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Short report

Should central venous catheters be rapidly removed to treat *Staphylococcus aureus* related-catheter bloodstream infection (CR-BSI) in neonates and children? An 8-year period (2010–2017) retrospective analysis in a French University Hospital

L. Boussamet^a, E. Launay^b, E. Thomas^c, C. Gras Leguen^b, D. Lepelletier^{a, c, *}

^a MiHAR Lab, University of Nantes, Nantes, FR-44000, France

^b Pediatric Department, Nantes University Hospital, Nantes, FR-44000, France

^c Bacteriology and Infection Control Department, Nantes University Hospital, Nantes, FR-44000, France

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SUMMARY

Catheter-related bloodstream infection (CR-BSI) treatment is based on empiric anti-biotherapy associated with or without catheter removal. The aim of this study was to compare the incidence of failures in neonates and children with *Staphylococcus aureus* CR-BSI with or without rapid catheter removal. Treatment failure was defined as the persistence of positive blood cultures, onset or aggravation of a local or systemic complication, or relapse. Fifty-four CR-BSI in 225 patients were analysed (33 and 21 conservative and non-conservative treatments) with three and 10 failures, respectively ($P < 0.002$). Non-conservative treatment with rapid catheter removal seems to be associated with a significantly lower failure rate and should be recommended.

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Introduction

Catheter-related bloodstream infection (CR-BSI) incidence ranges from 0.2 to 11 per 1000 catheter days in neonates and

children, and is associated with various clinical symptoms and morbidity [1]. These infections are associated with high morbidity, especially for at-risk patient groups, such as preterm neonates, immunocompromised children, and children with renal insufficiency.

The most commonly reported causative pathogens remain coagulase-negative staphylococci and *Staphylococcus aureus* [2]. The treatment of CR-BSI is based on empiric antibiotherapy (in France mainly with vancomycin, sometimes in association

* Corresponding author. Address: Nantes Univ, [CHU Nantes], The Microbiotas Hosts Antibiotics and bacterial Resistances Lab, F-44000 Nantes, France.

E-mail address: didier.lepelletier@chu-nantes.fr (D. Lepelletier).

with other antibiotics) with two possible options regarding the catheter: non-conservative treatment (catheter removal <72 h) or conservative treatment (the catheter is not removed or removed ≥ 72 h). Contrary to adult patients, withdrawing the catheter is not systematic in neonates and children, mainly because of difficulties in the anatomic site approaches, as well as the risk of new infection on to the new catheter. Conservative treatment is therefore more common in neonates and children than in adults even if local and general complications can occur [3]. The aim of this study was to compare the incidence of failure in children with *S. aureus* CR-BSI with or without conservative treatment, in order to help hospitals and paediatricians to develop specific strategies for *S. aureus* CR-BSI management.

Methods

Study design, patients and definitions

A retrospective analysis was performed on a cohort of children hospitalized from January 2010 to December 2017 at the Nantes University Hospital including a 60-bed Neonatal Department with an average of 1100 admissions per year. All positive *S. aureus* blood cultures from the were selected laboratory database during the study period among hospitalized neonates and children <18 years old. The following data were collected: age, sex, gender, type/dates of placement and removal of central venous catheter (CVC), clinical symptoms of CR-BSI, microbiological data related to the *S. aureus*-positive blood cultures, initial and adapted antibiotic therapy, failure associated with the CVC after treatment (relapse or recurrence, outcomes). CR-BSI was included when *S. aureus* was isolated from the blood culture with standard definition [4]. Non conservative treatment was defined when the CVC was rapidly removed before 72 h after the onset CR-BSI. Conservative treatment was defined when the catheter was not removed during the treatment duration or after 72 h [5]. Treatment failure was defined as the persistence of positive blood cultures, onset or aggravation of a local infectious complication (abscess, tunnelitis) or systemic complication (thrombosis, endocarditis, sepsis) or relapse (infection with the same *S. aureus* in 4–12 weeks). Salvage was considered successful if the catheter was still in place after 12 weeks and there was no recurrent bacteraemia or CR-BSI death [6].

Statistical analyses

Results were analysed using STATA V15® software (StataCorp LP, Texas, USA). Categorical variables were evaluated using the Chi-squared or Fisher's exact test. Continuous variables were compared using the *t*-test or the Mann–Whitney *U*-test, where appropriate. All tests of significance were two-tailed, and *P*-values <0.05 were considered statistically significant. Predictive factors for catheter salvage outcome were analysed by performing a backwards stepwise logistic regression analysis.

Results

Patient characteristics

During the 8-year study period, 471 blood cultures positive for *S. aureus* were extracted from the laboratory database. A

Table 1

Characteristics of neonates and children with catheter-related bloodstream infection (CR-BSI) (2010–2017)

Patients	N=57 (%)
Sex ratio M/F	35/22
Median age, years	4 [0.1–17.7]
Underlying diseases	
Prematurity	14 (24.6)
Immunosuppression	7 (12.3)
Digestive	4 (7.0)
Neurologic	2 (3.5)
Cutaneous	1 (1.8)
Renal failure	8 (14)
Cardiovascular	10 (17.5)
Indication of central venous catheter	
Parenteral nutrition	23 (40.4)
Median duration of catheterization (days)	12.3 [3–1305]
Preventive lock antibioprophyllaxis	0
CR-BSI	
Respiratory distress	5 (8.8)
Severe sepsis	11 (19.3)
Thrombophlebitis	5 (8.8)
Mean CRP (mg/L)	35.8 [3.5–319.0]
Polymicrobial blood culture	10 (17.5)
Meticillin-resistant <i>Staphylococcus aureus</i>	1 (1.8)

