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Primary bloodstream infection related to central venous catheter in neonatal intensive care unit: incidence evaluation after implementation (bundle)

Infecção primária de corrente sanguínea associada a cateter venoso central em unidade de terapia intensiva neonatal: avaliação da incidência após implantação de pacotes de intervenção (bundle)

Naiara Bozza Pegoraro[1], Anne Mei Miyake[1], Gabriela Maria Santos Rocha[1], Gabriela Pissaia Boarão[1], Aristides Schier da Cruz[1], Talita Moroz Leite Aladino[2], Thais Ariela Machado Brites[1], Juliana Baratella André Roveda[1]

ABSTRACT

Introduction: To improve practices related to intravenous device care, a strategy currently applied is the adoption of bundles or intervention packages that, when applied together and systematically, are capable of preventing infections.

Objective: To evaluate the incidence of neonatal infection with the use of central venous catheters, before and after implementation of the bundle.

Method: Analytical, observational, and retrospective study. The medical records of hospitalized newborns who used a central venous catheter (CVC) or peripherally inserted central catheter (PICC) were evaluated. A bundle was developed and implemented from 2020 onwards, comprising 2 groups: pre-intervention and post-intervention phases.

Results: Of the 751 patients with central catheters, 123 (16.4%) developed catheter-associated infection. Gestational age at birth and birth weight were significantly lower in the group that suffered. In this same group, the number of days of catheter use and hospitalization period were significantly higher compared to the group that did not suffer the infection. Apgar scores at one and five minutes did not interfere with the probability of developing primary bloodstream infection associated with the catheter. There was no significant difference in the proportion of patients who suffered infection associated with the catheter in the pre- and post-intervention phases.

Conclusion: The lower the birth weight and the lower the gestational age, the greater the probability of infection associated with the catheter. The intervention did not promote a significant reduction in the incidence associated with the catheter.

KEYWORDS: Bundle. Catheterization. Neonatal. Infection.

Central Message

To improve practices related to the care of intravenous devices, the strategy currently applied is the adoption of bundles or intervention packages that, when applied together and systematically, are capable of preventing infections. This study aimed to evaluate the incidence of neonatal infection with the use of central venous catheters, before and after bundle implantation. The results can better guide its use and when it is effective.

Perspective

Newborn care procedures in NICUs require the use of advanced technology, and among the invasive procedures used in these patients, the central venous catheter is one of the most necessary, despite its risks. The neonatal mortality rate from sepsis is high; Therefore, surveillance measures are necessary to direct actions to reduce infection rates, providing data that allow comparing and evaluating the impact of control measures.

RESUMO

Introdução: Para melhorar as práticas relacionadas aos cuidados com dispositivos intravenosos, estratégia atualmente aplicada é a adoção de bundles ou pacotes de intervenção que, quando aplicados em conjunto e de forma sistemática, são capazes de prevenir infecções.

Objetivo: Avaliar a incidência de infecção neonatal com uso de cateter venoso central, antes e depois da implantação de bundle.

Método: Estudo analítico, observacional e retrospectivo. Foram avaliados os prontuários dos recém-nascidos internados que fizeram uso de cateter venoso central (CVC) ou peripherally inserted central catheter (PICC). Foi desenvolvido bundle e implementado a partir 2020, perfazendo 2 grupos: fases pré-intervenção e pós-intervenção.

Resultado: Dos 751 pacientes com cateteres centrais, 123 (16,4%) desenvolveram IPCS associada ao cateter. A idade gestacional ao nascer e o peso de nascimento foram significativamente mais baixos no grupo que sofreu IPCS. Nesse mesmo grupo, o número de dias de uso de cateter e dias internados foram significativamente maiores em relação ao grupo que não sofreu a infecção. O Apgar no primeiro e quinto minuto não interferiu na probabilidade de desenvolvimento de infecção primária de corrente sanguínea (IPCS) associada ao cateter. Não houve diferença significativa na proporção de pacientes que sofreram IPCS associada ao cateter na fase pré- e pós-intervenção.

Conclusão: Quanto menor o peso de nascimento e menor a idade gestacional, maior é a probabilidade de IPCS associada ao cateter. A intervenção não promoveu redução significativa na incidência de IPCS associada ao cateter.

PALAVRAS-CHAVE: Bundle. Cateterização. Neo-natal. Infecção.

