

Association between sedation and adverse events in intensive care patients

Associação entre sedação e eventos adversos em pacientes de terapia intensiva

Asociación entre sedación y eventos adversos en pacientes de terapia intensiva

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Keywords

Intensive care units; Conscious sedation; Nursing care; Patient safety

Descritores

Unidade de terapia intensiva; Sedação consciente; Cuidados de enfermagem; Segurança do paciente

Descriptores

Unidades de cuidados intensivos; Sedación consciente; Atención de enfermería; Seguridad del paciente

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Abstract

Objective: Identify the level of sedation and daily interruption and associated them with adverse events such as accidental extubation, pressure injury, phlebitis, loss of devices and patients falls at an intensive care unit.

Methods: Retrospective and quantitative study, involving 204 patients, whose sedation was assessed by means of the Richmond Agitation-Sedation scale, followed by a search in the electronic files and analysis of the nursing notes. Fisher's test was used for statistical analysis.

Results: Out of 204 patients, 168 were under deep and 36 under light sedation. In approximately half of the deep sedation cases, daily sedation was not interrupted, and the same was true for the light sedation cases. Twenty-eight adverse events happened in deep sedation patients and 13 in light sedation cases, particularly pressure injury.

Conclusion: Most patients were under deep sedation. The adverse events were not associated with the daily interruption of sedation, but with work processes involving nursing care for the patient.

Resumo

Objetivo: Identificar nível de sedação, interrupção diária e associar com eventos adversos como extubação acidental, lesão por pressão, flebite, perda de dispositivos e queda de pacientes em unidade de terapia intensiva.

Métodos: Estudo retrospectivo e quantitativo, realizado com 204 pacientes, avaliados quanto à sedação por meio da Escala Richmond de Agitação-Sedação, e posteriormente, realizado busca em prontuário eletrônico e análise das notificações de enfermagem. Utilizou-se teste de Fisher para análise estatística.

Resultados: De 204 pacientes, 168 estavam com sedação profunda e 36 leve. Em sedação profunda, aproximadamente metade, não foi desligada a sedação diariamente, e com sedação leve, também. Ocorreram 28 eventos adversos naqueles com sedação profunda, e 13 em leve, destacando-se a lesão por pressão.

Conclusão: A maioria dos pacientes estava em sedação profunda. Os eventos adversos não se associaram com a interrupção diária da sedação, mas com processos de trabalho envolvendo a assistência de enfermagem ao paciente.

Resumen

Objetivo: Identificar nivel de sedación, interrupción diaria y asociar con eventos adversos como extubación accidental, lesión por presión, flebitis, pérdida de dispositivos y caída de pacientes en unidad de terapia intensiva.

Métodos: Estudio retrospectivo y cuantitativo realizado con 204 pacientes, evaluados respecto a sedación mediante la Escala Richmond de Agitación-Sedación, efectuándose luego búsqueda en historia clínica electrónica y análisis de notificaciones de enfermeras. Se utilizó test de Fisher para análisis estadístico.

Resultados: De 204 pacientes, 168 estaba en sedación profunda y 13 en leve. Aproximadamente la mitad de los pacientes bajo sedación, tanto profunda como leve, no fue despertada diariamente. Ocurrieron 28 eventos adversos en pacientes en sedación profunda y 13 en leve, destacándose la lesión por presión.

Conclusión: Mayoría de los pacientes bajo sedación profunda. Eventos adversos no asociados con interrupción diaria de la sedación, sino con procesos de trabajo involucrando atención de enfermería al paciente.

