



Usefulness of catheter tip culture in the diagnosis of neonatal infections

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Abstract

Objective: To determine the number of colony-forming units (CFU) that best correlates with catheter-related infections (CRI) in newborns.

Methods: This was a prospective study of semiquantitative cultures of catheter tips obtained from newborns in the neonatal unit at Faculdade de Medicina de Botucatu, state of São Paulo, Brazil. The microorganisms isolated from catheter and peripheral blood cultures were identified and submitted to a drug susceptibility test. The optimal cutoff point was determined by the receiver operating characteristic (ROC) curve.

Results: A total of 85 catheters obtained from 63 newborns were studied. *Staphylococcus epidermidis* was the predominant species in the catheters (75%). Eight of 11 (72.7%) CRI episodes were associated with coagulase-negative staphylococci, six of which were of the *S. epidermidis* type. ROC curve analysis indicated that the optimal cutoff point for the diagnosis of CRI was 122 CFU.

Conclusions: The cutoff point of 122 CFU correlated best with the diagnosis of CRI in newborns.

J Pediatr (Rio J). 2009;85(1):80-83: Catheter-related infection, catheter culture, semiquantitative culture, newborn, coagulase-negative Staphylococcus.

Introduction

A progressive increase has been observed in the survival of low birth weight and premature newborns. The use of invasive procedures, such as intravascular catheters, constitutes a significant risk factor for the development of nosocomial infections, among which catheter-related infections (CRI) stand out.^{1,2}

CRI are diagnosed when identical microorganisms are isolated from catheter cultures and from blood cultures, without any other apparent source of infection except for the catheter.³ The semiquantitative culture method proposed by Maki

et al.⁴ is the most commonly used in these cases, and it is recommended for the diagnosis of CRI by the Centers for Disease Control and Prevention.³ According to the criteria proposed by Maki et al.,⁴ positive catheter cultures are those that present a colony-forming unit (CFU) growth rate ≥ 15 , since this is the number that best correlates with the presence of infection when compared to the qualitative catheter-culture method, which does not distinguish between infection and contamination. Although other authors have already conducted studies to assess cutoff points in adult patients,^{4,5} we have not found any studies evaluating the best semiquantitative culture cutoff point for the diagnosis of CRI in newborns.

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Thus, the objective of this study was to determine the number of CFU that best correlates with the presence of CRI in newborns.

Methods

This prospective study included 85 catheter tips that had been used in 63 newborns hospitalized in the neonatal unit at Hospital das Clínicas, Faculdade de Medicina de Botucatu (UNESP), state of São Paulo, Brazil, in a period of 2 years, from September 2001 to August 2003. The study protocol was approved by the research ethics committee of the institution.

Microorganisms isolated from catheter tips and from blood cultures of patients whose samples had been collected close to the catheter removal date were included in this study. On the other hand, we excluded isolated samples of newborns whose clinical and laboratory data referring to a period of 1 week before up to 1 week after the catheter removal date could not be found.

Catheter tip cultures were performed using the semiquantitative method described by Maki et al.,⁴ whereas blood cultures were collected and cultivated using the BACTEC automated system, according to the guidelines described by Koneman et al.⁶ Identification of microorganisms was performed as preconized by Koneman et al.,⁶ and identification of coagulase-negative staphylococci (CNS) was performed according to the criteria proposed by Kloos & Scheifeir⁷ and Kloos & Bannerman,⁸ i.e., using a simplified scheme of biochemical tests. Antimicrobial susceptibility test was performed using the agar diffusion technique employing impregnated disks, as recommended by the National Committee for Clinical Laboratory Standards (NCCLS).⁹ Inhibition halos were measured (mm), and results were analyzed comparing germs isolated in the same newborn (from the catheter and the blood cultures) to assess similarity of the samples.

The definitive diagnosis of CRI was established based on the criteria proposed by the Centers for Disease Control and Prevention (CDC),³ i.e., by the presence of two or more of the following signs or symptoms: fever (≥ 38 °C), hypothermia (< 36 °C), sleep apnea, bradycardia or signs of shock, in addition to the presence of at least one positive blood culture in a patient whose vascular catheter presented a positive semiquantitative culture. The diagnosis of CRI was confirmed when the same microorganism (same species and same drug susceptibility profile) was isolated from catheter and from peripheral blood cultures, without any other apparent focus of infection except for the catheter.

In order to determine cutoff points for semiquantitative culture in the diagnosis of CRI, we calculated the sensitivity and specificity of the number of CFU in each culture. The gold standard corresponded to the definitive diagnosis of CRI, namely, isolation of the same microorganism (same species

and same antibiogram) from both catheter tip cultures and blood cultures.

The optimal cutoff point was determined by the receiver operating characteristic (ROC) curve, by representing true positive rates (sensitivity) on the y-axis, and false positive rates ($1 - \text{specificity}$) on the x-axis. All counts obtained from catheter tip cultures were analyzed: 1, 2, 7, 8, 9, 11, 12, 17, 22, 23, 30, 36, 60, 73, 122, 125, 130, 150, 193 and 300 CFU.