[1] Evangelical Mackenzie Faculty of Parana, Curitiba, PR, Brazil;
[2] Mackenzie Evangelical University Hospital, Curitiba, PR, Brazil

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INTRODUCTION

Advances in intensive care, such as the availability of invasive devices such as central venous catheters (CVCs), mechanical ventilation devices, and formulas for total parenteral nutrition, have provided indisputable improvements in neonatology, mainly due to the increase in the survival of premature and low birth weight newborns.[1,2] Paradoxically, the use of these advances, associated with prematurity, low birth weight, and the presence of malformations, were identified as risk factors for infections in neonatal units.[2] Nosocomial infections are one of the main causes of mortality and morbidity in newborns admitted to neonatal intensive care units (NICUs).[3,4] The incidence of infections varies widely between NICUs (7-25%), depending on environmental factors and differences in clinical practice.[3]

According to the material and caliber, the CVC can be inserted at the bedside - as is the case with the peripherally inserted central catheter - and remain for a long time to allow the administration of solutions and medications, test collection, transfusion of blood products and hemodynamic monitoring. Among the complications related to its use, infections stand out in frequency and potential for morbidity and mortality.[5] The use of invasive devices compromises the skin's natural physical barrier, which leads to the invasion of the bloodstream by opportunistic microorganisms. Bacteremia, when it evolves into severe sepsis, can lead to hemodynamic changes and even death.[3]

To improve practices related to care with intravenous devices, the strategy currently applied is the adoption of "bundles" or intervention packages. The Institute for Healthcare Improvement defines structured recommendations to promote the care process that favors patient discharge, that is, a group of practices that, when applied together and systematically, are capable of favoring discharge.[2] The intervention package or bundles for catheters should combine practices and conducts to prevent contamination, catheter migration, adhesion and colonization. When strongly evidence-based prevention strategies are applied during insertion, dressing changes, and catheter removal, infection rates are expected to decrease.[2,6]

The objectives of this study were to evaluate the incidence of neonatal infection related to the use of central catheters in NICUs, before and after the implementation of an intervention pack; to analyze which microorganisms are the most frequent; to analyze whether the population of preterm infants with low birth weight (<1500 g) has a higher chance of catheter-associated infection; and to verify whether Apgar, the use of antibiotics influences the risk of infection compared to the incidence of negative outcomes in the groups that did or did not suffer the infection.

METHOD

This research was approved by the Human Research Ethics Committee of the Evangelical Mackenzie Faculty of Parana, Curitiba, PR, Brazil – CAAE no.43694720.6.0000.0103. This is an analytical, observational, and retrospective study with a population composed of neonates hospitalized in the NICU of a tertiary hospital - Mackenzie Evangelical University Hospital, Curitiba, PR, Brazil - who used CVC or peripherally inserted central catheter (PICC) during hospitalization. The medical records of newborns admitted to the NICU from December 2016 to February 2022 were evaluated in the hospital's computerized system, and those who used CVC or PICC were selected. Those who did not undergo blood culture, who had CVC or PICC installed for a very short time (less than 24 h), and who failed to fill in the research variables were excluded.

A bundle was considered a set of measures and care adopted by health professionals for the management of CVC or PICC for the prevention of PBEMI. Such measures include adequate hand washing, antisepsis of the puncture region with 70% alcohol or alcoholic chlorhexidine and waiting for the action time (2 min), use of full clothing and avoiding multiple punctures, avoiding the use of PVPI, preferential use of silicone or polyurethane catheters. Regarding the PICC, it was avoided to pull the catheter or cut the tip of the catheter for insertion due to the risk of mechanical complications. Regarding the change of dressings, this was done every 48 h or sooner if necessary. If there was a break in technique or failure to carry out any guidance, the catheter would be immediately changed.

Neonates with late-onset sepsis were those who presented clinical and laboratory criteria for hemodynamic decompensation after 48 h of life (tachycardia, hypotension, fever, alteration in capillary perfusion, hypoactivity or lethargy, abnormal blood count and C-reactive protein) associated or not with positive blood culture, according to the definition of the National Health Surveillance Agency (ANVISA) and the Centers for Disease Control and Prevention - CDC.

Neonates with primary catheter-associated bloodstream infection (PBSI) were those who developed late-onset sepsis without any sign of localization and who were using central catheters at the time of diagnosis.

