Research Article

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Hemodialysis Catheter-Related Sepsis

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Abstract

Introduction: *Hemodialysis (HD) patients are exposed to various complications. Infectious complications are the second leading cause of morbidity and mortality after cardiovascular complications. The aim of our study is to describe the clinical, paraclinical and bacteriological aspects of the HD catheter-related infection.*

Patients and methods: *We carried out a retrospective study over a period of one year, involving 25 HDs patients hospitalized in the Department of Infectious Diseases, Cardiology and Nephrology of Ibn Rochd University Hospital Center in Casablanca.*

Results: *The majority of these patients were male (72%) with an average age of 59 years. Twenty patients had a jugular catheter. Fever was the main symptom found in all patients, associated with sepsis signs in 88% of cases, while 12% of patients were classified as a septic shock. All patients had a biological infectious syndrome with leukocytosis and positive CRP. Peripheral and catheter-based blood cultures, and culture of the distal tip of the catheter were performed in all patients., allowing the determination of the causative germ in 72% of the cases. The most frequently isolated germs were Staphylococcus aureus (66.7%), Gram-negative bacilli (16.7%), coagulase-negative staphylococci (11.1%), and Candida sp (5.5%). All patients received a probabilistic antibiotherapy based on vancomycin and amikacin combination adapted to the renal function andthe antibiogram results thereafter. Six patients had associated endocarditis. The evolution was favourable in 76% of the patients. Six patients died. The main cause of death is the septic shock (3 cases).*

Conclusion: *Vascular access in HD deserves special attention. The prevention of infectious complications in this category is based on compliance with hygiene rules and the temporary use of catheters and then the creation of native arteriovenous fistula.*

Introduction

In patients with chronic hemodialysis (HD), permanent vascular access, in the type of an arteriovenous fistula (AVF), is the preferred method for performing HD sessions. When intravenous catheters are used, morbidity and mortality increased. In our context, all patients with CKD initiate chronic HD from a catheter as the first vascular access, either because the fistula is still immature or non-functional. But for long-term use, the European (EBPG) and American (KDOQI) guidelines recommend the central venous catheter as a second-line vascular access, with a prevalence not exceeding 10% per service [1,2]. In practice, the aging of the dialysed population, the associated pathologies with chronic renal failure, and sometimes late management are all reasons for the increased use of the catheter. The direct consequence of the increase in the use of catheters compared with other accesses is an increase in the relative risk of death [3]. The catheter is functional with no prior maturation time, and is applicable to the majority of patients, whereas associated pathologies with CKD often make it difficult to create AVF. In the long term, however, its use is associated with a higher incidence of infectious complications. Catheter-related septicemia is associated with significant morbidity, hospitalization and mortality. The most common causative pathogens are Gram-positive cocci accounting for 77.8% of the germs isolated. The objective of this work was to study the clinical, biological, particularly bacteriological and evolutionary characteristics of HD catheter-related septicemia through a retrospective study.

Methods

All hospitalized patients in various departments (Cardiology, Nephrology and Infectious Diseases) of the Ibn Rochd University Hospital Center in Casablanca were included retrospectively for HD catheter-related infection between 1 January 2016 and 31 December 2016. These patients are monitored for chronic hemodialysis in different hemodialysis centers in Casablanca. The data were collected from the medical records of hospitalization on case report form.

Results

1.Epidemiological Features

Twenty-five patients were included in this study, hospitalized in the Department of Infectious Diseases, Nephrology and Cardiology. Patients receive their HD sessions in different hemodialysis centers in Casablanca. The mean age of the patients was 59 years, with extremes from48 years to 82 years. The male sex was predominant with a sex ratio of 2.5. Twenty patients had a jugular catheter over 72 days on average.

2. Clinical Features

All patients were admitted because of chronic fever, 88% had sepsis signs, while 12% were in septic shock with hemodynamic disorders. The clinical symptomatology was associated with digestive signs in 40%, marked by fluid diarrhea and vomiting, respiratory symptoms in 36% of cases, neurological symptoms in 24% of cases, and 16 % of patients had associated urinary dysuria. The mean time between onset of symptoms and consultation was 10 days [3-60]. Eighty per cent of patients had a jugular catheter and 20% had a femoral catheter for more than 72 days, 40% of whom had signs of local infection. The clinical data are reported in Table 1.