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Introduction

Sedation and analgesia in an intensive care unit (ICU) collaborate in the treatment of severe patients, as it improves respiratory distress and adaptation to invasive mechanical ventilation (IMV), thus ensuring greater safety.⁽¹⁾ Excessive sedation is associated with prolongation of mechanical ventilation time, increased rates of delirium and mortality though.⁽²⁾

The daily interruption of sedation (DIS) is being studied in recent times, and Kress et al. were the pioneers in this process, which consists in switching off the infusion of sedatives until the patient awakens and is able to respond to verbal commands or demonstrates agitation.⁽³⁾ It is performed daily until the multiprofessional team realizes that the patient is fit for endotracheal extubation.⁽⁴⁾

Interventions that facilitate the total reduction of analgesic and sedative drug administration, such as the use of protocols to guide nurse-controlled sedation, combination of arousal and spontaneous breathing tests, and the use of short-acting medications are associated with better outcomes for the patient, as verified by bedside scores such as the Ramsay Scale, Richmond Agitation-Sedation Scale (RASS) and Adaptation to the Intensive Care Environment (ATICE) Scale.⁽⁵⁾

The score used to assess the patients' sedation level in this study was the Richmond Agitation-Sedation (RASS) scale.⁽⁶⁾ It is based on scores ranging from aggressive, violent and dangerous patients to the extreme that is disability to awaken, without response to sound and physical stimuli.⁽⁷⁾

In the ICU, when the patient is in light sedation, (s)he requires greater attention from the team, as the risks of accidental extubation, loss of invasive devices and falls increase, causing inconvenience to the patient and greater stress for the team, with increased risk of adverse events (AE).⁽⁸⁾

Under the hypothesis that DIS performed according to the RASS score favors more superficial sedation, and that this behavior increases the risk of AE, which requires greater attention from the nursing team, the objective in this study was to identify the level of sedation and daily interruption and as-

sociate them with adverse events such as accidental extubation, pressure injury, phlebitis, loss of devices and patient falls in intensive care units.

Methods

A prospective, quantitative study was performed at a teaching hospital in the Northwest of São Paulo with approximately 800 beds, a reference for high complexity treatment.

The data were collected in two ICUs: a general one, with general surgery, traumatology, oncology, pneumology, nephrology and gastrology as the main specialties, and the other neurological, having neurosurgery as the main specialty, totaling 27 beds. The data collection period was January 2016 to January 2017 (13 months). The nursing team consisted of twelve assistant nurses, one supervisor and 52 nursing technicians, distributed among the morning, afternoon and evening shifts. From a total of 240 patients, the sample consisted of 204 patients who were under IMV and sedation.

Inclusion criteria were patients who stayed in the ICU for more than 24 hours, submitted to IMV and sedation. Exclusion criteria were those who died or were discharged within 24 hours after admission to the ICU or were not sedated. Forty-six patients were excluded.

For data collection, the Richmond Agitation-Sedation Scale (RASS) was used, as shown in figure 1.

Score	Description
+4	Aggressive, violent, dangerous
+3	Highly agitated, aggressive conduct, removal of tubes or catheters
+2	Agitated, frequent nonpurposeful movements
+1	Restless, anxious, but without vigorous or aggressive movements
0	Alert, calm
-1	Drowsy. Not fully alert, but has sustained awakening to voice (>10sec)
-2	Light sedation. Briefly awakens with eye contact to voice (<10sec)
-3	Moderate sedation. Movement or opening of the eyes to voice, but without eye contact
-4	Deep sedation. No response to voice, but movement or eye opening to physical stimulation
-5	Unarousable. No response to voice or stimulation

Source: Bugeo G, Tobar E, Aguirre M, Gonzalez H, Godoy J, et al. Implantação de protocolo de redução de sedação profunda baseado em analgesia comprovadamente seguro e factível em pacientes submetidos à ventilação mecânica. *Rev Bras Ter Intensiva*. 2013; 25(3): 188-96.

