Chapter 13

Catheter-Related Bloodstream Infections in Critical Care

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Additional information is available at the end of the chapter

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1. Introduction

1.1. High-yield facts

- Central line insertion is a very common procedure in critical care settings, and is associated with infectious complications such as local colonisation and bloodstream infection which leads to bacteremia and sepsis.
- Causative microorganisms are commonly missed on blood cultures, so that empiric therapy must be started in absence of a known pathogen.
- Diagnosis is based on clinical suspicion and microbiological confirmation by means of local and blood cultures (quantitative or semiquantiative).
- The mainstay of treatment is a combination of early antibiotic treatment and catheter removal with insertion at a new site.
- Prevention is the cornerstone of catheter-related infections.
- Multimodular programs (education, surveillance and quality management) and the sophistication of catheter-associated devices have shown benefit on CRBSI rate reduction.
- Strategies must be grouped into bundles.
- CRBSI reduction plans are part of the general ICU quality improvement plan.
- Team work is crucial to the construction and follow-up of the strategies aimed at reducing the infection rate in critically-ill patients.

2. Epidemiology of catheter related bloodstream infections

Central lines are inserted on a routine basis in critical care settings, for IV fluid administration, vasoactive medication infusions and monitoring purposes. As there has been worldwide expansion of intensive care facilities in the last few decades, the insertion of

central catheters has increased exponentially. Unfortunately, this procedure carries a risk of morbidity that includes local and bloodstream infections, which translates into higher healthcare costs and eventually into mortality[1-3].

The incidence of catheter-related bloodstream infections (CRBSI) varies widely among different healthcare institutions, ranging between 2,1 per 1.000 catheter-days for peripherally inserted central catheters (PICCs) to 2,7 per 1.000 catheter-days for non-tunneled central lines[4-6]. In the US, it has been estimated that approximately 31.000 deaths per year are attributable to bloodstream infections[7], representing an expenditure of about $18.000 per CRBSI[8]. In Spain the rate of CRBSI has been estimated in the range of 2,1 to 3,4 per 1.000 hospitalized patients[9]. Tacconelli et al. showed that the incidence of CRBSI varies widely among four european countries (France, Germany, Italy and the UK), from 1,12 to 4,2 per 1.000 catheter days[10]. Finally in Latin America and Africa incidence of CRBSI is unknown.

3. Pathogenesis

CRBSI might occur as a result of the entry of pathogenic microorganisms to the bloodstream via four different routes[11]: local insertion site colonisation, catheter hub contamination, hematogenous seeding and infusión of contaminated fluids. Attention has been focused on the two first routes[12-14]. The spread of infection from the insertion site has been widely recognized as the main cause of CRBSI, and the risk factors related to its development have been matter of research during the last two decades. However, hub contamination is relevant for long-term tunneled catheters[15]. CRBSI co-morbidity risk factors identified are insertion technique, insertion site, type and frequency of dressing, frequency of manipulation, duration of catheterization, number of catheter lumens, local and systemic antibiotic use, type of antiseptic solution use and experience of the person in charge of catheter care[16-19]. On the other hand, the presence of renal failure and hemodialysis are independent risk factors for CRBSI[20-21].

Several studies have shown that the causative agent of CRBSI sometimes is difficult to isolate. However, some series have reported that the most common organisms responsible of infection are: *coagulase-negative Staphilococcus, Enterococci, gram negative bacteria (Klebsiella Pneumoniae and E. Coli) and Candida Albicans*[22-24]. Healthcare personnel and patient skin colonization with Staphylococci is common, and is related to CRBSI, whereas *C. Albicans* and *C. Parapsilosis* may be responsable of infusate contamination.

The causative microorganisms of CRBSI are able to produce an exopolysaccaride-rich layer that adheres to the catheter. This layer supports the formation of a microbial biofilm, that allows bacteria to grow on the surface of foreign bodies in contact with bloodflow. This situation confers the causative agent some resistance to antibiotic, making necessary catheter removal in order to erradicate infection. Soon after catheter insertion, a thrombin sheath is formed on the outer and inner surfaces of the device, facilitating adherence of pathogens. This sheath is rich in proteins such as fibronectin, fibrinogen, thrombospondin, laminin and adhesin[25-29]. This last protein is an endogenous protein attractive to coagulase negative

Staphylococci. Once bacteria are attached to adhesin, biofilm covers the microorganisms from the action of immune system and antibiotic action.

Unfortunately, information regarding the causative agent in a particular case is sometimes useless, due to the low rate of positive blood cultures in an ICU population receiving antibiotics for diferent reasons[30,31]. The isolation of a pathogen in blood cultures is a negative prognostic factor[32], whereas it is useful to verify the appropriateness of empiric therapy, which is related to morbidity and mortaity[33,34]. On the other hand, positive cultures at the insertion site do not predict reliably positive blood cultures[35]. Furthermore, false positive cultures may lead to unnecessary anibiotic treatment, prolonged hospital stay[36] and emergence of resistant species[37,38].

