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State of the Science Review

Clinical usefulness of catheter-drawn blood samples and catheter tip cultures for the diagnosis of catheter-related bloodstream infections in neonatology: A systematic review

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Key Words:

Catheter-related sepsis

Neonate

Newborn

Objectives: Neonatal sepsis is the most frequent health care-associated infection in neonatal units. This study aimed to analyze articles on the clinical usefulness of catheter-drawn blood samples and catheter tip cultures for the diagnosis of intravascular catheter-related bloodstream infection (CRBSI) in neonates.

Methods: A systematic search was performed for studies published from 1987-2017, without language restriction. Observational studies carried out in neonates with CRBSI diagnosed using catheter-drawn blood samples or catheter tip cultures were included.

Results: A total of 412 articles were identified in the databases and 10 articles were included. The 7 studies that evaluated central venous catheter tip cultures and cultures of catheter fragments presented sensitivities ranging from 58.5%-100% and specificities ranging from 60%-95.7%. Three studies that evaluated catheter-drawn blood cultures, paired with peripheral blood cultures, reported sensitivity and specificity of 94% and 71% when evaluated for the differential time to positivity. When quantitative evaluation was performed, the sensitivity and specificity were 80% and 99.4%.

Conclusions: Most of the studies analyzed cultures from the central venous catheter tip and catheter fragments for the diagnosis of CRBSI in neonatal populations. The results of this review suggest that the analysis of the catheter-drawn blood samples and catheter tip cultures, paired with peripheral blood cultures, are efficient methods for the diagnosis of CRBSI in neonates.

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Neonatal sepsis represents a common adverse event in health care in neonatal intensive care units (NICUs), causing increases in morbidity, mortality, and prolongation of hospital stays.¹⁻³

The incidence density of central line-associated bloodstream infections, which is the number of episodes of sepsis per 1,000 central line-days, varies among countries and institutions, and is associated with factors such as quality of health care, as well as the number of suitably trained health professionals. Thus, the incidence density of catheter-associated sepsis in neonatology ranges from 4.1-8.8 episodes per 1,000 central line-days in European countries, whereas the results of studies carried out in Latin America range from 3.0-12.6 infections per 1,000 central line-days. The national studies performed in neonatal

units in Brazil present rates around 18 infections per 1,000 central line-days.⁴⁻¹⁴

Prematurity and low birth weight are considered to be 2 of the most important risk factors for neonatal sepsis, due to immaturity of both the immune system and the protective barrier of the skin. The main exogenous risk factors related to health care are the length of hospitalization in the NICU, surgical procedures, the use of parenteral nutrition, and use of invasive devices such as mechanical ventilation and central venous catheters (CVCs).¹⁵⁻¹⁷

Preterm and low-birth-weight neonates usually need prolonged treatments with vesicant medication (that may cause tissue damage) that are harmful to the vascular endothelium, indicating the need for a CVC. Intravascular devices, such as peripherally inserted central catheters, are widely used in neonatology; however, they may be associated with adverse events such as failure during insertion, obstruction, rupture, and bloodstream infection.¹⁸⁻²⁰

Despite increasing knowledge of the related pathophysiology and treatment, neonatal sepsis remains a pathology that is difficult to

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manage clinically. The diagnosis of neonatal sepsis is difficult due to the nonspecific clinical manifestations with low predictive value that may be attributed to the clinical conditions during that period, such as transient tachypnea, apnea of prematurity, and bronchopulmonary dysplasia.²¹⁻²⁴

Catheter-related bloodstream infection (CRBSI) should be suspected when sepsis occurs in the setting of a CVC with no other apparent source. Because the CVC may be the focus of the infection, the diagnostic approach to CRBSI consists of clinical evaluation and microbiologic confirmation using paired blood samples drawn from the catheter and a peripheral vein or tip cultures when the catheter is removed.^{25,26}

The drawing of paired blood samples from the catheter and a peripheral vein is considered the best approach to reduce suspicion of colonization of the device; contamination of the sample; or true bloodstream infection caused by common commensal microorganisms, such as coagulase-negative *Staphylococcus* (CNS), the main etiologic agent of neonatal sepsis.^{22,27-31}

However, the definitive diagnosis of CRBSI in preterm and low-birth-weight infants is complicated because the drawing of paired blood samples from the catheter and peripheral vein is not always possible. Therefore, many cases of CRBSI are only identified by culturing the tip when the device is removed.^{28,31-33}

The aim of this study was to carry out a systematic review evaluating the clinical usefulness of catheter-drawn blood samples and catheter tip cultures for the diagnosis of CRBSI in neonates.

METHOD

Literature search strategy

This review followed the guidelines described in the preferred reporting items for systematic reviews and meta-analyses statement.³⁴

We conducted a systematic search for studies published from 1987-2017, without language restriction, in databases such as Medline, Embase, Biblioteca Virtual em Saúde, Scopus, Google Scholar, and grey literature (ie, publications available in electronic media not reviewed by scientific editors).

