Central Venous Catheter-Related Bacteremia in Chronic Hemodialysis Patients:Saudi Single Center Experience

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Abstract

Introduction: Central vein catheters (CVC) are an important means of delivering hemodialysis (HD) to patients who require immediate initiation of dialysis but are without a mature functioning arterio-venous fistula or graft. The frequency of catheter-related bacteremia (CRB) reported in several large series ranged between 2.5 and 5.5 cases/1,000catheter-days.

Aim of the study: The aim of the study was to evaluate the incidence, spectrum of infecting organisms, risk factors, and optimal treatment for catheter-related bacteremia.

Methodology: This retrospective study of clinical records was conducted between January 2005 and January 2009 where all episodes of catheter related bacteremia in the preceding 4 years were a subject of our study. Data recorded for each patient included the number of catheter-days, episodes of suspected bacteremia, blood culture results, method of treatment, complications, and outcomes. All patients with CRB were treated with a 21-day course of intravenous antibiotics, with surveillance cultures obtained 1 week after completing the course of antibiotics.The CVC was removed if the patient had uncontrolled sepsis or if other vascular access was ready for use. Once the infection was controlled, catheter salvage was considered successful, leaving the original CVC in place.

Results: 93 chronic hemodialysis (HD) patients, 42 male (45.25%) and 51 female (54.8%) were included, with median age 51.67 years. During this study, there were 37087catheter-days, with 52 episodes of CRB, or 1.4 episodes/1,000 catheter-days. Thirty- five infections (67.3%) were caused by *gram-positive cocci* only, including *Staphylococcus aureus, Staphylococcus simulans*, and *Staphylococcus haemolyticus*. Seventeen infections (32.7%) were caused by gram-negative rods only, including a wide variety of enteric organisms. Five CVCs were removed because of severe uncontrolled sepsis, of the remaining 47 cases; attempted CVC salvage was successful in (90.3%). The only important complication of CRB was endocarditis, occurring in 1 of 52 episodes (1.9%).

Conclusion: We conclude that in our study, CRB is relatively near the lower limit of normal range with low incidence of complication and frequently involves gram-positive bacteria. CVC salvage is significantly improved when CVC was treated by antibiotic based on blood culture results.

Introduction

Central venous catheters (CVC) are an important means of delivering hemodialysis (HD) to patients who require immediate initiation of dialysis but are without a mature functioning arterio-venous fistula or graft. Types of central venous catheters used for chronic HD include tunneled cuffed catheters and nontunneled catheters. The risk of developing bacteremia varies with site of CVC insertion; type of device and duration of CVC use. The incidence of CRB associated with catheters was highest for femoral catheters, followed by internal jugular catheters then subclavian catheters [1].

Aim of the study

The aim of the study was to evaluate the incidence, spectrum of infecting organisms, and optimal treatment for catheter-related bacteremia

Methods

Patients, setting, and data collection

A retrospective study of clinical records was conducted for cases between January 2005 and January 2009 where all episodes of catheter related bacteremia in the preceding 4 years were a subject of our study. The study included 93 chronic hemodialysis (HD) patients from Prince Salman Center for Kidney Diseases (PSCKD), they were 42 male patients (45.2%) and 51female patients (54.8%), Data recorded for each patient included the number of catheter-days, episodes of suspected bacteremia, blood culture results, method of treatment, complications, and outcomes. All patients with CRB were treated with a 21-day course of intravenous antibiotics, with surveillance cultures obtained 1 week after completing the course of antibiotics.

Diagnosis of CRB

1– The diagnosis of Catheter-related bacteremia was established when a hemodialysis patient with a dialysis catheter has:Clinical symptoms: fever or chills, unexplained hypotension, malaise, nausea, changes in mental status, hypothermia, lethargy, hypoglycemia, or diabetic ketoacidosis.

2– 2 - No other source of infection.

