Incidence and Challenges in Management of Blood Stream Infections in Hemodialysis

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Abstract: Bloodstream infections pose a significant threat to patients undergoing hemodialysis, leading to hospitalizations, increased morbidity, and mortality. The Centers for Disease Control and Prevention (CDC) has prioritized the prevention of bloodstream infections in hemodialysis through their Making Dialysis Safer initiative.Most bloodstream infections linked to vascular access primarily occur in patients undergoing dialysis using central vein catheters. The Centers for Disease Control and Prevention (CDC) advocates core interventions as the best practices for catheter care in hemodialysis, demonstrating their effectiveness in reducing catheter-associated bloodstream infections. However, bloodstream infections linked to hemodialysis catheters persist at undesirable levels, it is likely due to failures in maintaining rigorous aseptic techniques or other factors beyond the scope of the CDC's core interventions. There is a urgent need for innovation of preventive measures. This review focuses on the current therapies, recent developments and also addresses potential drawbacks and adverse effects associated with thealternatives. This review also highlights the challenges and future perspectives which might prove to be beneficial in reducing infection rates in hemodialysis patients.

1. INTRODUCTION

In terms of frequency, infection appears to be the most prevalent cause of death. Patients undergoing hemodialysis with a catheter have a higher risk of hospitalization due to infection or even death as compared to those with a permanent access likearteriovenous fistula or graft [1]. In chronic hemodialysis (HD) patients, infections related to catheters represent a significant contributor to both mortality & morbidity.[2]

More than 75% of deaths related to infections are attributed to septicemia. The arteriovenous fistula is the favored vascular access for hemodialysis (HD) due to its lower infection rates and improved delivery of effective dialysis. In contrast, cardiovascular catheters (CVC) exhibit lower patency rates, elevated infection rates, and increased incidents of hospitalization and mortality primarily attributed to catheter-related bloodstream infections. [3]

The primary factors for use of CVCs includes: Loss of permanent hemodialysis access (arteriovenous fistula or graft), Delay in initiation of dialysis, the need to await maturation of Arteriovenous Fistulas (AVFs) and because of limited options for access in patients with severe peripheral vascular syndrome.[5]

Management of patients with catheter-related infections (CRI) poses a significant challenge, as it involves frequent hospital visits and continuous engagement with multiple healthcare professionals.[6]Clinical practice guidelines outline specific approaches for managing both catheter-related bacteremia and bacteremia unrelated to catheters. Additionally, healthcare professionals should emphasize the importance of closely monitoring cases where attempts are made to salvage the dialysis catheter. [4]

This review focuses on the ongoing therapies and their short comings also new future perspectives in reducing the rates of blood stream infections in hemodialysis patients in order to increase their survival.

2. EPIDEMIOLOGY OF INFECTIONS AMONG HD PATIENTS

Several published studies examining bacterial infections in outpatient hemodialysis have reported a monthly occurrence of bacteremia ranging from 0.6% to 1.7% of patients, and vascular access infections (VAIs), including those with or without bacteremia, ranging from 1.3% to 7.2% of patients per month.[7] Recognizing the significance of bacterial infections among hemodialysis patients, the CDC launched a voluntary and continuous monitoring system in the United States known as the Dialysis Surveillance Network (DSN) in 1999.[8]The rates per 100 patient-months were 3.2 for all vascular access infections (comprising both access infections with and without bacteremia), 1.8 for bacteremia associated with vascular access, 1.3 for non-vascular access-related wound infections, 0.8 for pneumonia, and 0.3 for urinary tract infections. In individuals with fistulas or grafts, infections predominantly occurred at wound sites, while for those with hemodialysis catheters, infections were most commonly observed at the vascular access site.[8]

Infections at the access site are significant as they have the potential to lead to widespread bacteremia or compromise the integrity of the vascular access. Observable indicators of vascular access infections include redness, warmth, hardening, swelling, tenderness, skin breakdown, localized fluid accumulation, or the presence of pus.[7.8]

