



EDITORIAL

Diagnosis and treatment of bacteremia associated with the use of vascular catheters: That provides a new clinical practice guide ☆



Diagnóstico y tratamiento de las bacteriemias asociadas con el uso de los catéteres vasculares: que aporta una nueva guía de práctica clínica

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The use of peripheral intravascular devices (PIVD) is a basic element of healthcare.¹ In the information provided back in 2017 by the EPINE Program we got confirmation that more than 70 per cent of hospitalized patients are carriers of some kind of PIVD, 2/3 of these patients carry one peripheral venous catheter (PVC), and more than 10 per cent one central venous catheter (CVC), or one peripherally inserted central venous catheter (PICC).² At the Intensive Care Units (ICUs), almost all patients are carriers of some kind of PIVD during most of their hospital stay.

The use of PIVDs associates the risk of suffering from some sort of related infection, with rates of occurrence that have been studied by different monitoring programs. The National Healthcare Safety Network (NHSN) program conducted in the United States says that the incidence density (ID) of CVC-associated bacteremias at ICUs has gone down significantly ever since the massive implantation of intensive programs of prevention to just 1 episode for every 1000

days of program use. However, in some high-risk units such as those managing severely burnt patients, or patients with severe trauma, the ID could amount to 3 episodes. Similarly, and probably due to the great scientific repercussion that prevention programs had at one time or another^{3,4} the figures are significantly lower in most conventional hospitalization units of US hospitals.⁵

In Spain, the data provided by the ENVIN-HELICS for the year 2016 show one ID of bacteremias of unknown etiology or catheter-associated bacteremias close to 2.8‰.⁶ The effectiveness of the program known as “Bacteremia Zero” in these units has been confirmed and its persistence over time is now a clear reality.⁷ On a much bigger picture, the data from the VINCAt Program provide information on the status of vascular catheter-related bacteremias (VCRB) in Catalan hospitals. After adding the annual indicators from 2007 through 2016, the ID is 0.24‰ of hospital stays. In this setting, 68 per cent of bacteremias are associated with CVC; 21 per cent with PVC; and 11 per cent with PICC. Also, it has been confirmed that up to 70 per cent of all episodes are diagnosed in patients admitted to conventional hospitalization units.^{8,9}

The relevance of VCRBs is huge, due not only to their high frequency but also to the impact they have on health itself, healthcare costs and, eventually, on the effectiveness of healthcare systems. In the United States, it is estimated that the associated mortality rate may be around 25 per

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cent, and the incremental cost of VCRBs some \$26,000. The data coming from the US, that experienced a reduction of 46 per cent of its ID from 2008 to 2013, means that thousands of lives have been saved and nearly \$1.8 billion have not been spent.¹⁰ One case and control study conducted in Spain analyzed the excess of mortality and the healthcare costs associated with VCRBs at ICUs and confirmed that the mortality rate attributed to VCRBs is 9.4 per cent and the ICU stays extend for another 13 days.¹¹

Yet despite the enormous importance and impact of VCRBs, scientific societies have not made any big efforts to try to establish clinical practice guidelines beyond mere prevention issues. In the diagnostic and therapeutic setting, the most commonly accepted recommendations are the IDSA Practice Guidelines – whose latest publication dates back to the year 2009.¹² In Spain, back in the year 2004, and as the product of a collaboration between the SEMICYUC and the SEIMC, one document with a list of recommendations from experts was published.¹³ In the present issue, we will expose the consensus document (CD) “Diagnosis and Treatment of Catheter-Related Bloodstream Infection: Clinical Guidelines” co-authored by the Spanish Society of Clinical Microbiology and Infectious Diseases (SEIMC) and the Spanish Society of Intensive Care Medicine and Coronary Units (SEMICYUC).^{14,15}

This CD includes aspects associated with the diagnostic methodology and clinical management of VCRBs in the adult population. The CD also includes recommendations for all catheters – whether temporal or permanent, inserted into venous routes, but there is no explicit reference to those used for monitoring purposes and inserted into arterial systems. The methodology used to elaborate these recommendations has followed the guidelines established by the SEIMC (www.seimc.org) and the recommendations provided by the AGREE Collaboration (www.agreecollaboration.org). Also, the guidelines published by the ECCMID to grade the level of recommendations and the quality of the scientific evidence supporting them were used.