The variables analyzed were: gestational age, birth weight, Apgar score in the 1st and 5th min of life, microorganism that caused the catheter infection, number of days of catheterization, occurrence of sepsis, necrotizing enterocolitis, use of antibiotics, death or hospital discharge, and number of days of hospitalization. The decision to evaluate the incidence of sepsis, necrotizing enterocolitis, and antibiotic use was motivated more with the purpose

of determining the level of severity of the patients than to establish that such complications were caused by the use of the catheter, since high-risk neonates suffer numerous types of complications that course with infection and necrotizing enterocolitis.

To determine the influence of the intervention package (bundle), patients were separated into 2 groups: pre-intervention phase (December 2016 to March 2020) and post-intervention phase (April 2020 to February 2022). To assess risk factors and negative outcomes in cases that experienced catheter-associated infection, patients were divided into 2 groups: with and without catheter-related PCIs.

Statistical analysis

The results were recorded in writing, according to the established data collection protocol, and subsequently tabulated in an Excel spreadsheet and expressed as mean and standard deviation or median and interquartile range for continuous variables, and as number and percentage for categorical variables. The comparison of the results of the different groups was analyzed using Student's t-test or Mann-Whitney test for continuous variables, and using Pearson's chi-square test or Fisher's exact test for categorical variables. For the analysis of risk factors, the Odds Ratio and 95% confidence interval (95%CI) were calculated. For the risk of complications analysis, the relative risk (RR) and 95%CI were calculated. The differences between groups were considered significant when $p<0.05$. Statistical analysis was performed using the BioEstat 5.3 software.

RESULT

During the pre-intervention period, 375 newborns were admitted to the NICU who required the installation of CVC or PICC and were included in the analysis, while in the post-intervention period, 376 newborns were included. Of the 751 patients with central catheters, 123 (16.4%) developed primary bloodstream infection (IPCS). There was positivity in 136 blood cultures performed on these 123 patients. The infecting microorganisms were Staphylococcus epidermidis (n=56), coagulase-negative Staphylococcus (n=36), Klebsiella pneumoniae (n=7), Enterobacter sp. (n=6), Staphylococcus aureus (n=5), other microorganisms (n=27).

Table 1 shows the characteristics of birth and clinical evolution of newborns at risk in the pre- and post-intervention periods. Most of the data analyzed did not differ significantly in the comparison of the 2 periods. In the post-period period, gestational age and birth weight were significantly higher, with a significantly lower proportion of preterm infants. The length of hospital stay was significantly shorter in the post-intervention group. During this period, the proportion of newborns who suffered sepsis was significantly higher, although antibiotic use was lower. There was no significant difference in the proportion of patients who underwent PCIS (17.$^{6\%}$ pre- and 15.4% in the post-operative phase, p=0.422, RR=0.88, 95%CI 0.63-1.21).

Table 2 presents the characteristics of birth and clinical evolution of newborns with central catheters, comparing the group that underwent PCIS (n=123) with those that did not (n=628). Apgar scores in the 1st and 5th min did not interfere with the probability of its development. Gestational age at birth and birth weight were significantly lower in the group that underwent IPCS than in the group that did not, with significantly higher proportions of preterm infants and those born below 1500 g. In the group that suffered, the proportion that received antibiotics was significantly higher, as was the number of days of catheter use and days hospitalized. The risk of developing necrotizing enterocolitis was significantly higher in the group that underwent IPCS (RR=4.22 – 95%CI 2.4 to 7.5) and also the risk of death (RR= 2.27 – 95%CI 1.2 to 4.4).

TABLE 1 — Neonatal characteristics and clinical data of newborns in the pre- and post-intervention period

