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Catheter-related blood stream infections (CRBSI): a European view

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In the July 2009 issue of the journal *Clinical Infectious Diseases*, the Infectious Diseases Society of America (IDSA) published an update of their 'Clinical Practice Guidelines for the Diagnosis and Management of Intravascular Catheter-Related Infection' [1]. The largest part of the IDSA text relates to non-dialysis catheters, and it is not always clear to what extent these general recommendations can be extrapolated to the haemodialysis condition. A specific but only brief section (~2 pages) of the IDSA guidelines is devoted to haemodialysis catheters.

In a position statement published in the June issue of *NDT Plus* [2] by the European Renal Best Practice (ERBP), these IDSA guidelines are amended with focus on haemodialysis conditions. ERBP is the new guidance body of the European Renal Association–European Dialysis and Transplantation Association (ERA–EDTA) replacing European Best Practice Guidelines (EBPG) since 2008. In contrast to the IDSA Guidelines, the ERBP position statement contains not only a section on treatment but also one on prevention and is entirely devoted to haemodialysis catheters. The publication was written according to the new philosophy of ERBP [3,4] and conforms to previously published documents [5–7].

The current editorial review offers a summary of this monograph [2], highlighting the most relevant statements. The reader is referred to the full text for the proper recommendations, a more extended rationale and several dialectic reflections on the original IDSA guidelines. At the end, the text in *NDT Plus* contains also a list of research suggestions.

General: tunnelled *vs* non-tunnelled catheters

Central vein catheters as an access for chronic haemodialysis are discouraged, in accordance with the previous EBPG guidance [8], although they are lifesaving in a substantial proportion of the dialysed population, who have run out of native access possibilities. If the use of a central vein catheter seems unavoidable, preference should be given to cuffed, tunnelled catheters unless contraindications are present, since the barrier they impose against inoculation is more efficient than with non-tunnelled catheters. It is considered mandatory to remove non-tunnelled temporary catheters as soon as possible, even in the absence of complications, and to have them replaced preferentially by an arteriovenous fistula (AVF), an arteriovenous graft (AVG), or a tunnelled central vein catheter, in that order of preference.

Prevention of infection

Catheter insertion and position

Catheters should be inserted under strict aseptic circumstances and according to the conditions formulated by EBPG [8]. Due to the complication profile [9], the use of the femoral and subclavian vein positions is discouraged. The right internal jugular vein is the preferred location for insertion, followed by the left internal jugular vein.

Nursing care

Universal precautions using sterile material and aseptic technique should be applied whenever a central vein catheter is manipulated, connected or disconnected.

The protective effect of masks and gowns against staphylococcal or other infections has not been proven. Therefore, their use should not be considered as an excuse to relax general hygienic and sterility standards.

Preventive antimicrobial catheter locks and catheter surface treatment

There is increasing evidence that certain antimicrobial locks applied within the catheter lumen are effective at preventing catheter-related blood stream infections (CRBSI). Some locks may have extra antimicrobial or biofilm-removing properties (e.g. citrate), in contrast to heparin which even tends to antagonize the bactericidal properties of certain antibiotics [10,11] and promotes biofilm formation [12].

The clinical advantages offered by citrate have been confirmed in at least two meta-analyses [13,14]. Over time, progressively lower concentrations of citrate have been applied (from 46.7% to 4%) with still significantly better results, even in the latter case, than those obtained with heparin locks [15–19].

One potential drawback of catheter locks is that some of the contents spill over into the circulation at injection and in between dialysis sessions [20,21], resulting in associated risks such as arrhythmias, toxicity and allergic reactions. These risks should be balanced with the benefits in terms of prevention of infection. For that reason, a low 4% concentration of citrate is proposed by the American Society of Diagnostic and Interventional Nephrology (ASDIN) [22]. For antibiotic locks, spillover may be a source of resistance [23]. Here, too, the use of antimicrobial locks should not be used as an excuse to relax the application of universal precautions and hygienic measures.