Various types of central venous catheters (CVC) employed for chronic hemodialysis include tunneled cuffed catheters and non-tunneled catheters. The likelihood of bacteremia occurrence depends on factors such as the insertion site of the CVC, the specific type of device used, and the duration of CVC utilization.[9]

3. PATHOGENESIS OF INFECTIONS IN HD PATIENTS

Infections caused by bacterial pathogens can originate either exogenous (through acquisition from contaminated dialysis fluids or equipment) or endogenous (resulting from the invasion of bacteria already present in or on the patient).Infections related to catheters typically occur when bacteria from the patient's skin colonize the external surface of the catheter or when there is direct contact, such as touch contamination by healthcare professional, with the catheter. This contact can result in the inner surface of the catheter becoming contaminated.[10]

The primary pathogens responsible for catheter-related blood stream infections (CRBSIs) are typically gram-positive bacteria, with Staphylococcus aureus and coagulase-negative staphylococci making up 40% to 80% of cases. Gram-negative organisms contribute to 20% to 40% of CRBSIs, while polymicrobial infections account for 10% to 20%, and fungal infections are less prevalent, constituting less than 5%. Complications arising from the spread of infection in catheter-related bloodstream infections (CRBSIs) include conditions such asseptic arthritis, septic pulmonary emboli, spinal epidural abscess, , endocarditis, brain abscess, and osteomyelitis.[11,12,13]

Factors that increase the risk of catheter-related bloodstream infections (CRBSIs) encompassprolonged catheter use, the insertion site prioritized as femoral > internal jugular >subclavian, diabetes, the use of non-tunneled catheters, recent surgery, a history of previous CRBSI, nasal carriage of Staphylococcus aureus, hypoalbuminemia, and suboptimal barrier precautions during catheter insertion.

4. EXISTING THERAPIES FOR TREATING CRBSIs

Diagnosis without removing the catheter involves utilizing paired quantitative blood cultures, wherein both sets reveal the presence of the same microorganism. The culture obtained through the catheter exhibits a colony count that is at least three times higher than that of the peripheral culture.[14] The catheter culture with a semi-quantitative assessment of equal to or greater than 15 colony-forming units (CFU) corresponds to the identification of the same microorganism in at least one percutaneous blood culture and the culture of the catheter tip.[15,16]

Catheter cultures should be conducted specifically when there is suspicion of catheter-related bloodstream infection (CRBSI) upon catheter removal. Routine catheter cultures are not recommended. In the case of Central Venous Catheters (CVCs), it is advisable to culture the catheter tip instead of the subcutaneous segment.[17,18] The diagnosis of exit-site infection is determined by the presence of hyperemia, induration, and/or tenderness within a 2 cm radius from the catheter exit site. This condition may be accompanied by fever and the discharge of purulent material from the exit site. Bacteremia may or may not be associated with this infection. In cases where purulent drainage is

observed, it should be collected and submitted for Gram staining and culture. Treatment duration typically ranges from 7 to 14 days, depending on the identified microorganism and local medical protocols.[19,20,21] Diagnosis of tunnel infection is established by the presence of tenderness, hyperemia, and/or induration that extends beyond 2 cm from the exit site, progressing along the subcutaneous tunnel. Bacteremia may or may not be linked to this infection. In instances of purulent drainage, it is advisable to collect and submit the discharge for Gram staining and culture.[22]It is recommended to always remove the catheter, avoiding exchange over a wire. A new catheter should be inserted at a different location. Initiate empiric broad-spectrum antibiotic treatment to address both gram-positive and gram-negative organisms.[16]

Adjust the antibiotic regimen based on the available culture and sensitivity results. Tunnel infections, when not accompanied by a concurrent catheter-related bloodstream infection (CRBSI), are usually managed for duration of 10 to 14 days, depending on the identified microorganism and local treatment protocols. If a CRBSI is also detected, the duration of therapy will be determined by the management approach for the CRBSI.[23] Empiric management for Catheter-Related Bloodstream Infection involves the initiation of broad-spectrum antibiotics to address both gram-positive and gram-negative organisms. Typically, antibiotics should provide coverage for methicillin-resistant S aureus (MRSA) and Pseudomonas. After initiating empiric antibiotic therapy, it is essential to promptly follow up with culture and sensitivity data to enable the use of the most suitable antibiotics based on sensitivity results.[16]

