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Prevention of primary bacteraemia

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Abstract

This overview provides information on recent advances in the prevention of primary bacteraemia, commonly defined as bloodstream infection without a documented source of infection, but including those resulting from an intravenous or arterial line infection. The potential to prevent community-acquired, primary bacteraemia is still limited and may be targeted mainly at vaccines for high-risk groups. In contrast, the prevention of catheter-related bacteraemia has seen substantial progress within the last 10 years. Consequently, intravascular device-related bacteraemia has become largely preventable under routine working conditions. Independent of the use of antibiotic-coated catheters, the implementation of clinical pathways and multimodal preventive strategies directed at several risk factors of catheter-related bacteraemia is a successful strategy to reduce this potentially life-threatening infection and deserves future health services research.

Keywords: Catheterisation; Central venous catheter; Cross-infection; Prevention & control; Guideline adherence; Patient care; Practice guidelines; Prospective studies; Septicaemia

1. Introduction

Bloodstream infections account for approximately 5–15% of all healthcare-associated infections and represent an important cause of death in hospitalised patients. Despite advances in the diagnosis and care of bacteraemic patients with organ dysfunction, case-fatality rates are still high, ranging from 10 to 60% [1].

Primary bacteraemia is commonly defined as microbiologically documented bloodstream infection without a known source. As in many previous reports, primary bacteraemia in the presence of an indwelling catheter is considered a catheter-related bacteraemia. Frequently, authors group together primary bacteraemia and catheter-related bacteraemia to describe their impact and draw clinically relevant conclusions [2] and we follow that practice in this review.

In the present overview, we discuss on the basis of a selection of articles some of the current challenges associated with the prevention of primary bacteraemia, describe recently published evidence and summarise ongoing controversies, with a particular focus on catheter-related bacteraemia. More specifically, we address the following questions:

1) What is the epidemiology of primary bacteraemia?
2) How can we prevent primary bacteraemia unrelated to indwelling devices?
3) What approach should be chosen to prevent catheter-related bacteraemia?
4) When are coated catheters required?
5) Are antibiotic stop locks indicated for prevention of primary bacteraemia?

2. Epidemiology of primary bacteraemia

Unfortunately, few population-based data are available to estimate the incidence of primary bacteraemia. A Danish population-based cohort study conducted between 1992 and 1997 obtained information on co-morbidities, source and outcome of 1844 patients with community-acquired bacteraemia [3]. Patients with an undetermined source accounted for 21% in 1992–95 and 13% in 1996–97. In 54 of 145 (37%) episodes of community-acquired *Staphylococcus aureus* bacteraemia the source of infection could not be established.

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The 30-day case-fatality rate for community-acquired bacteraemia with a miscellaneous source of infection was 15% (42 of 275 patients died).

Critically ill patients are at particularly high risk of primary bacteraemia. An international study performed in 28 intensive care units from eight countries determined between May 1997 and May 1998 the incidence of bloodstream infections in this patient population [4]. Among 4277 infected patients who stayed more than 24 h, 536 (12.5%) had primary bloodstream infection. The relative frequency of primary bloodstream infection was 5.8% among patients with community-acquired infection, 11.3% in patients with hospital-acquired infection and 15.3% in those with intensive-care-unit-acquired infection. In all three groups, Gram-positive cocci were the predominant pathogens in primary bloodstream infection (Fig. 1).

In a 3-year retrospective cohort study performed at the surgical intensive care unit of the Geneva University Hospitals (Geneva, Switzerland), we determined the epidemiology of bloodstream infections [5]. Among 4530 admissions to this intensive care unit, 224 clinically significant episodes of bloodstream infection were recorded (incidence, 4.9%), with a 28-day fatality rate of 36%. A total of 110 patients had primary bacteraemia, among which 39 (36%) were microbiologically proven, catheter-related infection. Another study published in 2001 described the relative frequency of intensive-care-unit-acquired bacteraemia [6]. Bacteraemia occurred in 5% of patients (111 episodes). These were divided into primary bacteraemia (no known source of infection, 29%); catheter-related bacteraemia with microbiological proof of catheter infection (26%); and secondary, nosocomial bacteraemia (45%). Only the latter type of infection had an increased risk of death compared to primary bacteraemia (odds ratio, 4.6; 95% confidence interval, 2.9–7.1).

