Use of sedatives and analgesics and hospital outcomes in pediatric intensive care: a cohort study

Uso de sedativos e analgésicos e desfechos hospitalares em terapia intensiva pediátrica: estudo de coorte

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ABSTRACT

BACKGROUND AND OBJECTIVES: Continuous infusion sedoanalgesia may favor negative hospital outcomes, thus, the objective was to analyze the relationship between continuous infusion sedoanalgesia and factors such as duration of mechanical pulmonary ventilation (MPV), extubation failure, hospital infections, length of hospitalization, and death in a mixed pediatric intensive care unit (PICU). The aim of this study was to identify the association of the use of sedatives and analgesics in continuous infusion with hospital outcomes through the control of confounding variables.

METHODS: Retrospective cohort with hospitalizations of children aged zero to 14 years, from 2012 to 2017. Use of continuous sedoanalgesia was considered a factor for the outcomes: duration of MPV, extubation failure, hospital infections (healthcare-associated infections - HCAI, fungal infection and catheter-related bloodstream infection), length of stay in the PICU and hospital, and death. Poisson regression was performed with adjustment by progressive models, with a significance level of 5%, calculation of relative risk (RR) and confidence interval (95% CI).

RESULTS: A total of 894 hospitalizations were analyzed, with a predominance of males (54.3%), non-malnourished children (70.7%) and without a diagnosis of chronic disease (55.1%). Infants accounted for half of the population. The outcomes that were associated with continuous sedoanalgesia in the final model were: MPV time > 4 days (RR=2.74; 95%CI=1.90-3.93), HCAI (RR=1.91; 95%CI=.32-2.80), fungal infection (RR=2.00; 95%CI=1.12-3.58), length of stay in the PICU > 3 days (RR=1.81; 95%CI=1.51 -2.17) and hospital stay > 10 days (RR=1.52; 95%CI=1.27-1.84), and death (RR=0.64; 95%CI=0.43-0.95).

CONCLUSION: MPV time longer than four days, diagnosis of HCAI, diagnosis of fungal infection, length of stay in the PICU longer than three days, and hospitalization time longer than 10 days were factors more present in children who received continuous infusion of sedoanalgesia. Death, on the other hand, was more related to severity variables than to the use of psychoactive drugs.

Keywords: Analgesia, Artificial ventilation, Cross infection, Deep sedation, Intensive Care Units, Length of stay.

RESUMO

JUSTIFICATIVA E OBJETIVOS: A sedoanalgesia em infusão contínua pode favorecer desfechos hospitalares negativos, assim, o objetivo foi analisar a relação entre sedoanalgesia em infusão contínua e fatores como tempo de ventilação pulmonar mecânica (VPM), falha de extubação, infecções hospitalares, tempo de internação e óbito numa unidade de terapia intensiva pediátrica (UTIP) mista. Este estudo buscou identificar a associação do uso de sedativos e analgésicos em infusão contínua com desfechos hospitalares por meio do controle de variáveis de confusão.

MÉTODOS: Coorte retrospectivo com internações de crianças de zero a 14 anos, de 2012 a 2017. Uso de sedoanalgesia contínua foi considerado fator para os desfechos tempo de VPM, falha de extubação, infecções hospitalares (infecções relacionadas à assistência à saúde - IRAS, infecção fúngica e infecção de corrente sanguínea relacionada a cateter), tempo de internação em UTIP e no hospital e óbito. Foi realizada a regressão de Poisson com ajuste por modelos progressivos com nível de significância de 5%, cálculo do risco relativo (RR) e intervalo de confiança (IC 95%).