Figure 1. Richmond Agitation-Sedation Scale in ICU

Through the RASS scale, the variables observed at the bedside of the sedated patient under IMV were associated with psychomotor agitation behaviors, according to the classification from 0 to +4, to the deepest sedation, from 0 (RASS between -3 to -5, and light sedation, RASS between -1 to +2).⁽⁹⁾ This instrument was applied by nurses during the first hour of their work shift. We also used the DIS process, in which sedative-analgesic medications such as midazolam, propofol and fentanyl were turned off at seven o'clock in the morning. In some cases, however, these medications could not be interrupted according to non-DIS exclusion criteria such as intracranial hypertension, acute respiratory distress syndrome (ARDS), use of neuromuscular blocker, status epilepticus, hemodynamic instability and palliative care.

According to the criteria established in the data collection instrument, patients were observed after 24 hours of ICU stay and for 48 hours of sedative-analgesic medication use. Two observations took place in the morning, two in the afternoon and two in the evening, totaling six observations per patient. Afterwards, patients submitted to DIS were reevaluated every two hours, so as to continue or not with weaning from sedation and possible programmed extubation.

In another research variable, data were collected through electronic medical records, reading the evolutions and daily notes of the nursing team, in order to verify the reports of AE the patients suffered during the ICU stay during the first 48 hours of sedative-analgesic medication use and according to the DIS.

Adverse event was considered to be an untoward effect, harmful to the patient, compromising the patient.⁽¹⁰⁾ In this study, the following AE were verified: accidental extubation, pressure injury (PI), phlebitis, loss of gastric tube, nasoenteral tube, indwelling bladder catheter, central venous catheter and falls.

The research project received approval from the ethics committee (CEP) of the São José do Rio Preto Medical School-FAMERP in accordance with the premises of Resolution 244/12 involving humans, under Opinion 984.505. The statistical

application of Fisher's comparison test was used to analyze the data.

Results

Of 204 sedated patients under IMV, 168 were considered in deep sedation and 36 in light sedation according to the RASS scale. Of those who were in deep sedation, 91 (54.2%) did not undergo DIS, against 16 (44.5%) patients under light sedation, which means that in approximately half of the patients, the administration of sedative-analgesic drugs was not interrupted daily.

Forty-one AE were also reported during data collection in the 13-month period, 28 of which involved patients under deep sedation, $p < 0.0531$, and 13 events in light sedation, with $p < 0.0369$, as shown in table 1.

Table 1. Association among level of sedation, daily interruption of sedative-analgesic medication and adverse events

Sedation	Interruption n(%)	Non interruption n(%)	Total patients n(%)	Total AE n
Deep sedation (RASS -3 until -5)	77(45.8)	91(54.2)	168(100)	28
Light sedation (RASS -2 until +1)	20(55.5)	16(44.5)	36(100)	13
Total	97(47.6)	107(52.4)	204(100)	41

During the study period, in patients under deep sedation with RASS -3 to -5, both in patients whose sedation was interrupted and in those who remained sedated, the number of AE was exactly the same, totaling 14 events, with $p < 0.6337$, without statistical significance in relation to DIS with the increase in AE.

In deep sedation, accidental extubation occurred in four patients, two (14.3%) with DIS and two (14.3%) without IDS, with $p < 0.8745$. When analyzing nurses' notifications and nursing team notes, in one of the patients, the event occurred due to psychomotor agitation after the DIS, despite the use of mechanical restraint, following institutional standard protocols. In this episode, the nursing report emphasized that, after the incident, the patient remained extubated, using an

oxygen mask. In two other cases, with DIS exclusion criteria, the event occurred during the bath, when turning the patient to change the sheet, and the last, during the change of fixation of the endotracheal tube, when the cuff was cut, causing extubation, unrelated to DIS. In these three events, the medical team immediately reintubated the patients and sedation was turned on.

Pressure injury (PI) in patients under deep sedation was the most frequent event (17 cases), however, there was no significant difference between the patients submitted to DIS and those who were not, with $p < 0.5468$, as it occurred in nine (64.3%) cases with DIS and in eight (57.1%) without interruption. Other factors are related to the risk of PI because, among the 17 reported cases, 11 involved extended hospitalizations, with more than 10 days of ICU, and six were due to non-change of decubitus due to hemodynamic instability.

