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Case Report

Salvage of Hemodialysis Catheter in Staphylococcal Bacteremia: Case Series, Revisiting the Literature, and the Role of the Pharmacist

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Keywords

Hemodialysis · Staphylococcal bacteremia · Lock solutions · Catheter salvage · Role of the pharmacist

Abstract

Catheter-related blood stream infections comprise a major concern in hemodialysis patients, leading to increased mortality, morbidity, and cost of treatment. Prompt appropriate systemic antibiotics treatment, which includes administration of appropriate systemic antibiotics and, frequently, catheter removal and replacement, is warranted. However, in hemodialysis patients, repeated catheter insertions may cause central vein stenosis and thrombosis which limits the future availability of hemodialysis access. Lock solutions containing antibiotics and anticoagulants, instilled directly into the catheter lumen after each dialysis, have been successfully utilized for catheter salvage but higher rates of recurrence and complications were observed in

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infections resulting from staphylococcal species. We report several cases of catheter salvage using antibiotic lock solution in staphylococcal bacteremia with the purpose of stimulating the interest in randomized clinical trials. Evaluating the risk and benefits of catheter salvage in this patient subset in light of optimized systemic antibiotic dosing, improved lock solution use, and multidisciplinary involvement, balanced with the critical need to prevent unnecessary vascular trauma, is of great importance.

Introduction

Ample evidence indicates the gravity and substantial impact of catheter-related blood stream infections (CRBSI) on morbidity, mortality, and the cost of health care. Insertion of long-term central venous catheters (CVC) is essential for the care of patients receiving chemotherapy and hemodialysis [1]. Reportedly, 5 million CVCs are inserted annually in the US associated with an incidence of 400,000 related blood stream infections (BSI) [2]. The National Nosocomial Infections Surveillance (NNIS) revealed the incidence is up to 5.2 BSI per 1,000 catheter days [3].

Although arteriovenous graft and arteriovenous fistula (AVF) provide more favorable dialysis access in most hemodialysis patients, CVCs are still used in 40% of these patients for various reasons, such as waiting for vascular surgery, maturation of fistula, lack of operable vascular anatomy, patient preference, or short life expectancy [4, 5]. Preserving venous access patency is crucial for those patients particularly in cases with limited remaining access sites. The drawback of traditional care for BSI in hemodialysis patients involving removal and replacement of CVC is the possibility of venous stenosis and thrombosis, which jeopardizes the availability of future dialysis access [4, 5].

Establishing an AVF is dependent on the peripheral veins' patency, sufficient size, and elasticity to allow for dilation and maturation of the fistula post-surgical construction. In addition, the AVF function requires a patent venous circuit. The frequent venipuncture and the excessive use of peripheral intravenous lines and peripherally inserted CVC (PICC) can damage the veins, impair venous circulation, and endanger future AVF construction. Smaller caliber CVCs (such as PICC and triple-lumen catheters) can also be associated with thrombus formation over a short term [6–8]. In addition, PICC lines are associated with central vein stenosis, thrombosis, and scarring of the peripheral veins [9, 10]. Approximately 40% of patients with subclavian vein catheters and 20% with jugular vein catheters will develop central vein obstruction (venous stenosis or occlusion) secondary to previously inserted CVC. Irrespective of the location (subclavian or internal jugular), a larger number and longer duration of CVC use increases the risk of developing central vein stenosis. It was shown that it may take only between a few weeks to months following PICC insertion to render a vein useless for hemodialysis access [9, 10].

Anatomical sites that are conductive for creating arteriovenous graft or AVF are the cephalic and basilic veins in each arm) and these veins should be preserved [11]. As a result, many nephrology associations and agencies in North America have launched campaigns to save the veins of chronic kidney disease patients [12–14].

Multiple pathogens are implicated in CRBSI including coagulase-negative *Staphylococci*, *Staphylococcus aureus*, *Enterococci*, Gram-negative bacilli, *Pseudomonas aeruginosa*, and *Candida* species. Several studies indicated the difficulty of treatment of staphylococcal infections without catheter removal and this is the recommended treatment strategy by the Infectious Diseases Society of America (IDSA) [15].

We are reporting eradication of CRBSI caused by *Staphylococcus* species in a series of 8 hemodialysis patients using antibiotic lock solution in conjunction with intravenous antibiotics to avoid the removal of catheter access. We documented all staphylococcal-related bacteremia cases after the implementation of catheter-related antibiotic lock policy at our institution in the following 18 months. In addition, we revisited the literature evaluating the plausibility of this approach.