RESULTADOS: Foram analisadas 894 internações, predominando o sexo masculino (54,3%), crianças não desnutridas (70,7%) e sem diagnóstico de doença crônica (55,1%). Lactentes representaram metade da população. Os desfechos que se associaram à sedoanalgesia contínua no modelo final foram: tempo de VPM > 4 dias (RR=2,74; IC95%=1,90-3,93), IRAS (RR=1,91; IC95%=1,32-2,80), infecção fúngica (RR=2,00; IC95%=1,12-3,58), tempo de internação na UTIP > 3 dias (RR=1,81; IC95%=1,51-2,17) e hospitalar > 10 dias (RR=1,52; IC95%=1,27-1,84) e óbito (RR=0,64; IC95%=0,43-0,95). The aim of this study was to identify the association of the use of se-

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datives and analgesics in continuous infusion with hospital outcomes through the control of confounding variables.
CONCLUSÃO: Tempo de VPM maior que quatro dias, diagnóstico de IRAS, diagnóstico de infecção fúngica, tempo de internação na UTIP maior que três dias e tempo de internação hospitalar maior que 10 dias foram mais incidentes nas crianças que receberam sedoanalgesia em infusão contínua. Já o óbito apresentou maior relação com as variáveis de gravidade do que com o uso de fármacos psicoativos.
Descritores: Analgesia, Infecções nosocomiais, Sedação profunda, Tempo de internação, Unidades de Terapia Intensiva Pediátrica, Ventilação artificial.

INTRODUCTION

Intensive care units (ICU) are environments in which severely ill patients remain under multiprofessional care until their clinical condition improves or stabilizes. They must have technological resources for diagnosis, monitoring and treatment of the hospitalized person. The ICU is classified according to age group as: neonatal, for patients between zero and 27 days of age; pediatric, for children between 28 days and 14 or 18 years of age; and mixed, when it cares for newborns and adolescents between 14 and 18 years of age, according to institutional norms[1].
ICU peculiarities, associated with invasive procedures inherent to the patient's status of severity, culminate in higher levels of stress, anxiety, and agitation, especially in children[2]. Thus, sedation and analgesia are essential in the therapeutic processes of the pediatric ICU (PICU)[3]. However, adjusting the ideal dose in this population is a challenge due to the large difference in age groups of children admitted to PICU of mixed profile[4]. Sedoanalgesia can be performed continuously or intermittently, i.e., with minimal interval between doses. The most commonly used classes of drugs are benzodiazepines and opioids[4,5].
Adverse effects resulting from the continuous use of these drugs can be observed due to their cumulative effects, which result in higher incidence of withdrawal symptoms and delirium, as well as longer mechanical ventilation time and hospital stay. However, the literature emphasizes these consequences by analyzing specific drugs and/or combinations of them[4,6,7].
In the case of children admitted to mixed profile PICU, comprehending how the use of these drugs is associated with negative outcomes, regardless of the drug class, by controlling confounding variables, will contribute to better direct the care provided, with the creation of protocols that allow differentiated management of these patients. Thus, the present study's objective was to analyze the relationship between the use of continuous infusion sedoanalgesia and health outcomes in a mixed PICU.