3– 3- Definitive diagnosis of catheter-related bacteremia was made when blood cultures obtained from both the catheter lumen and

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a peripheral vein grow the same organism [2], and also, there was no difference regarding the infecting organism between blood cultures drawn from the catheter or a peripheral vein if the cultures are drawn during the dialysis.

Treatment

Our protocol for treatment of CRB once it is diagnosed consisted of initial empiric antibiotic regimen included both vancomycin (20 mg /kg /weekly) and broad-spectrum gram-negative bacterial coverage (third-generation cephalosporin) Ceftazidime (1g post every session). The systemic antibiotic regimen was modified after the blood culture report was obtained. Protocol success, was defined as catheter salvage plus resolution of symptoms within 48 h of initiation of therapy and negative cultures 1 week after completion of the regimen. The PC was removed if the patient had uncontrolled sepsis, haemodynamically unstable, or if other vascular access was ready for use.

Results

Patients demography

During the 4-year study period, 93 eligible patients were dialyzed using double-lumen, tunneled, and cuffed catheters. Average patient age was 51.67 years. Causes of ESRD included: diabetes mellitus (48.3%), hypertension (26.8%), glomerulonephritis (2.2%), unknown (13.9%), systemic lupus erythematous (2.2%), Alport syndrome (2.2%), autosomal dominant polycystic kidney disease (1.1%), obstruction (1.1%), and other (2.2%), (Table 1).

Most PCs were used as a bridge to arteriovenous fistula in patients with newly diagnosed as ESRD or in established patients with access failure. The catheters were inserted by the vascular surgeons.

Incidence of CRB

Fifty-two episodes of CRB occurred in 93 patients during the study period (Table 2). Twenty-seven patients had one episode of CRB, and 25 patients had two or more episodes (Figure 1). There were

Parameter	Patient's number	%
Gender	Male (42) Female(51)	M 45.2 F 54.8
Age (years)	51.67(18.5)	
Disease duration (years)	12.2 (7.84)	
Hemodialysis duration (years)	2.23 (1.66)	
HCV+	10	10.8
HBV+	2	2.2
Original kidney disease		
DM	45	48.3
HTN	25	26.8
Unknown	13	13.9
Alport syndrom	2	2.2
SLE	2	2.2
IgA nephropathy	1	1.1
PCKD	1	1.1
Scleroderma	1	1.1
Obstructive uropathy	1	1.1
	1	1.1
Mesangial post streptococcal GN	1	1.1

Data are mean (SD) or number (%).

Table 1: Demography of the 93 patients included in the study.

Parameter	Mean ± SD
Kt/V	1.36 (0.2)
Hemoglubin g/dL	11.1 (1.33)
White blood cell (K/uL)	7.65 (3.38)
Neutrophil (K/uL)	4.43 (2)
Platelet (K/uL)	255 (80)
Total protein (g/L)	69.86 (7.7)
Albumin (g/L)	32.25 (5.42)
Ferritin (ng/ml)	522 (422)
Iron saturation (%)	29.7 (19.85)
PTH (Pmol/l)	31.7
Calcium (mmol/L)	2.2 (0.2)
Phosphorus (mmol/L)	1.44 (0.56)
EPO dose (IU/kg/week)	188 (109)

Data are mean (SD)

Table 2: Laboratory findings of the 93 patients included in the study.
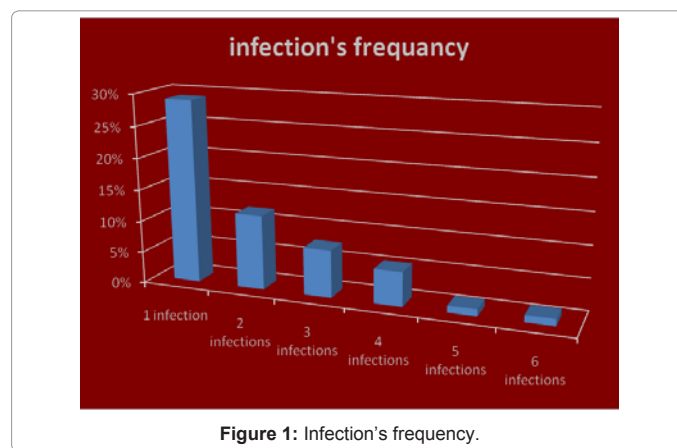
Figure 1: Infection's frequency.

