care Med 42:233–244. https://doi.org/10.1007/s00134-015-4136-z
18. Jin HS, Yum MS, Kim SL, Shin HY, Lee EH, Ha EJ et al (2007) The efficacy of the COMFORT scale in assessing optimal sedation in critically ill children requiring mechanical ventilation. J Korean Med Sci 22(4):693–697. https://doi.org/10.3346/jkms.2007.22.4.693
19. Shehabi Y, Bellomo R, Kadiman S, Ti LK, Howe B, Reade MC et al (2018) Sedation intensity in the first 48 hours of mechanical ventilation and 180-day mortality: a multinational prospective longitudinal cohort study. Crit Care Med 46(6):850–859. https://doi.org/10.1097/CCM.0000000000003071
20. Rose L, Burry L, Mallick R, Luk E, Cook D, Fergusson D et al (2016) Prevalence, risk factors, and outcomes associated with physical restraint use in mechanically ventilated adults. J Crit Care 31(1):31–35. https://doi.org/10.1016/j.jcrc.2015.09.011

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