Case Series

All of the cases presented here involved staphylococcal infections including coagulase-negative as well as methicillin-sensitive and -resistant species conveniently reviewed between 2013 and 2014 at a dialysis center affiliated with a community hospital serving several cities in Southwestern Ontario, Canada. To attempt catheter salvage, antibiotic lock solutions were locally instilled in the catheter space concomitantly with the appropriate intravenous antibiotics administration for the same duration. Patients were prescribed lock solution when the treating physician judged catheter salvage to be critical. The selection of systemic antibiotic and the composition of antibiotic lock solution (Table 1) were based on the culture and sensitivity results reported by the hospital's microbiology department. The lock solutions were prepared by aseptically reconstituting commercially available products and admixing with the desired anticoagulant, if applicable, in a sterile syringe for instillation into the catheter space at the end of each dialysis session where it dwelled until the next dialysis session (i.e., 44–68 h).

Case 1

In a 47-year-old Caucasian male (weight 70 kg, height 177 cm), with a known history of hypertension, beta-lactam-documented allergy, and on hemodialysis for 3 years prior to this event, a dialysis catheter was inserted 30 months prior to the incident. Peripheral blood cultures as well as blood drawn from the catheter revealed methicillin-sensitive *S. aureus* (MSSA) bacteremia. To avoid possible allergic manifestations, the patient was treated with vancomycin 2,000 mg i.v. (28.5 mg/kg) as a loading dose in the last 90 min of dialysis followed by 1,000 mg i.v. (14.2 mg/kg) after each subsequent dialysis (in the last 30–60 min of dialysis) plus combination vancomycin (2.5 mg/mL)/4% citrate antibiotic lock for 3 weeks. Vancomycin pre-hemodialysis concentrations were >15 mg/L (target 15–20 mg/L) during the 2 weeks of intravenous antibiotic therapy. The treatment was initiated while the patient was an outpatient. The patient experienced complete resolution of bacteremia confirmed by negative blood cultures. The catheter was removed 5 months after transplant surgery.

Case 2

A 34-year-old white female (weight 46 kg, height 166 cm) with a medical history significant for type I diabetes, hypertension, ischemic heart disease, and on hemodialysis for 3 years prior to this encounter, grew coagulase-negative *Staphylococcus* from her CVC (oxacillin susceptible), where the catheter was changed on the same day of suspected blood stream infection. The patient was treated with parenteral cefazolin 2 g thrice weekly after each dialysis session in addition to cefazolin (5 mg/mL)/heparin (5,000 units/mL) lock solution for the duration of 1 week as deemed appropriate by the prescribing physician. The treatment was initiated and completed in the inpatient setting. Repeated cultures were all negative and the catheter remained in place with no recurrence in the 3-month follow-up period.

Case 3

A 37-year old African-Canadian male (weight 77 kg, height 180 cm), with a documented history of hypertension and type II diabetes, had been receiving hemodialysis for 4 months prior to this encounter. MSSA was recovered from blood samples withdrawn via CVC (which was inserted 2 months earlier) and peripheral veins. The treatment regimen consisted of cefazolin 2 g i.v. thrice weekly after dialysis plus cefazolin (5 mg/mL)/heparin (5,000 units/mL) antibiotic lock instilled at the end of each dialysis for 2 weeks; the treatment started as inpatient and continued in the outpatient dialysis unit. All repeat cultures were negative and the permanent catheter was not removed for the follow-up period of 3 months.

Case 4

An 81-year-old quadriplegic African-Canadian female (weight 64 kg, height 152.5 cm), with a known history of hypertension, type II diabetes, and requiring hemodialysis 55 months prior to this encounter, was diagnosed with MSSA bacteremia, with blood samples collected from the CVC (which was inserted 21 months before the incidence of bacteremia) and peripheral veins. A prescription for cefazolin 2 g i.v. after each dialysis and cefazolin (5 mg/mL)/heparin (5,000 units/mL) lock solution for 2 weeks were administered. Treatment was started in the outpatient dialysis unit. All repeat cultures were negative and the catheter was conserved intact. The patient expired 60 days later after admission; she was found unresponsive at a nursing home.

