British Intestinal Failure Alliance (BIFA) Recommendation

Diagnosis of Catheter Related Blood Stream Infections (CRBSIs)

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Aim

This document aims to provide the UK standard for the diagnosis of CRSBI in adult patients receiving parenteral support (PS; includes parenteral nutrition and/or fluids).

Background

Central-venous catheter related blood stream infections (CRBSI) are a significant cause of morbidity and mortality in patients requiring home parenteral support (HPS) (1, 2). There is a wide variation in the incidence of reported CBRSI, even amongst internationally-recognised Intestinal Failure (IF) centres. A systematic review of 39 studies published in 2012 reported a range of 0.38-4.58 per 1000 catheter days (1). A more recent series from the U.K. gave a lower rate of 0.31 per 1000 catheter days (3). This is in contrast to a series from the U.S.A. which gave a much higher rate of 11.5 per 1000 catheter days (4). It is not clear if the difference between centres relates to differing catheter care protocols, patient factors and/or criteria for CRBSI diagnosis. Since the incidence of CRBSIs is considered to be a marker of the safety and quality of HPN care, it is used for benchmarking units, research and quality improvements. For the incidence of CRBSI to be meaningful, the same definition for CRBSI needs to be applied nationally (5).

BIFA Recommendations

- Patients suspected of having a CRBSI should have peripheral and central blood cultures (at least 20mL from peripheral and 20mL from central (10 ml into each pair of bottles); a greater volume may be required for suspected infective endocarditis) taken within 10 minutes of each other (6). It is important that the same volume of blood is taken for the peripheral and central cultures. The inoculated blood culture bottles should be incubated as soon as possible (within 4 hours).
- All isolated organisms should be characterized, using standard laboratory techniques, to determine whether they are different from each other or indistinguishable.
- A CRBSI should be diagnosed using paired qualitative (as measured using differential time to positivity (DTP)) and/or using paired quantitative (as measured using pour plates) blood cultures from a peripheral vein and from the catheter.
- For centers using DTP, a CRBSI is diagnosed if the same organism is isolated from blood obtained through the catheter hub and from blood obtained from a peripheral vein <u>and</u> the DTP is more than 2 hours (catheter hub culture positive first). The results of DTP must be interpreted with care if a polymicrobial infection is found.
- For centers using pour plates, a CRBSI can be diagnosed if the same organism is isolated from blood obtained through the catheter hub and from blood obtained from a peripheral vein <u>and </u>the colony count of microbes grown from blood obtained through the catheter hub is at least 3-fold greater than the colony count from blood obtained from a peripheral vein.
- If a catheter is removed the tip should be sent for culture and if the same organism as from blood cultures is isolated CRBSI is confirmed.
- Integrated and HPN centers with no current access to DTP or pour plate methodology should work with their microbiology teams to introduce this service.
- All Integrated and HPN centers should report annual CRBSI rates/1000 catheter days with the associated method of diagnosis.

- Policies should be devised by via a regional network to ensure Integrated IF centers and HPN centers are informed within 24 hours when patients with suspected CRBSIs present to local hospitals.

Appendix

Current definitions of CRBSI

The current European Society for Parenteral and Enteral Nutrition (ESPEN) guidelines are based upon the Centre for Disease Control and Prevention (CDC) criteria and are defined by a "positive culture of the catheter (on removal), or paired blood cultures from a peripheral vein and the catheter (when left in place) with isolation of identical organisms (both species and antibiograms) from cultures of catheter segments and blood drawn from a peripheral vein in a patient with clinical symptoms of sepsis and the absence of another source of infection." The ESPEN guidelines also states "a diagnosis of CRBSI should be achieved by (a) quantitative or semi-quantitative culture of the catheter (when the CVC is removed or exchanged over a guide wire), or (b) paired quantitative blood cultures, or paired qualitative blood cultures from a peripheral vein and from the catheter with continuous monitoring of the differential time to positivity (if the catheter is left in place). A probable CRBSI is characterized by a colonized catheter in association with clinical signs suggesting septicaemia, despite the lack of a positive peripheral blood culture. Blood cultures should not be taken on a routine basis in the absence of suspicion of a catheter-related infection."(7-9)

The Infectious Disease Society of America (IDSA) diagnostic criteria are similar to the ESPEN ones with peripheral and central blood cultures, stating as follows: (10) For quantitative blood cultures, the colony count of microbes grown from the catheter hub blood sample is at least 3-fold greater than the colony count from the peripheral blood. For differential time to positivity (DTP), the growth of microbes from the catheter hub blood sample occurs at least 2 h before any microbial growth is detected in the peripheral blood sample.