Regarding phlebitis, three cases (21.4%) were reported in patients who did not undergo DIS, and the analysis of the reports could not identify the main factor of this occurrence, the outcome being tube withdrawal and new puncture.

Regarding the gastric / nasoenteral, indwelling bladder catheter and central venous catheter loss, three (21.4%) events were reported in the patients who underwent DIS and only one (7.2%) without interruption. In those patients whose sedation was interrupted, the three events occurred due to psychomotor agitation and withdrawal of the devices, two events being described as loss of nasoenteral catheter, which needed to be reinstalled, and the removal of a central venous catheter, which was not reinstalled, but only peripheral venipuncture occurred. One event occurred when sedation was not interrupted, due to a nasogastric tube obstruction. The tube needed to be removed and reinstalled, which happened without difficulty.

There were no reports of falls during the period of data collection, which is justified by the fact that most patients are sedated or restricted to the bed, following a standardized fall protocol. The data are shown in table 2.

Table 2. Identification of adverse events according to daily interruption of sedation in patients under deep sedation (RASS between -3 and -5)

RASS -3 until -5	Accidental extubation n(%)	Pressure injury n(%)	Phlebitis n(%)	Loss of devices n(%)	Falls n(%)	Total events n(%)
Daily interruption of sedation (n= 77 patients)	2(14.3)	9(64.3)	-	3(21.4)	-	14(100)
Non interruption (n= 91 patients)	2(14.3)	8(57.1)	3(21.4)	1(7.2)	-	14(100)
Total	4(14.3)	17(60.7)	3(10.7)	4(14.3)	-	28(100)
$p < 0.05^*$	0.8745	0.5468	0.1565	0.2924	-	0.6337

*Significance level $p < 0.05$

In relation to the patients with light sedation (RASS -2 until +1), accidental extubation was not reported at any time during DIS or not in the analysis of the nursing team reports. This is considered important as, according to with this classification, patients usually present a level of consciousness and psychomotor agitation, which may cause incidents.

Pressure injuries in patients under light sedation were the most frequent AE, totaling 11 cases, six (54.5%) of which were justified by not performing the change of decubitus, due to hemodynamic instability and, consequently, non-DIS. Also, there was no statistical significance when associated with patients who underwent DIS ($p < 0.4478$).

Phlebitis was reported in only one (14.2%) patient who underwent DIS. In the reports, continuous administration of high dosage of antibiotics was emphasized, in a single peripheral venous access. The outcome was the puncture of central venous access for greater patient safety, however, there was no relationship with DIS regarding possible motor agitation and withdrawal of the device.

In relation to the loss of gastric, nasoenteral, indwelling bladder and central venous catheters, there was one (14.2%) event involving a patient who underwent DIS. The loss of the nasoenteral catheter was due to psychomotor agitation, corrected by a new tube passing, without problems and without statistical significance, with $p < 0.5556$.

As with deep sedation, there were no reports of falls in patients under light sedation, as shown in table 3.

Table 3. Identification of AE according to daily interruption of sedation or not in patients under light sedation (RASS between -2 and +1)

RASS -2 until +1	Accidental extubation n(%)	Pressure injury n(%)	Phlebitis n(%)	Loss of devices n(%)	Falls n(%)	Total events n(%)
Daily interruption of sedation (n= 20 patients)	-	5(71.6)	1(14.2)	1(14.2)	-	7(100)
Non interruption (n= 16 patients)	-	6(100)	-	-	-	6(100)
Total	-	11(84.6)	1(7.7)	1(7.7)	-	13(100)
p<0.05*	-	0.4478	0.5556	0.5556	-	0.8817

*Significance level p<0.05

Discussion

In this study, AE occurred in the same proportion, regardless of DIS or not, and also according to deep and light sedation. A Cochrane meta-analysis compared DIS with other non-interruption strategies and observed no difference in the duration of mechanical ventilation, ICU and hospital stay, nor in events that caused patient damage as, in 1282 patients, no evidence was found that DIS affected the total length of IMV, reducing its use by only 13%. Similarly, the rate of orotracheal tube removal was 1.07% and of catheter removal 1.48%.⁽¹¹⁾