Case 5

A 36-year-old white male (weight 71 kg, height 175 cm) with hypertension, type I diabetes, heart disease, and on hemodialysis 51 months prior to this incident, developed MRSA bacteremia as shown by both CVC (which was inserted 1 week before the incidence of infection due to poor blood flow) and peripheral line blood cultures. The patient was treated with vancomycin 1,000 mg i.v. (14 mg/kg) initially, then 1,500 mg (21 mg/kg) after the subsequent dialysis (due to low trough level) followed by 1,000 mg i.v. after each subsequent dialysis with pre-hemodialysis concentrations >15 mg/L (MRSA MIC was 0.5 mg/mL). Treatment was initiated in the inpatient setting and was completed in the outpatient dialysis unit. The patient was also treated with vancomycin (2.5 mg/mL)/4% citrate lock solution for a 2-week period. Microbiological eradication and resolution of symptoms were observed. The catheter was removed 1 month later after the patient had a successful kidney transplant.

Case 6

A 67-year-old white female (weight 67 kg, height 160 cm) with a medical history significant for type II diabetes, hypertension, heart disease, and on hemodialysis for 23 months, developed MRSA bacteremia from the arterial line, CVC (which was inserted 4 months prior to this infection incident), and peripheral lines during her hospital admission and was started on both vancomycin 2 g (31.5 mg/kg) loading dose during the last 90 min of dialysis followed by 1 g after each subsequent dialysis with a pre-hemodialysis level between 13 and 15 mg/L (MRSA MIC of ≤0.5 mg/L). The patient also received vancomycin (2.5 mg/mL)/4% citrate lock solution. Due to catheter blockage by a blood clot irresponsive to dissolution by tissue plasminogen activator local treatment, the catheter was removed 6 months later due to loss of function. However, during the interim when the catheter was in use, there was no infection seen.

Case 7

An 82-year-old Asian female (weight 55 kg, height 167 cm), with a known history of hypertension, heart disease, and on hemodialysis 28 months prior to this incident, developed bacteremia with *Acinetobacter baumanii* and coagulase-negative *Staphylococcus*. The patient was treated with vancomycin loading dose of 1,500 mg i.v. (27.2 mg/kg) during the last 60 min of dialysis followed by vancomycin 1,000 mg maintenance dose after each subsequent dialysis, along with parenteral gentamicin 160 mg (2.9 mg/kg) loading dose and 60 mg maintenance dose at the end of each dialysis, oral ciprofloxacin 500 mg daily, plus gentamicin 5 mg/mL solution in normal saline lock. The three antibiotics and lock solution were started in the outpatient dialysis unit and were continued for 2 weeks without requiring hospital admission. The patient did not experience recurrent infection for a follow-up period of 1 year and continued dialysis through the same catheter.

Case 8

A 62-year-old white male (weight 125 kg, height 167 cm), with a known history of type II diabetes, heart disease, hypertension, stroke (paraplegic), and on hemodialysis 98 months prior to this infection incident, developed bacteremia secondary to coagulase-negative *Staphylococcus* from the CVC. The patient received vancomycin 2,000 mg i.v. (16 mg/kg) for 2 consecutive dialysis sessions followed by vancomycin 1,000 mg i.v. after each subsequent dialysis plus vancomycin 2.5 mg/mL/4% citrate lock for 2 weeks total with complete cure, and the patient continued using the same catheter in the 6-month follow-up period.

Discussion

Staphylococcal bacteremia in patients with long-term CVCs carries the risk of hematogenous complications and recurrence which often necessitates catheter removal and replacement. In hemodialysis-dependent patients suffering from paucity of alternative hemodialysis access, catheter salvage is of upmost importance. In this case series, we have documented the utility of antibiotic lock solutions in salvaging the long-term dialysis catheter in patients with staphylococcal bacteremia in whom maintenance of patent dialysis access was critical.

Earlier studies examining the utility of antibiotic lock solutions in catheter salvage yielded varying results. Maya et al. [16] reported that of 113 hemodialysis patients with staphylococcal bacteremia, 35% experienced persistent fever until the next dialysis session and in additional 24% the infection recurred within 90 days. The pharmacokinetic/pharmacodynamic profile and target attainment was not discussed in the study; however, doses of antibiotics administered in the protocol were expected to achieve levels lower than the standard of practice today.