Table 1: Clinical features associated with catheter-related infections

Clinical symptoms	N (%)
General signs	
Fever	n= 25 (100%)
Sepsis	n= 22 (88%)
Septic shock (hemodynamic instability)	n= 3 (12%)
Digestive signs	n= 10 (40%)
Fluid diarrhea	n= 6 (24%)
Vomiting	n= 5 (20%)
Pulmonary signs	n= 9 (36%)
Cough	n= 8 (32%)
Purulent sputum	n= 3 (12%)
Neurological disorder	n= 6 (24%)
Consciousness	n= 6 (24%)
Agitation	n=2 (8%)
Convulsion	n=1 (4%)
Urinary signs	n= 4 (16%)
Dysuria	n=4 (16%)
Burning urination	n=4 (16%)
Local infection signs	n= 10 (40%)

3. Paraclinical Features:

All patients benefited a blood count, showing inflammatory anemia in 92%, moderate to major hyperleukocytosis in 80% and 20% respectively, while 12% of the patients had thrombocytopenia. Protein-C-Reactive (CRP) was performed in all patients, positive in 100% of cases with an average of 214.9 mg /l, while procalcitonin was only done in 56% with an average titre to 5.83ng/l.

Bacteriological exploration was carried out by the peripheral blood cultures and from the catheter, before its removal and its culturing, carried out systematically in all the patients, thus allowing the identification of the causative germ in 72% of the cases. Staphylococcus was the most prominent germ of HD catheter infection in our series, isolated in 78% of the positive samples. The distribution of the isolated germs is shown in FIG.1

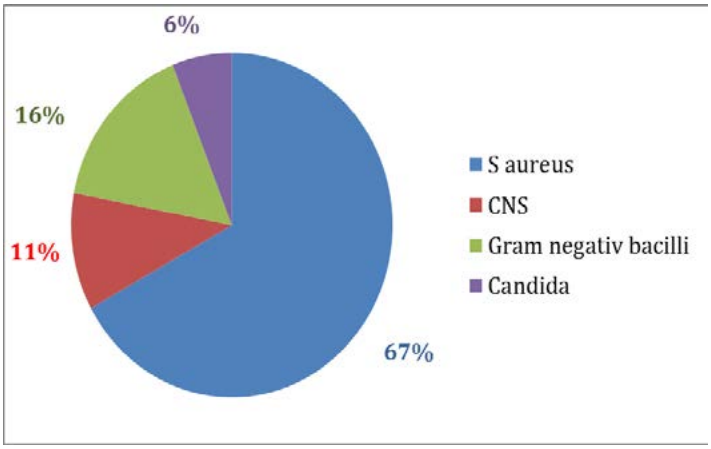

Figure1: Causatives germs during hemodialysis catheter-related infections
Note: CNS: Coagulase-negative staphylococci

4. Treatment

All patients received an initial antibiotherapy based on vancomycin and amikacin combination. The doses were adapted to the renal function and were given according to the HD sessions and adapted by following the bacteriological data. Six patients had an endocarditis (24%), with meningitis in 1 patient (4%).

5. Evolution

The evolution was favourable in 19 patients, 76% of the cases. Death occurred in 24% of patients, the main cause of which was septic shock (50%), followed by cardiac arrhythmias (33%) and heart failure (17%).

Discussion

Infections are common complications among patients on chronic hemodialysis. Hemodialysis patients with a catheter have a 2 to 3 fold increased risk of hospitalization for infection and death compared with patients with an arteriovenous fistula or graft [4]. Catheter-related bloodstream infections (CRBSIs), exit-site infections, and tunnel infections are common complications related to hemodialysis central venous catheter use. Catheter-related bloodstream infections alone have a reported incidence of 1.1 to 5.5 episodes per 1000 catheter days and are associated with increased morbidity, hospitalization, and death [5-6].

The two main pathway of colonization of catheters are the endoluminal route by contiguity from the first fitting to the vein, it mainly concerns catheters of short duration (<10 days), and the extraluminal route from the skin and moving along the outside of the catheter to the vein, it is secondary to septic manipulations and instead concerns long-term catheters (>10 days) in particular hemodialysis catheters [7].