	Pre-intervention n=375	Post-intervention n=376	p	OR ou RR (IC 95%)*
Men - n (%)	211 (56,3)	211 (56,1)	0,974	OR=0,99 (0,75 a 1,33)
Gestational age in weeks - mean (SD)	33,0 (4,4)	35,0 (4,0)	<0,0001	
Birth weight in grams - median (IQR)	1920 (1313-2825)	2228 (1484-3106)	0,0006	
Prematurity - n (%)	253 (68,8)	232 (61,7)	0,0436	OR=0,73 (0,54 a 0,99)
Weight <1500g - n (%)	129 (34,4)	95 (25,3)	0,0062	OR=0,64 (0,47 a 0,88)
Air 1st minute - mean (SD)	5,8 (2,5)	5,7 (2,5)	0,7310	
Apgar 5th minute - mean (SD)	8,0 (1,6)	7,7 (1,7)	0,0233	
Antibiotic use - n (%)	349 (93,1)	309 (82,2)	<0,0001	RR=0,88 (0,84 a 0,93)
Necrotizing enterocolitis - n (%)	15 (4,0)	75 (7,2)	0,0579	RR=1,8 (0,97 a 3,32)
Sepsis - n (%)	193 (51,5)	259 (68,9)	<0,0001	RR=1,34 (1,19 a 1,51)
Catheter-associated PCIS - n (%)	66 (17,6)	58 (15,4)	0,422	RR=0,88 (0,63 a 1,21)
Positive blood culture - n (%)	69 (18,4)	67 (17,8)	0,8363	RR=0,97 (0,71 a 1,31)
Death - n (%)	24 (6,4)	15 (4,0)	0,1905	RR=0,62 (0,33 a 1,17)
Hospitalized days - median (IIQ)	31 (16 – 54)	24 (14 – 44)	0,0088	
Catheter Use Days - Median (IIQ)	10 (6 -18)	9 (6 - 15)	0,213	

*OR or RR (95% CI)=the calculation was performed by evaluating the proportions of the post-intervention phase compared to pre-intervention phase

TABLE 2 — Neonatal characteristics and clinical data of newborns

with and without occurrence of catheter-associated IPCS

	With IPCS * n= 123	No IPCS* n=628	p	OR ou RR (IC 95%)**
Men - n (%)	55 (44,7)	366 (58,3)	0,0056	OR=0,579 (0,39 a 0,85)
Gestational age in weeks - mean (SD)	32 (4,3)	34 (4,1)	<0,0001	
Birth weight in grams - median (IQR)	1420 (975 – 2198)	2210 (1493 – 3030)	<0,0001	
Prematurity - n (%)	102 (82,6)	383 (61,6)	0,0001	OR=3,18 (1,9 a 5,3)
Weight <1500g - n (%)	66 (53,7)	158 (25,2)	<0,0001	OR=3,44 (2,31 a 5,12)
Apgar 1st minute - mean (SD)	5.48 (2,6)	5,81(2,5)	0,227	
Apgar 5th minute - mean (SD)	7.80 (1,7)	7,85 (1,6)	0,719	
Antibiotic use - n (%)	122 (99,2)	536 (85,4)	<0,0001	OR=20,9 (2,9 a 151,7)
Necrotizing enterocolitis - n (%)	19 (15,5)	23 (3,7)	<0,0001	RR=4,22 (2,4 a 7,5)
Death - n (%)	12 (9,8)	27 (4,3)	0,0126	RR=2,27 (1,2 a 4,4)
Hospitalized days - median (IIQ)	61 (38 – 82)	23 (13 – 41)	<0,0001	
Catheter Use Days - Median (IIQ)	24 (16 – 35)	8 (6 – 13)	<0,0001	

*IPCS=primary bloodstream infection; **OR or RR (95% CI)=the calculation was performed with the evaluation of the proportions in the group with catheter-associated PICS compared to the group without catheter-associated PCIS

DISCUSSION

During the more than 5 years of research, 16% of newborns at risk in NICUs with CVC or PICC installation developed IPCS. In the 2-year period in which the intervention package was adopted, there was no significant decrease in the occurrences of IPCS, compared to the pre-intervention period. Length of hospital stay and antibiotic use were significantly lower. The incidence of deaths did not decrease significantly. The study showed that the lower the birth weight and the lower the gestational age, the greater the probability of IPCS This occurrence is accompanied by a significantly higher risk of death, necrotizing enterocolitis, antibiotic use, long catheter use, and hospitalization.

Low birth weight and gestational age are criteria established as risk factors for the development of sepsis, and the incidence of IPCS is inversely proportional to these parameters. In addition, necrotizing enterocolitis, although multifactorial in cause, is also often associated with sepsis.[1] These data explain the higher incidence of these variables in the group that underwent IPCS compared to the group that did not.[4]

Patients with CVC installation require a longer period of parenteral nutrition and antibiotic therapy, which leads to a more complicated hospitalization[2], corroborating these findings, in which the group that suffered PCIS received more antibiotics, required catheter use for more days, and stayed longer in hospital.