Ashby et al. [17] observed that in hemodialysis patients, attempted salvage was successful in 66.1% with no recurrence or complications, recurrent bacteremia was observed in 33% in the salvage group compared with 8.1% in the replacement group, but complications occurred in 0.9% in the former versus 14% in the latter group. Of note, *S. aureus* was the causative agent in 15.9% of cases, vancomycin dosing targeted trough of 5–10 mg/L, and lock solutions contained only heparin. Krishnasami et al. [18] found 69% of staphylococcal bacteremia to be eradicated successfully per protocol with a low incidence of *S. aureus*, the load dose of vancomycin was 20 mg/kg and the maintenance dose was 500 mg.

Based on the above studies and others, IDSA guidelines [15] that were published in 2009 recommended catheter removal for staphylococcal bacteremia; however, targeting higher vancomycin levels as the standard of practice, availability of diverse antibiotic lock solutions [19–22], and dire need of hemodialysis patients to minimize the frequency of catheter insertions should instigate clinical trials to re-examine the applicability of antibiotic lock solutions in maintaining the catheter in place and consequently conserving the options for dialysis access.

Central vein stenosis and thrombosis are well-described complications related to placement of short, long-term catheters. Endothelial damage occurs as a result of vein by an indwelling biologically incompatible foreign body. The injury is exaggerated further by constant movement of the catheter concomitant with respiration, movements of body parts, and changes in posture, as well as increased flow and turbulence from the arteriovenous access, alter the shear stress, resulting in platelet deposition and venous wall thickening. Trauma to the vessel wall results in thrombin generation, platelet activation, and expression of P-selectin with inflammatory response [23–25].

It is noteworthy to mention the role of nephrology-trained clinical pharmacists in providing effective therapy by selecting appropriate antibiotics which could be dosed after dialysis to conserve dialysis access. For example, the pharmacist recommended the use of cefazolin instead of cloxacillin/naficillin in MSSA and/or coagulase-negative *Staphylococcus* cases to mitigate the need of medication administration on non-dialysis days [26]. Selecting certain anti-infective agents promoted the early discharge from the hospital (i.e., patients did not have to remain in hospital for the full duration of antibiotic therapy), thereby reducing the overall cost of the patient's hospital admission. The pharmacist also served as liaison between infectious diseases and nephrology physicians, observed appropriate drug dosing and monitoring, and finally provided education to minimize vascular trauma to hemodialysis patients [27, 28]. The majority of antibiotic lock solutions are labeled with a short stability period, so they need to be prepared just before instilling them into the patient's catheter (especially for the long inter-dialytic time). Ideally, antibiotic lock solutions are prepared at the beginning of the dialysis session in the pharmacy and transferred to the dialysis unit at the end of the session, this coordination of delivery of care is another role for the nephrology pharmacist.

The observations in this report highlight the feasibility of successful microbiological eradication and clinical resolution of staphylococcal bacteremia in hemodialysis patients while maintaining the catheter in place to sustain the availability of dialysis access. The realization of the goals of infectious diseases [14, 29, 30] and renal groups [7] guidelines can be achieved through the selection of a treatment approach with a comprehensive view of the patient, maximizing the efficacy of systemic antibiotics, choice of the appropriate lock solution, and collaborative efforts of various health care disciplines. The successful treatment reported herein could be attributed to appropriate systemic therapy alone or in combination with antibiotic lock solutions; this remains to be a subject for a future study.

The cases presented in this report could provide insights for a randomized controlled clinical trial to investigate catheter salvage in this patient population where it is needed most. Nonetheless, several factors remain to be defined – for instance, the optimal antibiotic/anticoagulant concentrations of lock solution, when to start lock solution, the adequate dwell time, the required spectrum of antimicrobial coverage, patient characteristics predicting success or failure, and involvement of various health care professionals in decision-making to support clinical decisions that consider the risks of microbiological eradication failure and permanent loss of feasible dialysis access.

Statement of Ethics

The study conforms to all guidelines for human research and the protocol has been granted exempt status from Research Ethics Board in our institution. Due to the retrospective nature of data collection, the need for informed consent was waived.

Disclosure Statement

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Table 1. Composition of different lock solutions used for catheter salvage

Drug	Concentration	Diluent	Anticoagulant concentration
Cefazolin	5 mg/mL	Normal saline	Heparin 5,000 units/mL
Gentamicin	5 mg/mL	Normal saline	N/A
Vancomycin	2.5 mg/mL	Sterile water	4% sodium citrate

The composition of antibiotic lock solutions was extracted from the literature and approved by the hospital pharmacy and therapeutics committee. Vancomycin/sodium citrate lock solution was chosen for practical aspects to avoid mixing polypeptide compounds.