METHODS

The study was conducted according to the international guidelines for observational studies (Strengthening the Reporting of Observational Studies in Epidemiology - STROBE). A retrospective cohort study composed of hospitalizations of children and adolescents from zero to 14 years of age in a tertiary care hospital PICU, located in a city in southern Brazil. At the time of the research, the city had 36 PICU beds, of which seven were in the public network, the location of this research, and 31 in private or philanthropic hospitals. The PICU studied is a reference for care provided to children and adolescents of the city and surrounding area, offering assistance in pediatric nephrology, child surgery, pediatric trauma, neurosurgery, major burns, and others.
The hospitalizations covered the period between January 1st, 2012 and December 31, 2017, which were listed and provided by the hospital's medical archive service. Cases of hospitalizations of children and adolescents who received continuous neuromuscular blockers and dissociative drugs (ketamine) intravenously were excluded due to the pharmacokinetic particularities of these drugs. Infusions of sedatives and/or analgesics that lasted less than 24 hours, a period considered insufficient for association with the outcomes analyzed, were also not considered. Patients diagnosed with encephalic death were excluded for characterizing peculiar diagnostic conduct with the potential to interfere in the proposed analyses. Not located medical records and ignored information on continuous infusion of sedoanalgesia were considered losses.
The variables analyzed in this research were: gender (male and female); age in years (< 1; 1 to 3; 4 to 6; 7 and more); Z-score classified according to weight measurement measured on admission, by age (malnourished: < -2; non-malnourished: ≥ -2), diagnosis of chronic disease on admission, considered as that with evolution longer than 30 days and in need of specialized pediatric follow-up (yes and no); main admission diagnoses, evaluated separately, such as respiratory failure, postoperative, sepsis, severe acute respiratory syndrome (SARS), and traumatic brain injury (TBI) (yes and no); need for mechanical pulmonary ventilation (MPV) (yes and no); and need for vasoactive drug (yes and no). These factors were assessed according to the need for sedatives and/or analgesics in continuous infusion (yes and no). The sedative drugs in this study were midazolam, thionembutal, clonidine, propofol, and dexmedetomidine. Fentanyl, morphine, and remifentanil were the analgesics considered.
The use of continuous sedoanalgesia (yes and no) was considered a factor for the following hospital outcomes: time of MPV, in days, according to the median (≤ 4 and > 4); extubation failure, that is, need for new tracheal intubation within 48h of withdrawal of invasive ventilatory support (yes and no); hospital infections, represented by healthcare-associated infections (HCAI), fungal infection, and catheter-related bloodstream infection (CRBI) (yes and no); length of ICU stay, according to the median, greater than 3 days (yes and no); length of hospitalization, according to the median, greater than 10 days (yes and no); and death (yes and no).
Data were obtained from medical records and transcribed to a form with the patients' sociodemographic characteristics, health history, data on admission to the PICU, information on hospitalization, and health outcomes. The data collection team was composed of nursing and medical students, as well as nursing residents in the field of child and adolescent health and medical residents in the field of pediatrics. All were trained by the research coordinators before the start of data collection. After this step, the forms were checked and coded for later typing.

This research followed the norms of Resolutions no. 466/2012 and no. 510/2016 and was approved by the Ethics Committee on Research Involving Human Beings of the institution (CAAE: 83069418.7.0000.5231).

Statistical analysis

Data were entered into the Epi Info® version 3.5.4 software and analyzed in the Statistical Package for Social Sciences (SPSS)® version 26.0 software. For statistical analysis, a 5% significance level was considered, with calculation of the relative risk (RR) and confidence interval (CI 95%). The Poisson regression model with robust variance was used, which is recommended in the case of a dichotomous and high frequency outcome. For analyses between factor (use of continuous infusion sedoanalgesia) and outcomes, the RR was adjusted by progressive insertions of group of variables (models) that were associated with these outcomes, with a p value < 0.20.

Models were grouped into demographic variables (model 1: gender and categorical age divided into 1 to 11, and ≥ 12 months). In the second model, the variables from the first model were added, plus the admission diagnoses, entered individually (model 2). In the third model, in addition to the previous variables, invasive MPV and vasoactive drugs use were added, characterized as severity variables (model 3).

RESULTS

In the five years assessed, there were 1182 hospitalizations. There were 61 losses, 60 of which were not located medical records and one was due to misinformation on the use of sedation and analgesia in continuous infusion, resulting in 1121 hospitalizations. Of these, 142 and 19 were excluded, respectively, for the continuous use of dissociative drugs and neuromuscular blockers, 52 for continuous infusion of sedatives and/or analgesics for less than 24 hours, and 14 for the confirmation of the diagnosis of encephalic death, resulting in 894 hospitalizations to be assessed. The admissions were characterized by a higher frequency of males (54.3%), hospitalization of non-malnourished children (70.7%) and without diagnosis of chronic disease (55.1%). Half of the children were infants (50.0%). Respiratory failure was the most commonly observed admission diagnosis (44.2%), followed by immediate postoperative care (39.8%). Just over half (51.1%) of the admissions required invasive MPV through orotracheal cannula and 20.8% used cardiocirculatory support through vasoactive drugs. The need for use of continuous sedoanalgesia was significantly associated with infants, with all admission diagnoses, and in children requiring use of MPV (RR=10.25; 95%CI=7.31-14.37) and vasoactive drugs (RR=2.59; 95%CI=2.28-2.95) (Table 1).