According to the results of this study, most extubations occurred in patients under deep sedation, without DIS and in none of the patients under light sedation, but the justifications for this event were mainly during nursing care. Extubation occurred in only one patient due to psychomotor agitation, one by cutting the endotracheal tube cuff during the fixation change, and two during the bed bath. It is important to highlight that the patients were assisted and reintubated immediately after the incident. Accidental extubation may entail severe consequences for ventilatory weaning, as reintubation is generally necessary.⁽¹²⁾ Consequently, the risk of hypoxemia, atelectasis, ventilator-associated pneumonia (VAP), tracheal injury, hemodynamic instability, cardiac arrest and death increases.⁽¹³⁾

The bed bath is usually a technique the nursing team masters, but extubation can occur during the lateralization of the body. This is explained by the

loss of the central position of the head. In this case, the nursing professionals are instructed that a technician be responsible for keeping the head in the lateral position, along the patient's body.⁽¹⁴⁾

These findings corroborate a study of clinical nursing practices, in which the accidental extubation rates found in the review by Yeh et al. between 1994 and 2002, indicated that the incidence ranged from 3% to 14%. Of these cases of unplanned extubation, 77.9 to 87% were self-extubations and 13 to 22.1% were accidental. Another study, however, points out that the incidence of unplanned extubation ranges from 2.8% to 20.6%. This percentage largely depends on the characteristics of the ICUs, duration of mechanical ventilation and sedation levels, without association with DIS.^(15,16)

In a study developed in the Brazilian South, accidental extubation occurred in 16.7% of patients under superficial sedation, and 25% in deep sedation. It was not associated with DIS, but with nursing care.⁽¹⁷⁾

Pressure injuries were the most reported AE in patients with deep and light sedation, in line with one study, with 20% of PI cases being related to sensory deficit caused by sedative-analgesic drugs, but unrelated to DIS.⁽¹⁷⁾ It is important to note that PI is considered to be any alteration in the integrity of the skin resulting from soft tissue compression between a bony prominence and a hard surface. It is a frequent complication in severe patients with great impact on their recovery and quality of life.⁽¹⁸⁾

The activities of the nurse in ICU are aimed at care for severe patients, including the diagnosis of their situation, interventions and evaluation of specific care, from a perspective focused on the quality of life.⁽¹⁹⁾ In the case of a sedated patient, as a result of the absence of sensory perception, this patient deserve better care regarding the occurrence of PI as, often they are unable to communicate the discomfort, becoming more vulnerable. The nurse should be able to identify this group of patients early, implementing actions that can reduce their complications.⁽¹⁸⁻²⁰⁾

Phlebitis was observed mainly in patients under deep sedation, without interruption of sedation, three (21.4%), but without justification being doc-

umented in the nursing reports. Only one (14.2%) occurred in patients under light sedation, who underwent DIS, justifying the administration of high doses of antibiotics. According to the Infusion Nurses Society (INS) standards, the acceptable rate of phlebitis is 5% or less.⁽²¹⁾ Research findings suggest a significant discrepancy in the reported incidence though. Thus, Webster mentions that the rate of phlebitis varies from 2.3% to 67%, in line with our study, but without being related to DIS.⁽²²⁾

It is also emphasized that no studies on the relationship between sedation and increased phlebitis rate were found. The findings suggest that the intense manipulation of peripheral venous accesses, common in ICU practice, in addition to the intrinsic factors due to the severity and instability of the patient's clinical condition, favor the proliferation of microorganisms, with consequent development of infectious processes.⁽²³⁾

Regarding the loss of invasive devices, higher rates were observed in patients under deep sedation, with DIS, justified by patients' psychomotor agitation, withdrawing the nasoenteral catheter and central venous catheter, in 21.4%, in line with a study in which the loss rate of these devices was 25%, due to motor agitation after DIS.⁽¹⁷⁾