After identifying 39 questions in an effort to adopt one single position, 103 recommendations were defined with different levels of grading. Thus, within category A there is a total of 41 recommendations – from B 29 to C 23. However, it is worth reminding here that when it comes to the categorization of recommendations, only 10 obtained a quality of evidence IA. This situation is a little better from the one published by the IDSA Practice Guidelines,¹² where only 6 out of 123 recommendations achieved this category. In both guidelines^{CD12,14,15} it is plain to see that we need more clinical studies with high levels of scientific evidence for a more adequate and rigorous implementation of their recommendations. We should also mention here that recommendations with a quality of evidence type III take up 42 per cent of the IDSA CD,¹² and 37 per cent of the Spanish guidelines, respectively.^{14,15}

Although it is difficult to obtain scientific evidences to reinforce the recommendations from the guidelines, it is convenient to stress out that the present CD makes very relevant contributions for the management of VCRBs in the adult population. On the issue of diagnostic suspicion, the CD also defines the clinical characteristics and factors that favor the initiation of all procedures for its microbiological confirmation, and the requirements that

need to be met to consider it within the category of complicated.

On the issue of diagnostic methodology, the CD explains, in a fairly rigorous way, both the sample collection process and blood culture processing – basic elements for the ultimate categorization of VCRBs, while a special emphasis is put on performing this technique prior to the administration of antimicrobial treatment. Interpreting the results of blood cultures in patients in whom the device is not immediately removed, and it happens to be the suspicious source of the bacteremia, is part of the scientific apparatus; also, an explicit reference should be made here to the adequate assessment of the two most widely used methodologies. When it comes to the most common causal agents of VCRBs, the CD exposes the utility of using the differential time to positivity of blood cultures technique, and the differential count of colonies technique with the quantitative blood cultures technique. In those cases of candidemia originated inside the vascular catheters, both techniques have not been quite validated yet, so their results are more difficult to interpret.

On the diagnosis of VCRBs in patients whose device was removed early, the indications and methodology for the adequate processing of catheters in the Lab of Microbiology advocate for the use of semi-quantitative or quantitative instead of qualitative cultures, since the latter do not distinguish between colonization and infection. Similarly, a special emphasis is put on the interpretation of results and on when such results should be considered indicators that the PIVD is causing the bacteremia or candidemia.

When it comes to the clinical management of VCRBs, one of the most significant contributions of the CD has to do with the non-immediate or systematic removal of all vascular catheters (VC) in patients with suspicion of associated infections, and with establishing the criteria that should be met in order to make this relevant clinical decision. The routine scheduled change of VCs using guidewires through the same vascular access would not be recommended due to the associated infectious complications; also, this routine change would positively be contraindicated in accesses that are the source of the bacteremia. Thus, the use of this conservative strategy would be limited to patients who cannot be operated using new vascular accesses and without clinical or diagnostic suspicion that the vein that will be used is a source of infection.

The therapeutic decision to be made when the blood culture from an extracted VC tests undoubtedly positive is a difficult one that has not been properly analyzed in well-designed prospective studies. Under certain circumstances, the CD suggests the administration of antimicrobial treatment but only in cases of infection due to *Staphylococcus aureus* or *Candida* spp.

The process of choosing the right empirical therapy for the management of patients with suspicion of VCRB is explained in one algorithm of the CD that includes elements associated with the diagnostic methodology and its results; indications for device removal; and the antimicrobial treatment indicated for every particular clinical situation. The therapeutic decision depends both on the high frequency of the staphylococcal etiology of this type of infections and on its potential associated clinical severity. The inclusion of an adequate coverage against other pathogens such as

gram-negative bacilli (GNB) and yeasts has limited scientific evidence, which is why this decision should be made individually.