Table 1. Demographic, health, and admission variables according to need for continuous infusion sedoanalgesia in a pediatric intensive care unit, Paraná, Brazil, 2012 to 2017

Variables*	n	%	Continuous sedoanalgesia			
			Yes		RR (CI 95%)	p-value
			n	%		
Gender (n=891)						
Male	484	54.3	216	44.6	1.15 (0.98-1.35)	0.082
Female	407	45.7	158	38.8	-	
Age (years) (n=894)						
< 1	447	50.0	215	48.1	1.30 (1.04-1.62)	0.023
1 to 3	174	19.5	63	36.2	0.98 (0.74-1.30)	0.865
4 to 6	114	12.8	38	33.3	0.90 (0.65-1.25)	0.523
7 and more	159	17.7	59	37.1	-	-
Z-score (n=858)						
Malnourished	251	29.3	111	44.2	1.11 (0.94-1.32)	0.214
Non-malnourished	607	70.7	241	39.7	-	
Chronic disease (n=894)						
Yes	401	44.9	164	40.9	0.96 (0.82-1.12)	0.567
No	493	55.1	211	42.8	-	
Diagnoses on admission (n=894)						
Respiratory failure	395	44.2	227	57.5	1.94 (1.65-2.27)	< 0.001
Postoperatory	356	39.8	109	30.6	0.62 (0.52-0.74)	< 0.001
Sepsis	111	12.4	64	57.7	1.45 (1.21-1.74)	< 0.001
SARS	74	8.3	52	70.3	1.78 (1.50-2.12)	< 0.001
TBI	41	4.6	24	58.5	1.42 (1.09-1.86)	0.010
Need for MPV due to orotracheal cannula (n=894)						
Yes	457	51.1	343	75.1	10.25 (7.31-14.37)	< 0.001
No	437	48.9	32	7.3	-	
Need for vasoactive drugs (n=893)						
Yes	186	20.8	152	81.7	2.59 (2.28-2.95)	< 0.001
No	707	79.3	223	31.5	-	

*Records with ignored information were excluded; RR = relative risk; CI = confidence interval ; SARS = severe acute respiratory syndrome; TBI = traumatic brain injury; MPV = mechanical pulmonary ventilation.

All outcomes in table 2 were associated with use of sedoanalgesia in continuous infusion, except extubation failure, highlighting HCAI (RR=3.76; 95%CI=2.80-5.06), fungal infections (RR=3.63; 95%CI=2.23-5.89), CRBI (RR=3.51; 95%CI=1.96-6.28) and length of stay at the PICU longer than three days (RR=3.31; 95%CI=2.83-3.88).

Table 3 shows the significant outcomes associated with the use of continuous sedoanalgesia with gradual adjustment of confounding variables. All variables except CRBI remained statistically significant in the final model, with reversal of the relative risk for death (RR=0.64; 95%CI=0.43-0.95). There was an impact on the magnitude of the association, after model 3, on the variables HCAI (RR=1.91; 95%CI=1.32-2.80), fungal infection (RR=2.00; 95%CI=1.12-3.58), and PICU length of stay greater than three days (RR=1.81; 95%CI=1.51-2.17).

Table 2. Raw analysis of outcomes associated with the use of continuous infusion sedoanalgesia in a pediatric intensive care unit, Paraná, Brazil, 2012 to 2017