A study on AE in an ICU in São Paulo found that, in a total of 113 events, there were predominant incidents involving tubes, drains and catheters in 40.7%, followed by medication errors (27.4%). In another ICU in São Paulo, it was verified that, of a total of 80 events, 20% were loss of invasive devices, in accordance with the findings of this study.⁽²⁴⁾

Regarding falls, no event was reported, neither in patients under deep nor light sedation, corroborating a study carried out by the São Paulo School of Nursing, in which the number of falls was low.⁽²⁴⁾ Despite the results found, this event is considered severe, as it entails consequences such as tissue injuries, fractures and even brain traumas, responsible for immobility, increased length of hospital stay and mortality. Investments in health prevention actions are needed.⁽²⁵⁾

Continuous sedation is associated with higher IMV rates and mortality. Therefore, strategies to improve the sedation process through care protocols such as the use of the RASS scale should occur,

making it lighter, more superficial and safer for the patient's ventilatory weaning.⁽¹⁶⁾ Daily interruption of sedation is not associated with a higher complication rate than non-interruption practices though.⁽³⁾

Conclusion

Most patients were under deep sedation according to the RASS scale, without daily interruption of sedation, according to the criteria for non-disconnection. In patients under light sedation, a greater number of adverse events occurred after the daily interruption of sedation. Pressure injury was the most reported event, however, it was not associated with the interruption but rather with nursing care. No association between the level of sedation and adverse events in intensive care unit patients was found at any time.

Collaborations

Barbosa TP, Beccaria LM, Silva Dc and Bastos As declare that they contributed to the research project and design, statistical analysis of the data, manuscript writing and critical review and approval of the final version for publication.

References

1. Mehta S, McCullagh I, Burry L. Current sedation practices: lessons learned from international surveys. *Anesthesiol Clin*. 2011;29(4):607-24.
2. Shinotsuka CR. Implementando protocolos de sedação: aproximando a diferença entre evidência e prática. *Rev Bras Ter Intensiva*. 2013;25(3):186-7.
3. Kress JP, Pohlman AS, Connor MF, Hall JB. Daily interruption of sedative infusions in critically ill patients undergoing mechanical ventilation. *N Engl J Med*. 2000;342(2):1471-7.
4. Pandharipande PP, Ely EW. Sedation and analgesia in the ICU: pharmacology, protocolization, and clinical consequences. Preface. *Anesthesiol Clin*. 2011;29(4):xv-xvi.
5. Namigar T, Serapa LS, Esra KS. Correlação entre a escala de sedação de Ramsay, escala de sedação-agitação de Richmond e escala de sedação-agitação de Riker durante sedação com midazolam-remifentanil. *Rev Bras Anestesiologia*. 2017;67(4):347-54.
6. Bugeo G, Tobar E, Aguirre M, Gonzalez H, Godoy J, et al. Implantação de protocolo de redução de sedação profunda baseado em analgesia comprovadamente seguro e factível em pacientes submetidos à ventilação mecânica. *Rev Bras Ter Intensiva*. 2013; 25(3):188-96.