Quantitative methods, such as pour plates, are thought (10) to have the best diagnostic accuracy and are recommended by international organisations, but may not be widely used (6,10-13). Differential time to positivity (DTP) has reasonable accuracy and is more widely available in most hospitals. (14) Quantitative and qualitative blood cultures rely upon careful sample labelling, with equal volumes of blood instilled into blood culture bottles (within 10 minutes) and that the samples are then handled identically. The samples require prompt transport to and processing within the laboratory (within 4 hours of being collected).

Notably, a recent study demonstrated that simply adopting a clinically-based approach to diagnosing CRBSI (for example, based on the presence of clinical symptoms, elevation of biochemical blood tests and a positive peripheral or central blood culture) rather than using quantitative or qualitative methods may lead to significant over-diagnosis by 46%, so contributing to antibiotic overuse, unnecessary admission to hospital, unnecessary central venous catheter removal and possible compromised vascular access. (5)

Pour Plate Methodology (example)

Samples

1ml of venous blood (central or peripheral) is injected aseptically into a universal containing 3ml of brain-heart infusion broth with 1% liquoid. A minimum of two samples (one central and one peripheral) is required*. Samples should be transported to the lab immediately. (If any delay is anticipated, the samples should be refrigerated at 4°C.) Samples must not be incubated prior to processing.

Method

For each sample, melt 20ml Columbia agar base in a universal container by placing the bottle into a heat proof jug with water and heating for 10-15 mins using a hot plate. (To avoid contamination, the water level must remain below the lid of the universal container.) Remove the bottle from the hot water and transfer it to a 55°C water bath. When the agar has cooled to 55°C, pour the agar into the vial containing the sample container (containing the broth/liquoid/blood). Mix by gently inverting, pour the contents into a sterile petri dish (total 24ml) and allow the agar to set at room temperature. Incubate the plate aerobically at 35-37°C for 5 days. Examine the plate daily and observe for any growth. If growth is observed, perform a gram stain on each type of colony. Characterise each morphotype using standard laboratory methods.

Interpretation

Count the number of colony forming units (CFUs). Check that paired peripheral and central samples were collected, received and processed together. If the number of CFUs from the central line blood sample is ≥3 times the number of CFUs from the peripheral blood sample, this is consistent with the central line being the source of infection.

Reporting

If positive, report the number of CFU/ml of each organism isolated. If negative, report no bacterial growth at 48 hrs (interim report) and no bacterial growth at 5 days (final report).

* Quantitative (pour plate) cultures test specifically for CRBSI and use a low volume of blood. They should not be regarded as general blood cultures and do not replace the need for conventional blood culture testing as part of a work-up for sepsis of unknown source.

Differential Time to Positivity (DTP) Methodology

Samples

A standard volume (usually 10ml) of venous blood is injected aseptically into a blood culture bottle designed for an automated, continuous monitoring blood culture system. A minimum of four samples (two central and two peripheral) is required*. Samples should be transported to the lab immediately. (If any delay is anticipated, the samples should be stored as per manufacturer's instructions and not pre-incubated). It is important that equal volumes of blood are injected into each bottle, as this will affect the time to detection, and to carefully label the source of each sample (central or peripheral; time of collection; lumen colour).

Method

Bottles are loaded onto the blood culture machine in accordance with the manufacturer's instructions. Positive cultures are flagged by the machine in accordance with pre-programmed positivity parameters. Time of loading and time of positivity for each bottle is recorded by the blood culture system. (If interfaced with the laboratory information system (LIMS), this data, together with date and time of sample collection, may all be available through the LIMS.) When a bottle is flagged as positive, perform a gram stain and culture on each positive bottle using standard laboratory methods. Examine subcultures daily and observe for any growth. Characterise each morphotype using standard laboratory methods.

Interpretation

Note the time of loading and the time of positivity for each positive bottle and calculate the time to positivity by subtraction. Check that paired peripheral and central samples were collected, received and loaded onto the machine together. If the time to positivity for a central line blood sample is more than120 minutes before the time to positivity for a peripheral blood sample, this is consistent with the central line being the source of infection.

Reporting

If positive, report the time to positivity for each bottle and the organism(s) isolated. (Note that the LIMS may not support automated extraction and reporting of all relevant data.) If negative, report no bacterial growth.

* The inclusion of 4 blood culture bottles (two sets) is consistent with a work-up for sepsis of unknown source, where CRBSI is part of the differential diagnosis, and will achieve the minimum recommended total blood culture volume of 30-40ml. Where only CRBSI is suspected, for example where an organism has already been identified in peripheral blood, it may be sufficient to inject only 10ml blood from each of paired central and peripheral samples into aerobic bottles only, thus minimizing the volume of blood and number of bottles required for the test.

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