Variables	n	%	Continuous sedoanalgesia			
			Yes		RR (CI 95%)	p-value
			n	%		
Length of MPV use (days) (n=473)*						
≤ 4	250	52.9	151	43.1	-	
> 4	223	47.1	199	56.9	2.91 (2.01-4.22)	< 0.001
Extubation failure (n=347)						
Yes	28	8.1	24	9.0	1.80 (0.64-5.03)	0.264
No	319	91.9	243	91.0	-	
HCAI (n=894)						
Yes	186	20.8	136	36.3	3.76 (2.80-5.06)	< 0.001
No	708	79.2	239	63.7	-	
Fungal infection (n=894)						
Yes	76	8.5	55	14.7	3.63 (2.23-5.89)	< 0.001
No	818	91.5	320	85.3	-	
CRBI (n=894)						
Yes	53	5.9	38	10.1	3.51 (1.96-6.28)	< 0.001
No	841	94.1	337	89.9	-	
Length of stay at PICU > 3 days (n=894)						
Yes	431	48.2	304	81.1	3.31 (2.83-3.88)	< 0.001
No	463	51.8	71	18.9	-	
Length of hospitalization > 10 days (n=894)						
Yes	437	48.9	251	66.9	1.87 (1.63-2.14)	< 0.001
No	457	51.1	124	33.1	-	
Death (n=894)						
Yes	109	12.2	72	19.2	2.69 (1.85-3.91)	< 0.001
No	785	87.8	303	80.8	-	

*Considered child in MPV by orotracheal tube and tracheostomy. RR = relative risk; CI = confidence interval; MPV = mechanical pulmonary ventilation; HCAI = health care related infections, CRBI = catheter-related bloodstream infection.

Table 3. Adjusted analysis of outcomes associated with the use of continuous infusion sedoanalgesia in a pediatric intensive care unit, Paraná, Brazil, 2012 to 2017

Variables	Raw analysis RR (CI 95%)	Adjusted analysis (Model 1) RR (CI 95%)	Adjusted analysis (Model 2) RR (CI 95%)	Adjusted analysis (Model 3) RR (CI 95%)
Time of MPV > 4 days	2.91 (2.01-4.22)	2.83 (1.96-4.08)	2.67 (1.86-3.84)	2.74 (1.90-3.93)*
HCAI	3.76 (2.80-5.06)	3.64 (2.69-4.92)	3.35 (2.45-4.56)	1.91 (1.32-2.80)
Fungal infection	3.63 (2.23-5.89)	3.49 (2.11-5.77)	3.12 (1.89-5.16)	2.00 (1.12-3.58)
CRBI	3.51 (1.96-6.28)	3.21 (1.78-5.78)	3.09 (1.70-5.64)	1.72 (0.74-4.00)
PICU length of stay > 3 days	3.31 (2.83-3.88)	3.13 (2.67-3.67)	2.76 (2.35-3.24)	1.81 (1.51-2.17)
Hospitalization length > 10 days	1.87 (1.63-2.14)	1.79 (1.56-2.05)	1.76 (1.53-2.03)	1.52 (1.27-1.84)
Death	2.69 (1.85-3.91)	2.65 (1.81-3.88)	1.89 (1.29-2.78)	0.64 (0.43-0.95)

RR = relative risk; CI = confidence interval; MPV = mechanical pulmonary ventilation; HCAI = healthcare-associated infections; CRBI = catheter-related bloodstream infection. Model 1: gender and age. Model 2: model 1 and admission diagnosis. Model 3: model 2 and MPV and vasoactive drugs needs. *In model 3, for adjustment of the outcome time of MPV greater than 4 days, model 2 was considered, plus use of vasoactive drugs.

DISCUSSION

A total of 894 PICU admissions were analyzed. The need for sedoanalgesia was frequent in infants, in all analyzed admission diagnoses and in children who required MPV and vasoactive drugs. As for the outcomes, the duration of MPV use greater than four days, diagnosis of HCAI, diagnosis of fungal infection, length of stay in the PICU greater than three days and length of hospitalization greater than 10 days were more present among those who used these drugs. In the end, the use of sedatives and analgesics proved to be a protective factor for death.

Continuous infusion sedoanalgesia is a common practice in intensive care settings, especially when there are clinical diagnoses of difficult management, requiring specific ventilatory strategies. However, the higher the dose and time of use, the higher the risk of adverse events related to these drugs[5]. In this context, iatrogenic abstinence stands out as a result of discontinuation of opioid and benzodiazepine drugs[8]. This condition, alone, can be associated with worse hospital outcomes by triggering, psychomotor agitation, mental confusion, uncoordination for feeding, and breathing difficulty in children, among other situations that end up prolonging their length of stay in the PICU[9].