7. Costa JB, Marcon SS, Macedo CR, Jorge AC, Duarte PA. Sedação e memórias de pacientes submetidos à ventilação mecânica em unidade de terapia intensiva. *Rev Bras Ter Intensiva*. 2014; 26(2):122-9.
8. Shinotsuka CR, Salluh JI. Percepções e práticas sobre delirium, sedação e analgesia em pacientes críticos: uma revisão narrativa. *Rev Bras Ter Intensiva*. 2013; 25(2):155-61.
9. Loss SH, Oliveira RP, Maccari JG, Savi A, Boniatti MM, Hetzel MP, et al. A realidade dos pacientes que necessitam de ventilação mecânica prolongada. *Rev Bras Ter Intensiva*. 2015;27(1):26-35.
10. Barbosa TP, Oliveira GA, Lopes MN, Poletti NA, Beccaria LM. Práticas assistenciais para segurança do paciente em unidade de terapia intensiva. *Acta Paul Enferm*. 2014; 27(3):243-8.
11. Burry L, Rose L, McCullach IJ, Fergusson DA, Ferguson ND, Mehta S. Daily sedation interruption versus no daily sedation interruption for critically ill adult patients requiring invasive mechanical ventilation. *Cochrane Database Syst Rev*. 2014 Jul 9;(7):CD009176.
12. McGahan M, Kucharski G, Coyer F. Nurse staffing levels and the incidence of mortality and morbidity in the adult intensive care unit: a literature review. *Aust Crit Care*. 2012;25(2):64-77.
13. Beccaria LM, Pereira RA, Contrin LM, Lobo SM, Trajano DH. Eventos adversos na assistência de enfermagem em uma unidade de terapia intensiva. *Rev Bras Ter Intensiva*. 2009;21(3):276-82.
14. Lanzillotti LS, Seta MH, Andrade CL, Junior WV. Eventos adversos e outros incidentes na unidade de terapia intensiva neonatal. *Rev Ciênc & Saúde Coletiva*. 2015; 20(3):937-46.
15. Webster J, Osborne S, Rickard CM, New K. Clinically-indicated replacement versus routine replacement of peripheral venous catheters. *Cochrane Database Syst Rev*. 2013 Apr 30;(4):CD007798. doi: 10.1002/14651858.CD007798.pub3. Review. Update in: *Cochrane Database Syst Rev*. 2015;(8):CD007798. PubMed PMID: 23633346.
16. Grap MJ, Glass C, Lindamood MO. Factors related to unplanned extubation of endotracheal tubes. *Critical Care Nurse*. 1995; 15(2): 57-65.
17. Alves EF. O cuidador de enfermagem e o cuidar em uma unidade de terapia intensiva. *Rev Cient Ciênc Biol Saúde*. 2013;15(2):115-22.
18. Olkoski E, Assis GM. Aplicação de medidas de prevenção para úlceras por pressão pela equipe de enfermagem antes e após uma campanha educativa. *Esc Anna Nery*. 2016;20(2):363-9.
19. Milutinovic D, Simin D, Zec D. Fatores de risco para flebite: estudo com questionário sobre a percepção dos enfermeiros. *Rev Lat Am Enfermagem*. 2015; 23(4): 677-84.
20. Palhares VC, Palhares Neto AA. Prevalência e incidência de úlcera por pressão em uma unidade de terapia intensiva. *Rev Enferm UFPE*. 2014;8:3647-53.
21. Reade MC, Finfer S. Sedation and delirium in the intensive care unit. *N Engl J Med*. 2014; 370(5):444-54.
22. Webster J, Osborne S, Rickard C, Hall J. Clinically-indicated replacement versus routine replacement of peripheral venous catheters. *Cochrane Database Syst Rev*. 2010 Mar 17;(3):CD007798. doi: 10.1002/14651858.CD007798.pub2. Review. Update in: *Cochrane Database Syst Rev*. 2013;4:CD007798.
23. Basto PA, Soares YO, Oliveira HS, Gonçalves WS, Balestra LF, Gardenchi G. Repercussões da sedação em pacientes internados em unidades de terapia intensiva: uma revisão sistemática. *ASSOBRAFIR Ciênc*. 2014; 5(2):59-72.
24. Moreira RM, Padilha KG. Ocorrências iatrogênicas com pacientes submetidos à ventilação mecânica em Unidade de Terapia Intensiva. *Acta Paul Enferm*. 2001; 14(2): 9-18.
25. Lima CS, Barbosa SF. Ocorrência de eventos adversos como indicadores de qualidade assistencial em unidade de terapia intensiva. *Rev Enferm UERJ*. 2015; 23(2):222-8.