The use of indwelling devices places large numbers of patients at risk for primary bacteraemia. It has been estimated that 50 000–100 000 bloodstream infections related to vascular devices occur every year in the United States; 90% of these infections originate from central venous catheters (CVC). Catheter-related infection may also be exit-site infection, infection of the tunnelled portion of a catheter, or combinations of the above. Most catheter-related bloodstream infections are due to coagulase-negative staphylococci, enterococci, and *S. aureus*. Less common pathogens are *Candida* species and various Gram-negative rods including *Escherichia coli*, *Klebsiella* species and *Pseudomonas* species [7].

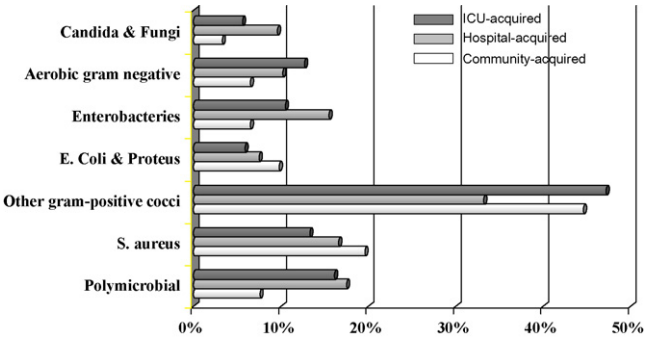

Fig. 1. Primary bacteraemia: description of micro-organisms according to the site of acquisition. Adapted with permission from [4].

The mortality rate for CVC-related bacteraemia ranges from 5% to 35%. The magnitude of effect may vary based on the pathogen, adequacy of treatment, and patient population studied [8]. In particular, microbiologically inappropriate therapy of severe CVC-related infections may increase the likelihood of death. Overall, between 14 000 and 28 000 deaths occur annually in the United States due to CVC-related infections. The excess costs attributed to such infections have been estimated to vary between $2000 and $40 000 per episode. Severe complications like endocarditis, septic arthritis and osteomyelitis are not uncommon.

3. Prevention of primary bacteraemia unrelated to catheters

The potential to prevent community-acquired, primary bacteraemia is still limited and may be targeted at high-risk groups only. Since the majority of these episodes are due to Gram-positive bacteria such as *S. aureus* and *Streptococcus pneumoniae*, preventive strategies may rely on eradicating the carriage status or increasing patients' immunity against invasive infection.

Multiple studies attempting to eradicate *S. aureus* colonisation and decrease associated *S. aureus* infection have been performed within the last 50 years, using different types of decontamination regimens. Despite these efforts, no clear evidence is available demonstrating that eradication of staphylococcal carriage in patients seen in ambulatory care and non-surgical settings may be beneficial and cost-effective. Moreover, no community-based intervention has ever attempted to decrease community-acquired *S. aureus* infections using this approach. Vaccines against *S. aureus* infection may be a promising approach, but have only been tested in high-risk patient groups. A vaccine directed against *S. aureus* capsular polysaccharide has shown short-term efficacy in haemodialysis patients [9]. However, development of the vaccine was stopped after it failed to show efficacy in a confirmatory phase III trial, which included 3600 dialysis patients. Despite these disappointing findings, further efforts are currently underway to assess new vaccines against staphylococcal infection. For instance, Roth et al. have recently suggested that a DNA vaccine targeting the penicillin-binding protein PBP2a could represent a new and valuable approach for passive immunisation against MRSA infections [10].

Vaccine development has been much more successful for *S. pneumoniae*. Pneumococcal vaccination clearly protects against invasive disease including primary bacteraemia [11]. Different types of studies suggest a greater than