The definitive treatment of Catheter-Related Bloodstream Infections (CRBSIs) should be customized based on factors such as the patient's clinical presentation, the identified microorganism, and the available vascular access options. For instance, the approach to managing a patient in septic shock due to MRSA CRBSI will differ from that of a hemodynamically stable patient who presents with a fever and is diagnosed with coagulase-negative staphylococcus. Treatment can be classified into three main groups: systemic antibiotics, antimicrobial locking (instillation) solutions, and catheter management.[23] For individuals with Catheter-Related Bloodstream Infections (CRBSIs), systemic antibiotics are essential and are generally prescribed for a duration of 2 to 6 weeks. The specific period of treatment depends on factors such as the microorganism involved, clinical presentation, and any complications. The choice of the specific antibiotic agent(s) is determined by the conclusive results of blood culture, sensitivities, and consideration of the patient's allergies.[24,25,26] In cases where Methicillin-Sensitive S Aureus (MSSA) infection is identified, cefazolin is the preferred option over vancomycin due to its association with reduced hospitalization and lower mortality rates resulting from the infection.[17]

5. CHALLENGES & FUTURE PERSPECTIVES

Centers for Disease Control and Prevention[29], and the Healthcare Infection Control Practices Advisory Committee [30], and the National Kidney Foundation[31, 32]has developed certain guidelines and incorporated fundamental measures to avert bloodstream infections (BSI) in individuals undergoing hemodialysis.

These essential measures include:

(1) Monitoring bloodstream infections through NHSN and providing feedback to clinical personnel;

(2) Observing hand hygiene practices and offering feedback to staff; (

(3) Conducting assessments of catheter/vascular access care to ensure adherence to aseptic techniques and optimal infection control practices by clinical staff (with subsequent feedback);

(4) Enhancing the infection prevention skills of staff, as demonstrated through competency assessments;

(5) Educating patients and involving them in infection control procedures;

(6) Reducing the prevalence of catheters;

(7) Disinfecting catheter hubs; and

(8) Applying bacitracin zinc/polymyxin B sulfate (Polysporin) triple ointment or povidone-iodine ointment to catheter exit sites.

Centers for Disease Control and Prevention (CDC)’s core intervention guidelines can be broadly classified into 4 categories:-

I. Patient Education

- Providing guidance on the proper care of catheters at home, including instructions on safely showering.
- Planning to decrease the use of catheters.
- Explore alternative options for kidney replacement therapy, such as peritoneal dialysis and kidney transplantation.
- Educate the patient regarding the potential hazards associated with prolonged use of a catheter.

II. Hemodialysis Staff

- Conduct regular observations of hand hygiene practices and communicate the findings with the hemodialysis staff on a monthly basis.
- Educate and assess the competency of staff every six months.
- Conduct surveillance for bloodstream infections and provide feedback utilizing National Healthcare Safety Network (NHSN) dialysis surveillance.
- Conduct assessments of staff performing catheter exit site care and connection or disconnection procedures, evaluating adherence to aseptic technique every six months.

III. Catheter Exit Site Care

- Applications of topical ointments, such as povidone iodine or Polysporin triple antibiotic ointment, during dressing changes.
- Novel therapy: Weekly replacement of dressings infused with chlorhexidine.
- Antiseptic for the skin during dressing changes: Utilize alcohol-based chlorhexidine (>0.5%), povidone-iodine 10%, or 70% alcohol.