CRP, c-reactive protein.

given patient, over a given period (several days mainly) could present several positive blood cultures during the same infectious episode. Thus, 225 infectious episodes were identified with *S. aureus* during the study period. One hundred and fifty-five *S. aureus* infectious in patients without CVC were excluded. In total, there were 57 CR-BSI among the 70 neonates and children with CVC; the median age was 4 years (± 5.6). The characteristics of the children are presented in Table 1. Blood cultures were positive for at least one other infectious agent in 10 neonates or children (18%), mainly *S. epidermidis*. Only one strain of *S. aureus* was meticillin-resistant (MRSA). The use of a preventive antibiotic lock was not common practice for children in this study.

Treatment and failures

Three dates of CVC removal were not available in the medical records. Empiric antibiotic therapy was prescribed within 2 days for all patients following the onset of infection. Vancomycin was the most used antibiotic (72%), usually in association with other antibiotics (62%). Thirty-three treatments were conservative without CVC removal within 72 h (61.1%) and 21 treatments were non-conservative with a rapid CVC removal (38.8%) for infection management. Three (9.1%) and 10 (47.6%) failures were observed in the two groups, respectively ($P < 0.002$). Failures in both groups are detailed in Table II.

Determination of predictive factors for conservative treatment failures

The predictive factors associated with failures after conservative and non-conservative treatment in 54 children were

Table II

Characteristics of failures after conservative ($N=33$) and non-conservative ($N=21$) treatments for *Staphylococcus aureus* catheter-related bloodstream infection*

Failures	Failures by type of treatment	
	Non-conservative ($N=3$)	Conservative ($N=10$)
Persistence of <i>S. aureus</i> positive blood cultures	—	4
Outcomes		
Tunnelitis	—	2
Thrombophlebitis	—	1
Local abscess	-	1
Relapse within 30 days	3	2
Infection attributable mortality	0	2

* The date of central venous catheter removal was not available for three children.

analysed. Sepsis within 3 days after the onset infection was the only risk factor identified, independently of the type of treatment (conservative or not) ($P=0.02$).

Discussion

National guidelines for non-conservative treatment with systematic removal of the CVC within 3 days for *S. aureus* CR-BSI in adults are based on different publications showing high rates of treatment failures (>40%) when the CVC is not rapidly removed [7]. But no study has been carried out and published in neonates and children in France. The aim of our study was to show whether the consequences of paediatric catheterization without systematic removal at the onset of CR-BSI may provide guidelines and confirm those used in adults. The main result of our study was that the incidence of failures occurring after conservative treatment is significantly higher than those after non-conservative treatment in neonates and children. This finding may be essential in helping paediatricians to manage CR-BSI in neonates and children, even if our results should be interpreted with caution due to the small size of our sample, the probable impact of age, and the type of CVC. *S. aureus* CR-BSIs are associated with high morbidity, especially for at-risk patients and non-conservative treatment to manage *S. aureus* CR-BSI should be beneficial. Moreover, if catheter removal is one of the main factors in preventing CR-BSI, prevention of CR-BSI should integrate a multidisciplinary bundle of measures involving healthcare professionals who prescribe the CVC insertion and removal, those personnel who insert and maintain CVC, infection control personnel, and healthcare managers. The goal of an effective prevention programme should be the elimination or drastic decrease of CR-BSI in intensive care units [8]. Although this is challenging, educational training has demonstrated success, but sustained elimination requires continued effort.

Most of the 57 neonates and children were young or very young, with high susceptibility to infections. The duration of catheterization was variable, from several days to several months. In case of long duration of catheterization, CVCs are

changed during hospitalization to treat them using a non-conservative treatment strategy or to prevent the occurrence of CR-BSI.

The conservative strategy of treatment without removal of the catheter or in a time greater than 72 h was also focused on. Catheter removal in neonates and children is less systematic, mainly because of the difficulty of the approaches. After identifying 21 infectious episodes with CVC conservation, the modality of therapeutic management was studied, as well as its failure rate and its causes. The initial antibiotic treatment is mainly a dual therapy, combining vancomycin with another antibiotic. This practice follows international recommendations for fast, broad spectrum management. However, the failure rate of conservative treatment was about 50%, compared to only 9% in a rapid removal strategy. The main causes of failure were the persistence of positive blood cultures as well as the occurrence of complications (thromboses, tunnelitis, etc.). It can be observed that there is a gap between international recommendations in adults and local practices in paediatric services. This discrepancy was noted due to a more frequent conservative treatment strategy, as well as the non-use of antibiotic lock. It was not possible to identify the factor associated with failure in the conservative group because of the small size of our sample. This is one of the limitations of our study, as those *S. aureus* CR-BSI are relatively rare events. Another limitation of our study was the lack of information related to the type of CVC in medical records. This information could have been relevant as occurrence of CR-BSI and failures of conservative treatment may be linked to the type of CVC. In conclusion, our study shows that non-conservative treatment with rapid removal of CVC is associated with significant lower failure rate and should be preferred by paediatricians managing *S. aureus* CR-BSI. Further multicentre researches with large cohorts of neonates and children are needed to confirm our finding and identify the role of host and CVC factors to prevent *S. aureus* CR-BSI.

Conflict of interest statement

None declared.

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