Several definitions for catheter-related infections are cited in the literature; however, consensus is not attained [8]. These commonly used and accepted clinical definitions of catheter-related infections in the literature are detailed in Table 2. Kidney Disease Outcomes Quality Initiative (KDOQI), Centers for Disease Control and

Prevention (CDC), Infectious Diseases Society of America (IDSA), and Public Health Agency of Canada [9-12].

Table 2: CRBSI clinical Definitions [8].

KDOQI	CDC	IDSA	Public Health Agency
Definite:same organism from a semiquantative culture of the catheter tip (>15 CFU/catheter segment) and from a BC in a symptomatic patient with no other apparent source of infection. **Probable:**Defervescence of symptoms after antibiotic therapy with or without removal of the catheter, in the setting in which BC confirms infection, but catheter tip does not (or catheter tip does, but blood does not) in a symptomatic patient with no other apparent source of infection. **Possible:** Defervescence of symptoms after antibiotic treatment or after removal of catheter in the absence of laboratory confirmation of BSI in a symptomic patient with no other apparent source of infection.	Clinical manifestations and at least 1 positive BC from a peripheral vein and no other apparent source, with either positive semiquantitative (>15 DFU/ catheter segment) culture, whereby the same organism (species and antibiogram) is isolated from the catheter segment and a peripheral blood sample; Simultaneous quantitative cultures of blood samples with a ratio of >3:1 (catheter vs peripheral); Differential period of catheter culture versus peripheral BC positivity of 2h; **OR** Isolation of the same organism from semi quantitative culture segment and from blood (preferably from a peripheral vein) of a patient with accompanying symptoms of BSI and no other apparent source of infection.	Bacteremia/fungemia in a patient with an intravascular catheter with at least 1 positive BC and with clinical manifestations of infections (ie, fever, chills, and/ or hypotension) and no apparent source for the BSI except the catheter **AND** One of the following should be present: A positive semiquantitative (>15 CFU/catheter segment or quantitative (>103 CFU/catheter segment) culture whereby the same organism (species and antibiogram) is isolated from the catheter segment and peripheral blood. Simultaneous quantitative BC with a >5:1 ratio catheter versus peripheral. Differential time period of caheter culture versus peripheral Bc positivity of >2h.	**Definite:** single positive BC and positive culture result of catheter segment with identical organisme or >10-fold colony count difference in BC draw from device and peripheral blood. **OR** Single positive BC and positive culture from discharge from exit site or tunnel with identical organism. Probable: >2 positive BC results with no evidence for source other than the device or single positive BC for S aureus or Candida species with no evidence for source other than the device **OR** Single positive BC for coagulase-negative staphylococci, bacillus, corynebacterium jeikeium, Enterococcus, Trichophyton, or Malassezia species in immunocompromised or neutropenic host or patient receiving total parenteral nutrition with no evidence for source other than a centrally place device. Possible: single positive BC result with no evidence for source except a centrally placed device, and patient or organism does not fit criteria for probable infection.

Note: CRBSI = catheter-related bloodstream infection; KDOQI = Kidney Disease Outcomes Quality Initiative; CDC = Centers for Disease Control and Prevention; IDSA = Infectious Diseases Society of America; CFU = colony-forming unit; BC = blood culture; S aureus = Staphylococcus aureus; BSI = bloodstream infection.

Fever or chills are the most sensitive clinical features, associated with positive blood cultures in 60% to 80% of patients. Only 5% of patients with CRBSIs will have a concurrent exit-site or tunnel infection.9 Other clinical manifestations of CRBSIs include hemodynamic instability, altered mental status, catheter dysfunction, hypothermia, nausea/vomiting, and generalized malaise. In some cases, complications related to a CRBSI may be the first clues to the presence of a CRBSI [13,14].

Treatment of Catheter-Related Infection

Exite-site infection:

Obtain cultures of any drainage from the exit site before administration of antibiotics. Treat empirically with antibiotics to cover Gram-positive organisms. Modify the antibiotic regimen once culture and sensitivity results are available. Exit-site infections are typically treated for 7 to 14 days, depending on the microorganism isolated and local practice [8].

Tunnel Infection

Obtain cultures of any drainage from the exit site and send blood cultures from the catheter. The catheter should always be removed, without exchange over a wire. A new catheter should be inserted at a separate site. Start empiric broad- spectrum antibiotics to cover both gram-positive and gram- negative organisms. Modify antibiotic regimen when culture and sensitivity results are available. Tunnel infections, in the absence of a concurrent CRBSI, are typically treated for 10 to 14 days, depending on the microorganism isolated and local practice. If a CRBSI is also present, then duration of therapy will be determined by the management of the CRBSI [8].