IV. Catheter Lumen & Hub Care

- Limited utilization of antibiotic locks as a preventive measure in patients with a history of catheter use and recurrent bloodstream infections despite adhering to aseptic techniques.
- Novel therapy: antimicrobial barrier cap with chlorhexidine rod or non-antibiotic lock
- Catheter Hub Cleaning/ disinfection- scrub the hub, Utilize alcohol-based chlorhexidine (>0.5%), povidone-iodine 10%, or 70% alcohol (Everytime catheter is connected or disconnected)

Further suggestions to prevent infections associated with hemodialysis catheters involve (1) employing a sterile technique and implementing maximal sterile barrier precautions (including a cap, mask, sterile gown, large sterile drapes, and gloves) during catheter insertion; (2) confining the use of non-cuffed catheters to a duration of 3 to 4 weeks; (3) limiting catheter manipulation and dressing changes to trained personnel; and (4) replacing the dressing at the catheter site if it becomes damp, loosened, or soiled.

6. CONCLUSION

Infection continues to be a devastating complication among patients on hemodialysis. Additional interventions are needed to further reduce the rates of blood stream infections.The most effective approach to minimize episodes of bloodstream infections is to avoid the use of catheters. Strategies like promptly referring patients to nephrologists, involving multidisciplinary teams and vascular access coordinators for patient education, implementing early-cannulationarteriovenous grafts for hemodialysis, and initiating peritoneal dialysis urgently have demonstrated effectiveness in reducing catheter utilization.

Yet, in cases where catheter use is inevitable, it is crucial to adopt a comprehensive strategy to prevent infections. Actively involving patients, educating staff on proper catheter care, and enhancing adherence to the core interventions recommended by the Centers for Disease Control and Prevention are essential components.

Ultimately, identifying obstacles to secure practices within the hemodialysis environment through the application of human factors systems engineering will undoubtedly be invaluable in diminishing infections in the future.

7. REFERENCES

[1] Dhingra RK, Young EW, Hulbert-Shearon TE, Leavey SF, Port FK. Type of vascular access and mortality in U.S. hemodialysis patients. Kidney Int. 2001 Oct;60(4):1443-51. doi: 10.1046/j.1523-1755.2001.00947.x. PMID: 11576358.

[2] Saran, R. et al. US renal data system 2016 annual data report: epidemiology of kidney disease in the United States. Am. J. Kidney Dis. 69(Suppl 1), 7–8 (2017).

[3] Vassalotti JA, Jennings WC, Beathard GA, Neumann M, Caponi S, Fox CH, Spergel LM; Fistula First Breakthrough Initiative Community Education Committee. Fistula fi rst breakthrough initiative: targeting catheter last in fi stula fi rst. Semin Dial. 2012 May;25(3):303-10. doi: 10.1111/j.1525-139X.2012.01069.x. Epub 2012 Apr 4. PMID: 22487024.

[4] Mermel LA, Allon M, Bouza E, Craven DE, Flynn P, O'Grady NP, et al. Clinical practice guidelines for the diagnosis and management of intravascular catheter-related infection: 2009 update by the Infectious Diseases Society of America. Clin Infect Dis. 2009;49:1–45.

[5] Allon M, Work J. Venous Catheter Access for Hemodialysis. In: Daugirdas JT, Blake PG, Ing TS, editors. Hand book of Dialysis. Philadelphia: Lippincott Williams. 2007; 87-104.

[6] Collins, A. J. et al. United States renal data system 2005 annual data report abstract. Am. J. Kidney Dis. 47, 5–6 (2006).

[7] Nguyen, D.B., Arduino, M.J. and Patel, P.R. (2019). Hemodialysis-Associated Infections. Chronic Kidney Disease, Dialysis, and Transplantation, pp.389-410.e8. doi:https://doi.org/10.1016/b978-0-323-52978-5.00025-2.

[8] Tokars JI, Miller ER, Stein G. New national surveillance system for hemodialysis-associated infections: initial results. Am J Infect Control. 2002;30(5):288–295.

[9] Manuti JK, Saadoon AM, Jawad TS, Alawn AG. Evaluation of catheter related bacteremia in patients with end stage renal disease on hemodialysis. J CliniNephrol. 2023; 7: 032-041.