4. Diagnosis

It has been found that reliability of clinical findings in CRBSI are not enough to diagnose the disease due to their por performance as diagnostic tests. Fever, one of the most common symptoms, has low specificity, whereas local insertion site inflammatory signs have por sensitivity. Remission of systemic inflammatory response after catheter removal is suggestive but not diagnostic of CRBSI[12,37-39].

The non-uniformity in definition of criteria to diagnose CRBSI has made difficult to compare studies and to issue accurate recommendations regarding diagnosis[12,23]. However, with surveillance purposes, the Centers for Disease Control (CDC) have established the definition of "laboratory confirmed bloodstream infection" (LCBI)[40], consisting in meeting at least one of the following criteria:

- Patient has a recognized pathogen cultured from one or more blood cultures and the pathogen is not related to an infection at another site.
- Patient has fever, chills and/or hypotension as well as positive laboratory cultures from two or more blood samples drawn on separate occasions which are not related to infection at another site and do not reflect contamonation.
- Patient < 1 year of age has at least one of the following signs or symptoms: fever, hypothermia, apnea, or bradicardia (in addition to the above criteria).

It is adequate to process only the catheter tip for culture[23]. Quantitative (positive $>10^2$ cfu) and semiquantitative (positive $>10^5$ cfu) culture techniques are recommended over qualitative cultures[41-45]. It is recommended to culture every catheter removed due to suspicion of infection, but it is not a good practice to send every catheter removed to culture. Secretion draining from the insertion site must be cultured[23].

According to the IDSA guidelines for the diagnosis and management of catheter related infection[23], it is recommended that as long as possible, blood cultures should be drawn prior to antibiotic administration. When dealing with blood cultures, contamination is an issue that must be taken into consideration. Contamination is significant when blood cultures are drawn from a catheter in use, as compared to an adequately obtained sample from a peripheral vein[46-50]. On the other hand, diagnostic accuracy is optimal when quantitative

paired blood cultures (concomitant catheter and peripheral) are drawn[51,52]. In summary, an accurate diagnosis of CRBSI can be achieved when clinical signs and symptoms are associated with positive local and paired blood cultures that match in microbiological terms.

5. Management

Empiric antibiotic treatment is a common practice when dealing with CRBSI. The choice of the antimicrobial agent depends on the severity of the systemic illness, the comorbidities, the most likely microorganisms and the local resistance profile. The combination of catheter removal and early antibiotic treatment have shown to be effective (negative blood cultures) in 88% of the cases[53]. Since methicilin-resistant *Staphylococcus Epidermidis* is the most common pathogen, it is reasonable to use Vancomycin as the first choice. In case of MIC ≥ 2 μg/mL, alternatives such as daptomycin are valuable. On the other hand, gram negative microorganisms (including *Pseudomonas Aeruginosa*) should be covered in neutropenic or severely-ill patients. It is not recommended to use linezolid as empiric treatment[23]. Regarding treatment duration, there is no strong evidence in favor of any recommendation. Our experience at Clinica de los Andes (unpublished results) have shown that five days from the first negative blood cultures is associated with no relapse and favorable outcomes. Femoral vein catheters are more prone to develop CRBSI due to the anatomical area of insertion. Furthermore, fungi growth is a common occurrence. This situation warrants antifungal empiric therapy in this subset of patients.

Catheter removal is a mainstay of treatment. However, when an ICU patient with moderate disease has fever, the recommendation is to draw blood samples from the device and from a peripheral vein before making the decision of removal. Most catheters from suspected cases of CRBSI end up being sterile[53-54]. If there is no other possible source of infection, or the patient is severely ill, catheter removal and insertion at a new site are recommended.

The antibiotic regimen must be "de-escalated" depending on blood and local site culture results in order to limit the probability of emergence of resistant species. At our institution we decide to continue the initial antibiotic depending on clinical response over the antibiogram. If the patient is not improving, then the sensitivity tests are taken into account to chang the antimicrobial agent.

6. Prevention: strategies and bundles

Significant efforts have been made at different levels in order to reduce the incidence of CRBSI in intensive care units[55-61]. Most of the initiatives have focused on preventive aspects[62-65], as evidence has shown that educational programs as well as multifactorial model implementation are effective[62-72].

During the last decade, several studies have investigated different strategies aimed at reducing CRBSI by means of prevention[73]. Most of the studies demonstrate benefit derived from multimodule programs including education, surveillance and quality management,

and from the development of devices (such as catheter biomaterial and locks, dressings and antiseptic solutions).