Catheter-Related Bloodstream Infection

Empiric management: Blood cultures should be sent from the catheter, dialysis circuit, and peripheral sites if possible. A recent prospective study of 178 suspected CRBSIs in hemodialysis patients showed that blood culture results are the most sensitive, specific, and accurate for diagnosis when taken from the hemodialysis circuit and the venous catheter hub, compared with any combination with peripheral vein cultures [16]. Broad-spectrum antibiotics should be initiated to cover both gram-positive and gram-negative organisms [17]. Antibiotics should generally cover methicillin-resistant S aureus (MRSA) and Pseudomonas

but are also dictated by local infection rates, dialysis center policies, and center-specific antimicrobial resistance patterns. Following initiation of empiric antibiotic therapy, it is crucial that culture sensitivity data are followed up in a timely manner, so that the most appropriate antibiotics based on sensitivity results can be used.

Definitive management. Definitive management of CRBSIs must be tailored to the clinical presentation of the patient, the microorganism isolated, and vascular access options of the patient. For example, management of the patient with septic shock secondary to MRSA, CRBSI will differ from that of a hemodynamically stable patient presenting with a fever and found to have coagulase-negative staphylococcus. Treatment can be categorized into 3 groups: systemic antibiotics, anti- microbial locking (instillation) solutions, and catheter management. Comparison of treatment strategies is very challenging because many studies are observational design with different methodologies, and have differences in CRBSI definitions, as well as different outcome measures [8].

Systemic Antibiotics

- All patients with a CRBSI should receive systemic antibiotics, which will typically be administered for 2 to 6 weeks depending on the microorganism, clinical presentation, and complications.
- Final decision on specific antibiotic agent(s) is dependent on final blood culture result and sensitivities, and whether or not patient has any allergies. If methicillin- sensitive S aureus (MSSA) infection is isolated, cefazolin is the preferred choice over vancomycin because it is associated with decreased hospitalization and death secondary to infection [18].
- Ease of administration is also a factor, ideally choosing agents that can be given to patients 3 times weekly for patients receiving conventional thrice weekly dialysis.
- Drug dose and timing vary for those who are not on conventional thrice weekly dialysis (eg, short daily or nocturnal dialysis) [8].

Antibiotic locks

- May be used as adjunctive therapy to systemic antibiotics.
- There are no randomized trials on the role of antibiotic locks in the treatment of CRBSIs, but several observational studies have shown similar eradication of bacteremia in patients treated with systemic antibiotics plus antibiotic lock compared with systemic antibiotics and catheter exchange or removal [19].

A recent systematic review and meta-analysis of hemodialysis patients with tunneled dialysis catheters, with a CRBSI, compared 3 treatment protocols for CRBSIs: (1) systemic antibiotics alone, (2) systemic antibiotics plus antibiotic lock (catheter not removed), and (3) systemic antibiotics plus guidewire exchange [20]. It included 28 retrospective and prospective studies, with a total of 1596 patients. Patients treated with systemic antibiotics and antibiotic lock had similar cure rates to those treated with systemic antibiotics and guidewire exchange, and both were superior to the rates obtained when antibiotics were used alone. Recurrence of infection with the same organism was not different between the systemic antibiotics plus antibiotic lock group and the systemic antibiotics plus guidewire exchange but was much higher in patients treated with systemic antibiotics alone, which further supports the practice to use an antibiotic lock or guidewire exchange in conjunction with systemic antibiotics.
Antibiotic locks should be used when immediate catheter removal is not possible and when catheter salvage attempted.

Catheter Removal with Replacement in New Site

► One option is immediate catheter removal, followed by placement of a temporary catheter, then conversion back to tunneled catheter. Indications for immediate removal are the following:

- Severe sepsis
- Hemodynamic instability
- If fever or bacteremia persist 48 to 72 hours after initiation of antibiotics to which the organism is susceptible
- Metastatic infection
- Signs of tunnel infection
- Fungal organism

► Consider catheter removal for patients with CRBSIs due to S aureus, Pseudomonas species, and fungus.
► A temporary nontunneled catheter should be inserted into another anatomical site.
► In some cases, patients may not have any alternative site available for catheter insertion, and in these patients, catheter exchange over a wire or catheter salvage might be considered instead of catheter removal, regardless of microorganism isolated [8].