[10] Nguyen DB, et al. National healthcare safety network (NHSN) dialysis event surveillance report for 2014. Clin J Am SocNephrol. 2017;12(7):1139–1146.

[11] Lata C, Girard L, Parkins M, James MT. Catheter-related bloodstream infection in end-stage kidney disease: a Canadian narrative review. Can J Kidney Health Dis. 2016 May 5;3:24. doi: 10.1186/s40697-016- 0115-8. PMID: 27152201; PMCID: PMC4857243.

[12] Lok CE, Mokrzycki MH. Prevention and management of catheterrelated infection in hemodialysis patients. Kidney Int. 2011 Mar;79(6):587-598. doi: 10.1038/ki.2010.471. Epub 2010 Dec 22. PMID: 21178979.

[13] Jaber BL. Bacterial infections in hemodialysis patients: pathogenesis and prevention. Kidney Int. 2005 Jun;67(6):2508-19. doi: 10.1111/j.1523-1755.2005.00364.x. PMID: 15882306.

[14] Vascular Access Work Group. Clinical practice guidelines for vascular access. Am J Kidney Dis. 2006 Jul;48Suppl 1:S248-73. doi: 10.1053/j. ajkd.2006.04.040. PMID: 16813991.

[15] O'Grady NP, Alexander M, Burns LA, Dellinger EP, Garland J, Heard SO, Lipsett PA, Masur H, Mermel LA, Pearson ML, Raad II, Randolph AG, Rupp ME, Saint S; Healthcare Infection Control Practices Advisory Committee (HICPAC). Guidelines for the prevention of intravascular catheter-related infections. Clin Infect Dis. 2011 May;52(9):e162-93. doi: 10.1093/cid/cir257. Epub 2011 Apr 1. PMID: 21460264; PMCID: PMC3106269.

[16] Mermel LA, Allon M, Bouza E, Craven DE, Flynn P, O'Grady NP, Raad II, Rijnders BJ, Sherertz RJ, Warren DK. Clinical practice guidelines for the diagnosis and management of intravascular catheter-related infection: 2009 Update by the Infectious Diseases Society of America. Clin Infect Dis. 2009 Jul 1;49(1):1-45. doi: 10.1086/599376. Erratumin: Clin Infect Dis. 2010 Apr 1;50(7):1079. Dosage error in article text. Erratum in: Clin Infect Dis. 2010 Feb 1;50(3):457. PMID: 19489710; PMCID: PMC4039170.

[17] Chan KE, Warren HS, Thadhani RI, Steele DJ, Hymes JL, Maddux FW, Hakim RM. Prevalence and outcomes of antimicrobial treatment for Staphylococcus aureusbacteremia in outpatients with ESRD. J Am SocNephrol. 2012 Sep;23(9):1551-9. doi: 10.1681/ASN.2012010050. Epub 2012 Aug 16. PMID: 22904350; PMCID: PMC3431413.

[18] Capdevila JA, Segarra A, Planes AM, Ramírez-Arellano M, Pahissa A, Piera L, Martínez-Vázquez JM. Successful treatment of haemodialysis catheter-related sepsis without catheter removal. Nephrol Dial Transplant. 1993;8(3):231-4. PMID: 8385290.

[19] Aslam S, Vaida F, Ritter M, Mehta RL. Systematic review and meta-analysis on management of hemodialysis catheter-related bacteremia. J Am SocNephrol. 2014 Dec;25(12):2927-41. doi: 10.1681/ASN.2013091009. Epub 2014 May 22. PMID: 24854263; PMCID: PMC4243345.

[20] Mermel LA, Allon M, Bouza E, Craven DE, Flynn P, O'Grady NP, Raad II, Rijnders BJ, Sherertz RJ, Warren DK. Clinical practice guidelines for the diagnosis and management of intravascular catheter-related infection: 2009 Update by the Infectious Diseases Society of America. Clin Infect Dis. 2009 Jul 1;49(1):1-45. doi: 10.1086/599376. Erratum in: Clin Infect Dis. 2010 Apr 1;50(7):1079. Dosage error in article text. Erratum in: Clin Infect Dis. 2010 Feb 1;50(3):457. PMID: 19489710; PMCID: PMC4039170.