Results

A total of 85 catheter tips used in 63 newborns hospitalized at UNESP were analyzed. Identification of the microorganisms isolated from catheter cultures revealed a predominance of CNS species (81.8%) (Table 1); *Staphylococcus epidermidis* was the most frequently found species (75%).

Analysis of the susceptibility profile of the microorganisms isolated from 17 patients whose catheter cultures and blood cultures were positive for the same species allowed diagnosis of CRI in 11 cases. Of the microorganisms associated with the etiology of CRI, eight (72.7%) were of the CNS type, and of these, six (54.5%) were of the *Staphylococcus epidermidis* species. We also found two cases of CRI caused by *S. aureus* and one caused by *Candida parapsilosis*.

ROC curve analysis revealed an optimal cutoff point of 122 CFU, with higher sensitivity (91%), higher specificity (81.1%), and higher positive (41.7%) and negative (98.4%) predictive values when compared to other cutoff points assessed. Calculation of the 95% confidence interval (95%CI) showed that the sample size was adequate for determining the cutoff points assessed; the area under the ROC curve was 0.860, indicating good adjustment. Ten of the 11 cases diagnosed with CRI (90.9%) showed a growth rate ≥ 122 CFU; a growth of 8 CFU was identified in only one case.

Discussion

The diagnosis of CRI in neonatal units has been performed as recommended by the CDC,³ using methods that are similar to those employed when diagnosing the infection in adult patients. This prospective study was conducted in view of the absence of literature dealing specifically with the diagnosis of CRI in newborns.

The species involved in the etiology of CRI in our study are in accordance with reports found in the literature, since the CNS have been associated with 81.8% of CRI cases, and they are the microorganisms most frequently involved with CRI in newborns.^{10,11} We also observed episodes of CRI caused by *S. aureus* and *Candida parapsilosis*; both microorganisms are considered frequent, although not predominant, etiologic agents of CRI in newborns.^{11,12}

Among CRI cases caused by CNS, *S. epidermidis* was the species most frequently found. A higher frequency of this microorganism was expected, since this is the predominant

Table 1 - Species of microorganisms isolated from semiquantitative catheter cultures

Microorganisms	Positive growth n (%)	CRI n (%)
<i>Staphylococcus epidermidis</i>	33 (75)	6 (54.5)
<i>Staphylococcus warneri</i>	1 (2.3)	1 (9.1)
<i>Staphylococcus simulans</i>	1 (2.3)	1 (9.1)
<i>Staphylococcus haemolyticus</i>	1 (2.3)	-
Total CNS	36 (81.8)	8 (72.7)
<i>Staphylococcus aureus</i>	2 (4.5)	2 (18.2)
<i>Acinetobacter baumannii</i>	1 (2.3)	-
<i>Candida parapsilosis</i>	4 (9.1)	1 (9.1)
Gram-positive bacillus	1 (2.3)	-
Total	44	11

CNS = coagulase-negative staphylococcus; CRI = catheter-related infection.

species in the flora of newborns. This predominance of *S. epidermidis* in the colonization of individuals and the high pathogenicity associated with some strains may explain why this microorganism is the one most frequently associated with infection processes in newborn infants, as described by Cunha et al.¹³

The ROC curve analysis showed that the 122 CFU cutoff point revealed higher specificity, without losing sensitivity, when compared with the 15 CFU cutoff point recommended by the CDC,³ whose sensitivity, specificity, and positive predictive values (PPV) were, respectively, 91.0, 71.6, and 32.3% in relation to our results. A study carried out by Collignon et al.⁵ involving adult patients concluded that the optimal cutoff point for detecting CRI is ≥ 5 CFU. Considering that the semiquantitative culture of catheter tips is useful for the diagnosis of CRI, a test characterized by high specificity and high PPV is both necessary and desirable. Nevertheless, the PPV found by Collignon et al.⁵ was only 8.8%. According to Brun et al.,¹⁴ those authors should have chosen a growth of ≥ 100 CFU as the optimal cutoff point, rather than ≥ 5 CFU, because a diagnostic test with a PPV < 10% cannot be considered adequate for the establishment of a clinical diagnosis. In our study, the cutoff point of ≥ 122 CFU corresponded to a lower number of false positive results and to higher specificity and PPV when compared with other values taken into consideration.

Although most cases of CRI present a growth rate > 122 CFU, we observed one case infected by *S. aureus* with a growth rate of only 8 CFU. Other authors have also identified CRI and semiquantitative cultures with growth rates < 15 CFU.⁵ These results can be explained by the use of antibiotics prior to the culture, or by intraluminal contamination of the catheter - this is a limiting factor in semiquantitative culture, since it only detects microorganisms adhering to the external

surface of the device.¹⁵ The need to remove the catheter in order to carry out the culture is another disadvantage of the semiquantitative method; therefore, other methodologies should be considered for the diagnosis of CRI, such as comparison of blood cultures isolated from peripheral veins and catheters, without the need to remove the device.

To sum up, semiquantitative cultures with a growth rate ≥ 122 CFU correlate best with the presence of CRI in newborns, which disagrees with the growth ≥ 15 CFU so far recommended in the literature. Nevertheless, interpretation of findings should be cautious, and culture results should be considered as a part of a broader scenario that determines diagnosis and a specific treatment.

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