Exit-site dressings

It is recommended to cover the insertion site [24], instruct the patient to respect strict hygiene and preserve the integrity and dryness of the dressing, to inspect the exit site at every haemodialysis session and replace the dressing if it is no more clean or intact.

Antibiotic ointments

The use of antibiotic ointment at the insertion site has a beneficial effect on CRBSI and exit-site infections [25–27]. Their application is especially recommended after catheter placement until the insertion site has healed [24]. Mupirocin, the most intensively studied agent, might be complicated by the development of resistance [28]. Another option is polysporin triple ointment, containing bacitracin, gramicidin and polymyxin B [29]. Prolonging antibiotic ointment application after site healing probably offers no advantage and has the potential to increase the risk of resistance [26] and *Candida* colonization [30].

According to ERBP, there is not enough evidence to propagate nasal antibiotic ointment in the haemodialysis setting.

Overall aspects

Diagnosis: cultures of intravenous catheter

Preferred laboratory approaches for catheter culture are the semi-quantitative roll-plate technique of 5 cm of the catheter tip or the quantitative broth culture. Although the IDSA guidelines explicitly recommend the culturing of catheter tips upon removal, the ERBP raises questions about the relevance of this labour-intensive and costly approach in view of the low yield [31].

Diagnosis: blood cultures

A diagnostic test proposed in the IDSA monography without requiring catheter withdrawal is simultaneous sampling from peripheral vein and catheter or from two different catheter lumens into appropriately marked bottles [32].

The ERBP, however, considers that, in many haemodialysis patients, an accessible peripheral vein will be unavailable, or that it will be preferred to preserve accessible veins for future access creation. Since many of the fever episodes necessitating blood culture sampling occur during dialysis, with high blood flows through the catheter, it is likely that blood cultures collected at that moment through the haemodialysis circuit will offer similar results as peripheral blood, so that peripheral sampling can be omitted [33].

Diagnosis: registration

To guide empiric antibiotic therapy, it is considered of utmost importance that each centre maintain a database of all suspected and proven CRBSI and episodes of bacteraemia in general, the causative organisms, their sensitivity pattern to antibiotics, the potential source (catheter related, pneumonia, urinary tract, etc.) and the outcomes after therapeutic intervention.

Unique aspects

Management of catheter infection in patients receiving haemodialysis

Catheter removal and preservation of existing and future access option. In Figure 1 of the publication in *NDT Plus*, a comprehensive flowchart of all options is given in a stepwise fashion [2].

Removal of the catheter should be considered as an additional intervention to systemic antibiotic treatment in severe complications (e.g. severe sepsis, suppurative thrombophlebitis, metastatic infection); persistent blood stream infection or persistent clinical signs of infection in spite of 48–72 h of appropriate antimicrobial therapy; infection with *Staphylococcus aureus*, *Pseudomonas aeruginosa*, multi-resistant organisms or fungi; tunnel infection with fever. For exit-site infection without fever, topical antibiotic application might be attempted first, but if infec-

tion does not resolve, here also systemic antibiotic treatment should be installed. If also systemic antibiotics fail, again catheter removal should be considered.

ERBP recommends the insertion of a new tunnelled catheter, preferably after the patient remains afebrile for 48–72 h and shows a normalization of C-reactive protein (CRP) and negative blood cultures. If the interval needs to be prolonged for >48–72 h, a haemodialysis catheter can be inserted during this interval at another site. A strategy of placement per single dialysis session and removal immediately afterwards might be considered as an option to minimize the risk of colonization. However, the risks of repetitive puncturing should be balanced against those of potential infection.