In this study, the greater need for psychoactive drugs in infants is consistent with the physiological disadvantages that can be aggravated in the presence of comorbidities. In addition, as it is the very characteristic of the sector to admit critically ill children who need ventilatory support and vasoactive drugs, it is expected that their use occurs more frequently, except in specific situations, such as postoperative care, in which the length of stay in the sector ends up being inferior after a short observation period.

Some strategies seek to minimize the adverse events of continuous sedoanalgesia. The first one is the adequate choice of drugs to be used. A Chinese study, for example, compared the use of midazolam alone (Group 1) and combined with remifentanil (Group 2), concluding that satisfactory sedation was achieved in both groups, but Group 2 awoke faster and had a shorter time of extubation, duration of mechanical ventilation, and PICU stay. This is a good strategy for mechanically ventilated children to achieve better outcomes, with a lower dose for maintenance of sedation and analgesia[6].

Authors[10] compared the sedative and anti-inflammatory effects of dexmedetomidine with midazolam in critically ill children with poly-trauma and found that dexmedetomidine decreased the level of pro-inflammatory cytokines, allowed shorter duration of mechanical ventilation (4.7 days versus 6.6 days) and PICU stay (9.5 days versus 12.3 days), and reduced the proportion of sepsis (33.3% versus 53.1%). Another study compared the isolated use of midazolam and fentanyl (different solutions) with the combined use in the same solution and found that in the latter case there was a higher cumulative dose of these drugs, longer time of need for vasopressor drugs and a higher number of children who developed tolerance to the adopted treatment[11].

This study did not identify the hospital outcomes according to the drugs used, nor according to the form in which they were administered, although the service in which the data were collected did not adopt combined sedoanalgesia solutions. On the other hand, the results consist of a large population of children in a PICU with a mixed profile, in which the use of sedatives and analgesics in continuous infusion, regardless of which was the chosen drug, favored longer MPV time, incidence of hospital infections and longer stays in the PICU and in the hospital, regardless of demographic factors, admission diagnosis and variables related to severity.

Finding the balance between offering or restricting these drugs is a complex goal. A research performed in a PICU in the Netherlands found a mean number of 11 painful and stressful procedures per patient per day. The most frequent were airway aspiration (endotracheal, oral and nasal), arterial and lumbar punctures and insertion of peripheral intravenous cannula. They also concluded that mechanical ventilation patients undergo twice as many painful procedures as non-ventilated patients, and yet there is no adequate pain control in these situations[12].

Another study carried out in Philadelphia (USA) identified that severe children with cognitive impairment received less sedoanalgesia than the others, but it was not clear if there is a lower incidence of pain in this population or if there is an inadequacy of the behavioral assessment instruments in these patients regarding the clinical signs of discomfort[13]. This difficulty in assessing individual needs in pediatrics, especially due to the heterogeneity of the mixed profile PICU, according to age range, injury, and selection of safer drugs in each case, can hinder the work of professionals less experienced in clinical management in children's intensive care environments[12,14].

This difficulty is also observed in the analyzed sector, because it is a teaching hospital with high turnover of professionals and less adherence to the practice of objective measurements through appropriate scales. Therefore, the indiscriminate use of certain psychoactive drugs for immediate sedoanalgesia ignores early and late pharmacological adverse effects, and its underuse has direct repercussions on the clinical and psychological condition of hospitalized children. A systematic review[15] suggests that sedation in the PICU is often not adequate to the demands of critically ill children and that there is a lack of assessment of this condition in this scenario. Excessive sedation is the most commonly observed situation and can prolong hospitalization and increase the incidence of complications.