The search strategy started with the definition of key terms, identified using Medical Subject Headings (MeSH): “catheter-related infections”[MeSH Terms] OR (“catheter-related”[All Fields] AND “infections”[All Fields]) OR “catheter-related infections”[All Fields] OR (“catheter”[All Fields] AND “related”[All Fields] AND “infections”[All Fields]) OR “catheter related infections”[All Fields] OR (catheter-related[All Fields] AND (“sepsis”[MeSH Terms] OR “sepsis”[All Fields])) AND (“infant, newborn”[MeSH Terms] OR (“infant”[All Fields] AND “newborn”[All Fields]) OR “newborn infant”[All Fields] OR “neonate”[All Fields]) AND (“diagnosis”[Subheading] OR “diagnosis”[All Fields] OR “diagnosis”[MeSH Terms]).

The following search terms were also used: *seps*, *infecção*, *cateter*, *neonatologia*, *neonato*, *recém-nascido*, *diagnóstico*, *seps* relacionada a *cateter*, and *infecção da corrente sanguínea associada a cateter*.

Inclusion and exclusion criteria

The research question was, Does catheter-drawn blood sample have a higher sensitivity and occurrence of adverse events than catheter tip culture for the diagnosis of CRBSI in a neonatal population? For the selection process, we used the population, intervention, comparison, outcome, study design strategy.^{34,35}

Thus, according to the population, intervention, comparison, outcome, study design strategy, we defined the eligibility criteria for the studies as P = neonates with a CVC, I = patients with CRBSI diagnosed by catheter-drawn blood sample, C = patients with CRBSI

diagnosed by catheter tip culture, O = definition of sepsis related to central venous catheter and occurrence of adverse events, and S = observational studies (cohort, cross-sectional or case-control).^{34,35}

The inclusion criteria were observational studies carried out in neonates with CRBSI, diagnosed by catheter-drawn blood sample or catheter tip culture. Congress abstracts, review articles, theses, dissertations, and letters to the editor were excluded.

Data extraction and quality assessment

The results of the literature search were assessed by 2 reviewers (JF and RMC). All the titles and abstracts identified in each database were analyzed to select studies that met the eligibility criteria.

The full texts of potentially relevant studies were obtained and they were evaluated for the study design, population, intervention, outcome, and presence of bias.

To evaluate the quality of the description of the observational studies, the strengthening the reporting of observational studies in epidemiology checklist was used.^{36,37} The information about the observational studies included was studied qualitatively.

Grading of recommendation, assessment, development, and evaluation (GRADE) was applied to evaluate the methodology, quality of the evidences, and outcomes reported in the studies, considering items such as risk of bias, inconsistency, indirectness, imprecision, and publication bias.³⁸

RESULTS

The literature database search retrieved a total of 412 references (207 on Medline, 100 on Embase, 53 on Biblioteca Virtual em Saúde, 51 on Scopus, and 1 on Google Scholar). Of these studies, 386 (93.7%) were excluded because they did not meet the eligibility criteria and 15 (3.6%) were excluded because they were duplicated. After reading the full text of the remaining 11 studies, 10 were selected for inclusion in this systematic review, and 1 article about CVC colonization survey was excluded because it was unrelated to the diagnosis of CRBSI (Fig 1).

Of 10 articles included in this systematic review, there were 7 prospective observational studies and 3 retrospective observational

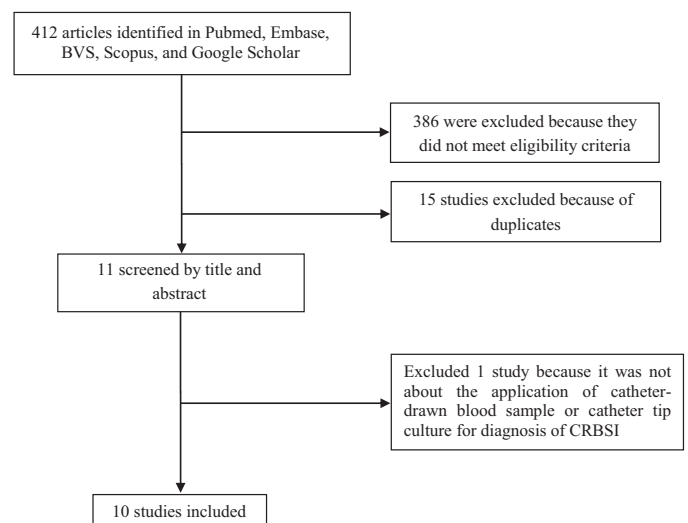


Fig 1. Flow diagram of the study selection on diagnosis of catheter-related bloodstream infections (CRBSI) in neonates. BVS, Biblioteca Virtual em Saúde.

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