37087 catheter-days, and the incidence of CRB was 1.4 episodes/1,000 catheter-days.

Microbiology

A single species of gram-positive coccus was responsible for 35of 52 episodes (67.3%) of CRB. A single species of gram-negative rod was isolated in 17 of 52 episodes (32.7%). No infections were associated with more than one organism (Figure 2).

The organisms isolated from all episodes of CRB are shown in (Table 3).

Treatment and outcome

Immediate PC removal because of severe and uncontrolled sepsis was required in five cases (8%) of 52 cases of CRB. The remaining 47 patients had PC salvage attempted. They were treated with empirical antibiotic alone which was modified later according to blood culture results.

Discussion

This study confirms that bacteremia is not a frequent occurrence in our chronic HD patients with long-term, tunneled, cuffed, venous catheter access. The incidence of CRB in our center was 1.4 episodes/1,000 catheter-days which is less than the rate of 3.9 episodes/1,000 catheter-days reported by Marr et al. [3] but all these rates are considerably greater than those reported in most previous
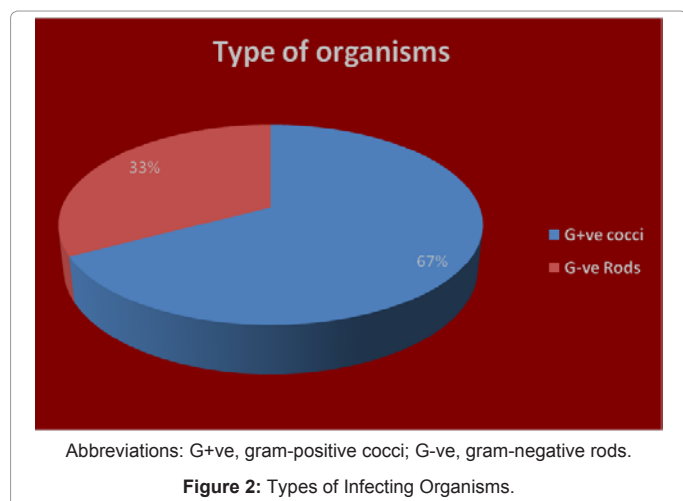
Abbreviations: G+ve, gram-positive cocci; G-ve, gram-negative rods.

Figure 2: Types of Infecting Organisms.

Organism	No. of Episodes	%
staphylococcus epidermides	26	50
Enterobacter cloacae	4	7.69
Pseudomonas aeroginosa	4	7.69
Staphylococcus haemolyticus	3	5.76
Enterococus faecalis	2	3.84
Staphylococcus aureus	1	1.92
Stahaylococcus auricularis	1	1.92
Acinetobacter baumanni haemolyticus	3	5.76
Escherichia coli	2	3.84
Cedecea davisae	1	1.92
Staphylococcus simulans	2	3.84
Pseudomonas stutzeri	1	1.92
Staphylococcus sciuri	1	1.92
Staphylococcus hominis subsp.Novobiosepticus	1	1.92
Total	**52**	**100%**

Data are number (%)

Table 3: Organism isolated from 52 episodes of CRB.

studies of long-term, tunneled, cuffed catheters. Moss et al. [4] reported 0.70 episodes/1,000 catheter-days in patients with median catheter duration of use of 18.5 weeks. Dryden et al. [5] reported 0.5 episodes of septicemia/1,000 catheter-days. They attributed this low rate in part to the strict aseptic technique practiced by nursing staff. The factors which are responsible for our relatively accepted rate of CRB are adequate skin disinfection and good placement technique, also, It is possible that our strict criteria for CRB diagnoses resulted in less diagnoses of CRB and contributed to the less infection rate than that reported by Marr et al. [3].