In this research, it is noteworthy that continuous sedoanalgesia was a protective factor for death in the final adjustment model. This means that this outcome is related more to the severity conditions of the child than to the psychoactive drugs, which are often used as adjuvants to stabilize the clinical condition and better therapeutic management of more complex cases.

A study[16] recommends in its review, as a target for favorable hospital outcomes in PICU, the use of sedation guided by assessment scales, management of protocols for daily interruption of sedatives and analgesics, and assurance of spontaneous breathing tests for children under mechanic ventilation. These measures shorten the time of mechanical ventilation as well as the length of hospitalization, and help control withdrawal and delirium without increasing the risk of morbidity and mortality[17].

Planning the discontinuation of sedoanalgesia is as important as its use in order to reduce the incidence of negative outcomes in

the pediatric population. Methadone, for example, is an allied drug in preventing withdrawal syndrome in patients who used opioids in continuous infusion during hospitalization, although the ideal therapeutic dose and treatment time are not so clear in the literature[18]. Another option to counteract the cumulative and adverse effects is drug rotation[19]. A study[20] verified that the daily interruption of continuous psychoactive drugs in critically ill children is a viable therapeutic option that results in decreased use of sedation, favors early extubation and reduces the length of stay in the PICU.

Despite the frequent use of these drugs in critically ill children, the choice must be based on criteria and evaluative scores to qualify care, facilitate mechanical ventilation, prevent accidental extubation, and minimize patient discomfort. A therapeutic plan should be established on an individual basis, with constant review of the goals to be achieved, and the drugs should be rotated and appropriate to the children clinic. Strategies of regional anesthesia and analgesia controlled by the patient with appropriate cognitive conditions could reduce the need for continuous intravenous infusion and nurse-guided protocols should be incorporated into the routine of these sectors due to the advantages already well documented in the literature[5,21].

There is also the possibility of titration of sedative and analgesic agents to reach the desired therapeutic goal. These actions, together or separately, can reduce the negative impact of continuous sedoanalgesia, regardless of the drug used, on the reported hospital outcomes[5]. In the research locus hospital, the rotation of sedatives and analgesics every 72h, as well as the daily interruption of these drugs, were started in mid-2015, with further strengthening of these strategies from 2020 on, a period that was not contemplated in the data collection.

The study presented some limitations, which can be improved in future methodological approaches. The first refers to the fact that the analysis was not classified according to the drug used and the combinations between them, which could identify those potentially more associated with unfavorable hospital outcomes. Also, relevant consequences associated with the use of continuous sedoanalgesia were not investigated, such as incidences of tolerance, abstinence, and delirium, which would allow a greater comparability of the intensity of this association with other scientific studies, since the applicability of objective scales to measure these diagnoses still does not occur routinely in the sector. Finally, it was not possible to use severity scores due to failure in the institutional records. Further prospective studies should be done covering these demands and following these patients after hospital discharge in order to identify potential long-term adverse effects on the developing human brain, especially in terms of neuropsychological damage.

These results reflect the features of a mixed PICU of a large university hospital in southern Brazil as to the outcomes associated with continuous sedoanalgesia, which may guide better planning of care for children and adolescents in these conditions. Updating the professionals who work in the care of critically ill children is also imperative, enabling a better quality of care, especially regarding pharmacodynamics, pharmacokinetics and caution in the administration of these drugs.

CONCLUSION

This study sought to identify the association of the use of sedatives and analgesics in continuous infusion with hospital outcomes. After all adjustments, MPV time greater than four days, diagnosis of HCAI, diagnosis of fungal infection, PICU length of stay greater than three days, and hospitalization time greater than 10 days were more present in these children. Death was more related to severity variables than to the use of psychoactive drugs.

AUTHORS' CONTRIBUTIONS

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Data Collection, Writing - Preparation of the original, Writing - Review and Editing
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Statistical analysis, Data Collection, Project management, Writing - Preparation of the original, Writing - Review and Editing
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Conceptualization, Writing - Review and Editing, Visualization
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Statistical analysis, Data Collection, Project Management, Methodology, Writing - Preparation of the original, Writing - Review and Editing, Supervision

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