One key element of the CD has to do with the conservative management of VCRBs in patients with devices used for hemodialysis. The specific recommendation here is that the use of combined antibiotic therapy (local and systemic) gives better results than the use of exclusive systemic antibiotics, with the exception of cases due to staphylococcus aureus in which this strategy can produce a large number of therapeutic failures.

When it comes to the etiological management of VCRBs due to *S. aureus* all the antibiotic alternatives available today are suggested, with different degrees of categorization and based on the sensitivity pattern of the pathogens; the existence of prior allergies to beta lactam drugs; or based on the lack of response to early therapy. There are not any specific recommendations in this CD on the combination of antibiotics as a feasible alternative in severe cases, or cases that do not respond to early therapy.

The CD advocates for the systematic management of VCRBs due to coagulase-negative species of staphylococcus or enterococcus spp, based on their antimicrobial sensitivity, although there is no clear scientific evidence supporting this decision and the therapeutic benefit is probably limited to just a scarce number of patients. In any case, in both etiologies, an antimicrobial course with an active drug for one (1) week may be adequate in most circumstances. There is no specific recommendation on the management of VCRBs due to GNB because no adequate clinical trials have been conducted on this issue, which is why the panel recommends antibiogram-based targeted antibiotic therapies that should not exceed a period of seven (7) days.

The recommendations made on the management of catheter-related candidemia have to do with the immediate removal of the device and the use of sequential therapy; one echinocandin; or one amphotericin B lipid formulation (ABLF) with fluconazole based both on the sensitivity of the *Candida* species and the clinical response of patients. The duration of the antifungal therapy should not exceed fourteen (14) days once there is confirmation that the blood cultures tested negative. If the catheter cannot be removed, then a course of drugs with high antifungal activity should be administered instead of biofilms; echinocandins; or ABLFs.

One of the most significant contributions of the CD has to do with the indications of sequence of oral administration of therapies to fight VCRBs. The clinical stability; the negativity of blood cultures after catheter removal; and the possibility of using oral antibiotics with good bioavailability make this decision one of the most important ones for clinical management purposes. The different therapeutic alternatives would cover a great deal of clinical situations and be extremely beneficial both for the patients and the healthcare system.

The CD provides a large detailed assessment on the utility of conservative management of VCRBs (the so-called "Antibiotic Look Therapy") together with all of its contraindications. Several recommendations, among them the requirements that the episodes need to meet for its indication, and the need to use combined antimicrobial therapies – local and systemic, are categorized as AI. Also, in the format of tables excellent information is provided on the

antimicrobials that can be used for this therapeutic modality; the concentration needed to prepare the formulations and how to administer them; the frequency of lumen catheter change; and the optimal duration of the lumen. The criteria for conservative therapy failure and need for immediate device removal are clearly established too. Finally, data are provided on the possible use of other substances such as ethanol; taurolidine; EDTA; or citrate for this therapeutic modality.

The recommendations for the management of local complications are dealt with in different sub-sections. The recommendation with the highest level of scientific evidence would be the immediate removal of the PVC with clear signs of infection in the insertion site. Similarly, it would be advisable to remove all CVCs that show any traces of inflammatory signs or exudation in the insertion site.

In the last section of the CD the methodology for the follow-up of patients with VCRB on how to conduct control blood cultures and echocardiographic studies is assessed. On how to conduct control blood cultures, their routine practice in cases of *S. aureus* and *Candida* spp. is advisable until they test negative or else, in all patients on conservative management. Lastly, if possible it is advisable to conduct one echocardiographic study through transesophageal access in most patients with VCRB due to *S. aureus* and also individualize the use of echocardiographic studies in the remaining etiologies.

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