Studies report wide variation in IPCS rates, ranging from 2-49 per 1,000 CVC-day.[5] In Brazil, sepsis associated with central catheters represents a serious health problem for the neonatal population.[2,5] The Informative Bulletin of the National Health Surveillance Agency (ANVISA) reports an incidence density of this IPCS in Brazilian NICUs ranging from 7.8 to 8.6/1,000 CVC-day, being higher in <750 g.

In the literature, comparisons of catheter-associated infection rates before and after the implementation of the intervention package (bundle) were found. In one of the studies, the authors reported a reduction in catheter-associated infection rates, from 8.6/1000 days of pre-intervention central venous catheter use to 5.78/1000 days post-intervention.[7] However, in another more recent study, it was reported that even with the application of the intervention package, catheter infection rates remained high, with the conclusion that catheter duration continues to be one of the most important factors for the occurrence of infection.[8]

In another study, with 551 neonates admitted to the NICU, 139 (25.2%) experienced late-onset neonatal sepsis, with an incidence rate of 16.1/1000 patient-days. The average length of hospital stay was 18.8 days. Potential risk factors for late-onset neonatal sepsis were gestational age <37 weeks, birth weight <1500 g, use of CVC, parenteral nutrition, and mechanical ventilation. In cases of late-onset neonatal sepsis, 66% were caused by Gram-positive cocci, 25% by Gram-negative bacilli, and 8% by Candida sp. Staphylococcus epidermidis was the most frequent agent (38%), followed by Staphylococcus aureus (13%). Among the gram-negative bacilli, Klebsiella pneumoniae was the most prevalent (8%). Rates of post-intervention late neonatal sepsis (14.7/1000 patient-days) decreased relative to pre-intervention rates (23.4/1000 patient-days).[9]

Data from the literature show that the microorganisms most associated with sepsis are gram-positive, especially coagulase-negative Staphylococcus,[4] and this microorganism was the second most common in our study.

One of the limitations of this study was the retrospective design, which often generates a situation in which non-standardized data recording promotes the loss of certain information in some patients. It should be noted that in this study, several clinical variables were compared in 2 different historical periods. In studies with this type of design, most of the significant changes, or non-changes, may occur only due to differences in the morbid profile of the problems analyzed, or changes in protocols or medical conducts. Thus, the significant changes observed between the 2 periods, or the non-changes, cannot be attributed to the intervention package.

Newborn care procedures in NICUs require the use of advanced technology, and among the invasive procedures used in these patients, CVC is one of the most necessary, despite its risks. As has been warned,5 the neonatal mortality rate due to sepsis is high, so surveillance measures are necessary to direct actions to reduce the rates of Health Care Associated

Infections, as surveillance is capable of providing data that allow comparing and evaluating the impact of control measures, in addition to enabling comparison with other health services with the same characteristics.

CONCLUSIONS

The intervention (bundle) did not promote a significant reduction in the incidence of CVC-related IPCS. However, there was a significant decrease in the length of stay of patients in the neonatal ICU. Regarding the most frequent microorganisms related to sepsis, the most found were the Staphylococcus epidermidis, followed by Staphylococcus coagulase negative. It has been shown that the lower the birth weight, Apgar and lower the gestational age, the greater the probability of IPCS. In addition, it contributes to the increase in the use of antibiotics and the number of days of hospitalization, in addition to increasing the risk of developing necrotizing enterocolitis and death in these patients.

Authors' contributions

Study design: Talita Moroz Leite Aladino

Data collection: Naiara Bozza Pegoraro, Anne Mei Miyake, Gabriela Maria Santos Rocha, Gabriela Pissaia Boarão

Statistical analysis: Aristides Schier da Cruz

Draft manuscript: Naiara Bozza Pegoraro, Anne Mei Miyake, Gabriela Maria Santos Rocha, Gabriela Pissaia Boarão, Aristides Schier da Cruz, Talita Moroz Leite Aladino

Manuscript review: Aristides Schier da Cruz, Talita Moroz Leite Aladino, Thais Ariela Machado Brites, Juliana Baratella André Roveda

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