The catheter insertion conditions are critical for the development of infections derived from the device. The current recommendation includes the use of a long sleeve gown, surgical cap, face mask, sterile gloves and large sterile sheets that completely cover the patient[74]. Hand hygiene should be the standard practice, but compliance by health care professionals is still poor. In an attempt to enhance compliance, hand rubbing with an alcoholic solution might be as good as hand washing[75]. Chlorhexidine, for example, has shown a better antiseptic performance as compared to regular povidone iodine solutions[76]. However, povidone iodine is preferred in some ICUs, especially in the developing world, due to its low cost and because of the low bacterial and fungal resistance development[77]. In this case, the povidone iodine solution must remain in contact with the skin for at least one minute in order to be effective[76].

The site of insertion of the catheter also influences the infection rate. In general terms, we can say that internal jugular approach is associated with a higher risk of CRBSI but a lower risk of mechanical complications such as pneumothorax. Conversely subclavian insertion requires more expertise but has a significant lower association with infection[2]. A higher infection rate is seen in the femoral approach. Thus, the subclavian approach must be preferred, especially for catheters expected to remain in place for more than 7 days[78]. Femoral catheters must be avoided unless the mechanical complication risks of the subclavian and jugular approaches are prohibitive [79].

Numerous studies have shown that catheter replacement on a scheduled basis does not reduce CRBSI in ICU[80-82]. In fact, the 2011 CDC guidelines argue against this practice[83]. However, guidewire exchange to prevent CRBSI is not recommended[84-86]. Nonetheless, Riveros recently showed that in a medical ICU, with a high average length of stay, the central catheter exchange scheduled on the eighth day was superior to the a change guided by signs of infection[87]. In that study, 315 catheters (163 patients), were analyzed. Significant catheter colonization rates (RR=0,4 CI 95%: 0,1-0,9 p<0,01) and catheter-related sepsis were significantly lower in the scheduled change group (RR=0,4 CI 95%: 0,1-0,97 p=0,05). Those findings allow for possibility of scheduled catheter change in selected long-term medical ICU patients. However, further research is needed before clear-cut recommendations may be issued.

Transparent and gauze dressings are supposed to be part of ICU general protocols, but their use is not systematically adopted in routine practice[88]. A randomized controlled trial reported a reduction from 1,3 to 0,4 catheter-days (hazard rate 0,24 95% CI 0,09-0,65) in CRBSI with the use of chlorhexidine-impregnated dressings[89]. Impregnated catheters have been extensively studied but have not been universally used. Despite the theoretical advantage of antibiotic-coated catheters, in a meta-analysis, Walder demonstrated that anti-infective effectiveness of chlorhexidine-sulfadiazine coatings is time-dependent, showing good anti-microbial activity for the first week only[90]. However, the Evidence-based Practice in Infection Control (EPIC) in the UK, recommends the use of impregnated catheters in adults who require the device for one to three weeks[91].

As stated above, the approach to CRBSI is multimodal. Recently, a lot of information has emerged from studies worldwide, regarding changing practices in ICU. These studies use the concept of the "bundle", which includes a definition of objectives such as training[92-94], insertion and catheter care. Simulation training, in addition to improving technical skills in catheter insertion, allows the resident and physician to easily comply with guidelines and checklists[95]. This technique has shown a significant decrease in CRBSI ranging from 71% to 84%[96,97].

Most bundle initiatives have followed to the Michigan bundle proposed by Provonoust[98-105]. The Michigan bundle includes hand hygiene, use of chlorexidine for skin preparation, use of barrier precautions during insertion, a preference for subclavian vein and the removal of unnecessary central lines. The bundle was implemented for the Institute for Health Improvement in the US as part of the 5 million lives campaign[106] and is considered a standard of care. The bundls *per se* is not capable of controlling CRBSI, so that observation and follow-up are mandatory for a prevention strategy to be successful. Riveros et al showed that the implementation of the bundles must be accompanied by a strong ICU quality management program, which ought to have solid foundations in terms of goal definition, follow-up, information system, education and improvement plans[107]. The institution of these plan at different health care centers has produced reports of experiences with impressive results[66]. Finally, the educational programs must be sustained over time, and in order to do so, involvement of ICU staff in the construction and follow-up stages of the process is crucial and has been able to keep CRBSI low[107].

Additional measures to prevent CRBSI include administration sets replacement, including secondary sets and add-on devices, between 96 hours and 7 days[108-112], use of central venous catheters coated with chlorhexidine and silver sulfadiazine to reduce device colonization[113,114], and heparin locks impregnated with antibiotics[115-117].

In conclusion, CRBSI has become more challenging in light of the exponential growth of the critical care patient population worldwide. In order to cope with these changes, ICU healthcare and administrative personnel must work as a team to achieve the goals of a quality plan focused on infection control. The different strategies evidence-based strategies must be part of a bundle, and must be followed on a routine basis as part of improvement plans.

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7. References

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