[21] Blot SI, Depuydt P, Annemans L, Benoit D, Hoste E, De Waele JJ, Decruyenaere J, Vogelaers D, Colardyn F, Vandewoude KH. Clinical and economic outcomes in critically ill patients with nosocomial catheter-related bloodstream infections. Clin Infect Dis. 2005 Dec 1;41(11):1591-8. doi: 10.1086/497833. Epub 2005 Oct 25. PMID: 16267731.

[22] Raad II, Hanna HA, Darouiche RO. Diagnosis of catheter-related bloodstream infections: is it necessary to culture the subcutaneous catheter segment? Eur J ClinMicrobiol Infect Dis. 2001 Aug;20(8):566- 8. doi: 10.1007/s100960100562. PMID: 11681436.

[23] Lisa MM, Edward C, Christine D, Swapnil H, Joanne K, Mercedeh K, Charmaine L, Rick L, Louise M, Matthew O, Jennifer M. Canadian Journal of Kidney Health and Disease. sagepub.com/journals. Permissions.nav. 2016; 3:1–11. DOI: 10.1177/205435811666912

[24] Safdar N, Fine JP, Maki DG. Meta-analysis: methods for diagnosing intravascular device-related bloodstream infection. Ann Intern Med. 2005 Mar 15;142(6):451-66. doi: 10.7326/0003-4819-142- 6-200503150-00011. Erratum in: Ann Intern Med. 2005 May 3;142(9):803. PMID: 15767623.

[25] Raad I, Hanna HA, Alakech B, Chatzinikolaou I, Johnson MM, Tarrand J. Diff erential time to positivity: a useful method for diagnosing catheter-related bloodstream infections. Ann Intern Med. 2004 Jan 6;140(1):18-25. doi: 10.7326/0003-4819-140-1-200401060-00007. PMID: 14706968.

[26] Moise PA, Sakoulas G, Forrest A, Schentag JJ. Vancomycin in vitro bactericidal activity and its relationship to efficacy in clearance of methicillin-resistant Staphylococcus aureusbacteremia. Antimicrob Agents Chemother. 2007 Jul;51(7):2582-6. doi: 10.1128/AAC.00939- 06. Epub 2007 Apr 23. PMID: 17452488; PMCID: PMC1913284.

[27] Lorente L, Jiménez A, Santana M, Iribarren JL, Jiménez JJ, Martín MM, Mora ML. Microorganisms responsible for intravascular catheter-related bloodstream infection according to the catheter site. Crit Care Med. 2007 Oct;35(10):2424-7. doi: 10.1097/01. CCM.0000284589.63641.B8. PMID: 17717493.

[28] Reboli AC, Rotstein C, Pappas PG, Chapman SW, Kett DH, Kumar D, Betts R, Wible M, Goldstein BP, Schranz J, Krause DS, Walsh TJ; Anidulafungin Study Group. Anidulafungin versus fluconazole for invasive candidiasis. N Engl J Med. 2007 Jun 14;356(24):2472-82. doi: 10.1056/NEJMoa066906. PMID: 17568028.

[29] Centers for Disease Control and Prevention. Guidelines for the prevention of intravascular catheter-related infections. MMWR Morb Mortal Wkly Rep. 2002;51(RR10):1–29.

[30] O'Grady NP, et al. Guidelines for the prevention of intravascular catheter-related infections. Clin Infect Dis. 2011;52(9): e162–93.

[31] NKF. Clinical practice guidelines for vascular access. Am J Kidney Dis. 2006;48(suppl 1):S176–S247.

[32] NKF. Clinical practice recommendation 8: vascular access in pediatric patients. Am J Kidney Dis. 2006;48(suppl 1):S274– S276.

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