The source of bacteria and route for bacterial entry to the bloodstream in CRB are not clear. Bacteremia is rarely associated with exit-site infection, and most episodes occur many weeks after PC insertion, when fibroblast growth into the catheter cuff should be well established, providing an effective barrier to bacterial migration up the catheter tunnel.

It is most likely that bacteria gain entry to the bloodstream through the PC ports during catheter access despite rigorous nursing adherence to access protocol.

Several interrelated factors have been proposed to participate in the pathogenesis of CRB, these Risk factors include Staphylococcus aureus nasal colonization, longer duration of catheter use, previous bacteremia, older age, higher total intravenous iron dose, lower hemoglobin levels, diabetes mellitus and recent hospitalization. Also, Hypoalbuminemia increases the likelihood of a recurrent episode of catheter-related bacteremia among patients treated for an initial catheter-related bacteremia [6].

In our study, about half of the patients were diabetic and there median age was more than fifty years which refers that older age and diabetic status was risk factors for CRB, while albumin and iron levels were within normal limits.

Diagnosis of CRB was based on blood cultures drawn directly from the PC port and peripheral circulation, and we did not depend on the positive cultures obtained from the catheter alone, It is possible that contamination of the catheter port or poor culture technique could result in false-positive culture results from the catheter, resulting in overdiagnosis of CRB, Moreover, the colony count should be 5- to 10-fold greater in the catheter blood culture than the peripheral vein culture [7]. Quantitative blood cultures are not available in our microbiology laboratory, an indirect approach requires showing that blood cultures obtained from the catheter become positive at least 2 hours earlier than those obtained from a peripheral vein [2]. However, for patients with a permanent (PC) catheter presenting with distinct signs and symptoms of systemic infection, the clinical suspicion for CRB must be high, and false-positive catheter-derived culture results are less likely.

Although positive catheter-tip cultures are commonly used as evidence for infection of temporary venous catheters, the same evidence does not exist for PCs, in most cases, the patient had already received several days of antibiotic therapy, and the blood culture results were diagnostic. Furthermore, the catheter tip was usually withdrawn through a nonsterile exit site, raising the possibility of false-positive tip culture results. For these reasons, in the setting of suspected CRB, we did not depend on catheter –tip cultures results for CRB diagnoses, although it was done routinely post each catheter exchange

Interestingly, many patients with CRB presented to dialysis with few or no symptoms but then developed fever, rigors, nausea, or severe manifestations of systemic sepsis during the HD session. This suggests that bacteria or pyrogens were sequestered in or around the PC and then released into the bloodstream after blood flow was established. Many of our patients with CRB were using high-flux dialyzers, and CRB presenting in this way may be indistinguishable from a sterile pyrogen reaction related to inadequate disinfection or poor water quality. However, most of the CRB presenting after the initiation of dialysis occurred well into the treatment (30 to 90 minutes) in contrast to sterile pyrogen reactions that would typically occur earlier. During this study, there were no sterile pyrogenic reactions diagnosed in a patient without a PC and no positive test results for pyrogens in the water treatment or reuse systems.

There was a wide variety of both gram-positive and gram-negative infections seen in this study, initial antibiotic coverage for our patients includes an agent effective against these organisms. Also, because of our relatively high incidence of staphylococcus, we have frequently used vancomycin (usually with ceftazidine) for initial empiric coverage of severe infections, With the increasing incidence of vancomycin-resistant staphylococcus, [8,9] there s considerable pressure to minimize its use. In hemodialysis patients with CRB S.aureus is an

independent risk factor for both infectious complications and failure of bacteremia treatment [10]. A single-center, retrospective study found that, compared with patients not on dialysis, those on dialysis (379 hemodialysis and 31 peritoneal dialysis patients) were four times more likely to die from S. aureus CRB staphylococcus induced (5.3% vs. 1.3%; P <0.001) [11].