Infection complications

Infection complications are thought to occur in 15-40% of CRIBSIs. These are most common for S. aureus infections, with endocarditis being the most common. Other complications include vertebral osteomyelitis or discitis (2%-15%), and less commonly, spinal epidural abscess, septic arthritis, and septic pulmonary emboli. Mortality rates are high: Reports in the literature vary between 6% and 34% in all cases of CRBSI. Mortality is highest with S. aureus infection complicated by metastatic complications, associated with 30% to 50% of mortality in these patients. [15,21,22].
In our study, 6 patients presented endocarditis (24%), and the mortality rate was 24%.

Prevention of Catheter-Related Infections

There are several risk factors for the development of infection, including conditions of catheter insertion, site of catheter insertion, and duration of use (Table 4) [15,23,24]. The most effective strategy for prevention of CRBSIs is reducing the use of catheters. Other basic measures include improved catheter care, good hand hygiene practices, and education for both patients and staff on vascular access care. As catheter use cannot be eliminated, CDC has recommended several core interventions to decrease infections (Table 5). Several of these recommendations are incorporated in catheter care bundles, which have been shown to reduce catheter-related infections in patients with central venous catheters [25-26].

Table 4. Risk Factors for the occurrence of CRBSIs [15,23,24].

Submaximal barrier precautions at the time of catheter insertion
Nontunneled catheter
Site of insertion – femoral > internal jugular > subclavian
Prolonged duration of catheter use
Previous episode of CRBSI

Staphylococcus aureus nasal carriage	
Diabetes	
Recent surgery	
Hypoalbuminemia	
Recent surgery	

Note: CRBSI= catheter-related bloodstream infection

Table 5. Core interventions for Dialysis BSI Prevention.

Surveillance and feedback	Conduct monthly surveillance for BSIs and other dialysis event using CDC's NHSN. Calculate facility rates and compare with rates in other NHSN facilities. Actively share results with front-line clinical staff.
Hand hygiene observations	Perform observations of hand hygiene opportunities monthly. Share results with clinical staff.
Catheter/vascular access care observations	Perform observation of vascular access care and catheter accessing quarterly. Assess staff adherence to aseptic technique when connecting and disconnecting catheter and during dressing changes. Share results with clinical staff.
Staff education and competency	Train staff on infection control topics, including access care and aseptic technique. Perform competency evaluation for skills such as catheter care and accessing every 6 to 12 mo upon hire.
Patient education/ engagement	Provide standardized education to all patients on infection prevention topics including vascular access care, hand hygiene, risk related to catheter use, recognizing signs of infection, and instruction for access management when away from the dialysis unit.
Catheter reduction	Incorporate efforts (eg, through patient education, vascular access coordinator) to reduce catheters by identifying and addressing barriers to permanent vascular acces placement and catheter removal.
Chlorhexidine for skin antisepsis	Use an alcohol-based chlorhexidine (>0.5%) solution as the first-line skin antiseptic agent for central line insertion and during dressing changes.
Catheter hub disinfection	Scrub catheters hubs with an appropriate antiseptic after cap is removed and before accessing. Perform every time catheter is accessed or disconnected.
Antimicrobial ointment	Apply antibiotic ointment or povidone-iodine ointment to catheter exit sites during dressing changes.

Source. Adapted from CDC approach to BSI prevention in dialysis facilities [27].
Note. BSI = Bloodstream infection; CDC: centers for Disease Control and Prevention; NHSN: National Healthcare Safety Network.

Conclusion

CRBSIs are major cause of hospitalization and mortality in HD patients. Prevention is key! Including maximal barrier precautions with catheter insertion and catheter care, topical antibiotics, education, and surveillance. Gram-positive organisms are responsible for most CRBSIs, with S aureus and coagulase-negative staphylococci in 78% which are responsible for a high mortality rate, and most likely to cause metastatic complications. The treatment strategies for CRBSIs can be categorized into systemic antibiotics, antibiotics locks and catheter management.

The prevention on infectious complications in this category is based on compliance with hygiene rules and the temporary use of catheters and creation of native arteriovenous fistule.

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