One of the most important additions in this section was the extension of interventional options beyond catheter removal and reinsertion after a >48-h interval, in view of the limited access possibilities in many patients on haemodialysis. Therefore, if any problems are anticipated, an alternative strategy is to exchange the catheter over a guidewire. The optimal time for guidewire-assisted replacement is after 48–72 h of appropriate and effective antibiotic treatment. However, guidewire-assisted replacement increases the risk of venous wall sclerosis and stenosis, and is associated with a high failure rate.

An even more conservative alternative is offered, leaving the catheter in place and attempting catheter salvage instilling an antibiotic lock (see below) in addition to systemic antibiotic therapy [34,35]. Both in the case of guidewire-assisted replacement and catheter salvage, close follow-up by assessment of clinical status and repetitive blood cultures is imperative, and if persistent clinical signs of infection and bacteraemia are found after 48–72 h, the catheter should still be removed.

Surveillance blood cultures should be obtained 1 week after completion of antibiotic treatment if the catheter has not been removed. If these cultures are positive, the catheter should still be removed.

Antibiotic and antimycotic treatment. In Figure 2 of the publication in *NDT Plus*, also in this respect, a comprehensive flowchart of all options is given [2].

In all circumstances, a systemic antibiotic therapy should be administered.

According to ERBP, empiric coverage for dialysis catheter infections should be inspired by the recorded infections in the unit (see above). If the registry indicates that current catheter infections are regularly caused by both Gram positives and Gram negatives, coverage for both classes should be provided, with eventual refinement of the regime once the responsible organism has been isolated and sensitivities are known. In settings where methicillin-resistant *S. aureus* (MRSA) is highly prevalent, vancomycin or teicoplanin are the first choices for empirical treatment of Gram-positive germs. In patients on empirical vancomycin or teicoplanin in whom an infection with methicillin-sensitive *S. aureus* appears, a switch to cefazolin is recommended. Continued treatment with vancomycin in the case of methicillin sensitivity substantially increases the risk of treatment failure [36].

Preferred antibiotics are those with a pharmacokinetic profile allowing administration after each dialysis session only (e.g. vancomycin, teicoplanin, cefazolin, ceftazidime and daptomycin). Although the same is correct for aminoglycosides, it might be impossible to reach appropriate trough levels with simple post-dialysis administration, enhancing the risk of complications. Nevertheless, in view of their rapid bactericidal effect, a single shot might be considered, or if no alternative is available, even a longer therapeutic course. For candidaemia, echocandin should preferably be used, with fluconazole only for selected cases (e.g. if risk of *Cancida krusei* or *Candida glabrata* is low) [37].

Usual length of treatment for uncomplicated cases is 3 weeks. For tunnel infection without bacteraemia or fungaemia, and if the catheter has been removed, 7–10 days are sufficient. A 6-week course is recommended if fungaemia or bacteraemia persists 48–72 h after catheter removal or in the case of endocarditis or intravascular infection. For osteomyelitis, even an 8-week treatment is advised.

For uncomplicated infections with other organisms than those mentioned above, antibiotic treatment without catheter removal should be attempted first (both systemic and lock). With a single blood culture positive for coagulase-negative *staphylococci*, a careful clinical evaluation and additional positive cultures should be obtained before therapy and/or catheter removal [38].

For antibiotics with substantial removal via kidneys and/or dialyser, renal function and dialysis adequacy should be taken into account when defining the dose and frequency of administration [39].

Antibiotic locks

If catheter removal is deemed unnecessary, undesirable or impossible, antibiotic lock is an important therapeutic option, but only if used in conjunction with systemic antibiotics (catheter salvage). For haemodialysis, lock renewal after every dialysis session is considered sufficient. In Table 2 of the publication in *NDT Plus* [2], suggested concentrations are provided.

The success rate of salvage in case of *S. aureus* is low (~40%) [40], and therefore should be considered only in problematic cases.

Antibiotic locks can be dissolved in different vehicles. Some of these might have extra antimicrobial or biofilm-removing properties (see above). Urokinase and other thrombolytic locks are not recommended as an adjunctive therapy for patients with CRBSI.

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