Relatively five catheters were removed early because of overwhelming sepsis. We attempted catheter salvage in many patients who presented with quite severe clinical sepsis as long as they responded well to initial therapy. Most patients were afebrile and asymptomatic within 24 to 48 hours. If the response to antibiotics was not prompt and complete, the catheter was removed

Presumably, the low success rate of curing catheter-related bacteremia with systemic antibiotics alone is caused by persistence of the bacterial biofilm in the catheter lumen because systemic antibiotics achieve negligible antibiotic concentrations in the catheter lumen [12], In approximately 10% of patients with catheter-related bacteremia, fever persists 48 hours after the initiation of broad-spectrum antibiotics, prompting removal of the catheter [13,14].

Infection-free survival for patients with catheter-related bacteremia treated with systemic antibiotics alone was inferior to that obtained with either immediate catheter removal [3] or catheter exchange over a guidewire [15]. However, the likelihood of a metastatic infectious complication was not increased by attempting therapy with systemic antibiotics alone [3].

It is possible that early detection and aggressive early antibiotic treatment are partly responsible for our high catheter salvage and low complication rates. Every episode of suspected bacteremia for which blood cultures were drawn was treated immediately with antibiotics, leaving no patient untreated pending culture results. This is especially important when CRB is treated on an outpatient basis and blood cultures turn positive on the day after HD. If appropriately treated with long-acting antibiotics after dialysis, outpatients can usually wait until after their next dialysis session to be redosed and only be brought back early if they have persistent symptoms of infection or if culture results are positive for organisms unlikely to be covered by the initial antibiotics.

CRB can result in life-threatening complications, including septic shock, infective endocarditis, septic arthritis, osteomyelitis, spinal epidural abscess, septic pulmonary emboli, or even death. The range in frequency is from 8, 7 to 50% depending upon the type of vascular access and the organism involved.

Metastatic complications are suspected when the patient remains febrile or has positive cultures after the catheter was removed.

In our study, no metastatic infections attributable to CRB was observed, Marr et al. [2] reported that 22% of the patients with CRB developed complications, including 10% with endocarditis. The reasons for our comparatively low rates are unclear, and this may be due to immediate treatment to every suspected bacteremia with effective antibiotic.

The relative risk for infection-related hospitalization and infection-related death is increased 2- to 3-fold among catheter-dependent hemodialysis patients compared with those using fistulas or grafts [12].

In our study, our patient died and the mortality was directly attributed to CRB, It was complicated by development of endocarditis.

1. A strict prophylaxis protocol has been reported to reduce the incidence of catheter-related bacteremia substantially in an observational study. The protocol included simple measures, such as wrapping the catheter hubs with iodine-saturated gauze for 5 minutes before removal of the catheter caps, having the dialysis nurse and patient wear masks during catheter connection and disconnection, and minimizing exposure of the catheter to air [16]. In addition, 2 types of pharmacological measures may be useful for the prophylaxis of catheter-related bacteremia. One potential approach is to use an antibiotic ointment to reduce skin flora around the catheter exit site. A second approach involves instillation of an antimicrobial solution into the catheter lumen to limit biofilm formaIt is imperative for every dialysis center to develop multidisciplinary approaches to minimize the use of catheters in hemodialysis patients. However, even with optimal adherence to the Kidney Disease Outcomes Quality Initiative guidelines on vascular access, [17] there will always be a subset of patients requiring dialysis catheters.

This study confirms that in our patients, bacteremia is not a frequent complication of PC access, and a wide variety of organisms, including gram-negative rods, may be responsible for these infections. Few serious complications occur, with the notable exception of endocarditis. This study also confirms acceptable catheter salvage rates when CRB is treated immediately and promptly with antibiotic alone.

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