

Evaluating a Novel Hemodialysis Central Venous Catheter Cap in Reducing Bloodstream Infections: A Quality Improvement Initiative

Steven Weiss¹
Muhammad Qureshi²

¹Quality and Support Services, Atlantic Dialysis Management Services, Ridgewood, New York, USA; ²Clinical Research, Mattoo & Bhat Medical Associates, P.C., College Point, New York, USA

Purpose: Central line-associated bloodstream infection (CLABSI) is the second leading cause of death in hemodialysis patients. Patients dialyzed via central venous catheters (CVCs) are more susceptible to vascular access-related bloodstream infection (VRBSI), sepsis, and mortality when compared to patients with other dialysis accesses.

Patients and Methods: A retrospective observational data analysis was conducted from 13 outpatient dialysis clinics in the United States to compare novel chlorhexidine-coated end caps to standard needlefree connectors for differences in CLABSI rates when utilizing CVCs for hemodialysis. There were two periods in this study: in the first study period over a 5-month period (May 2018 to September 2018), data were evaluated from a group of patients undergoing hemodialysis using chlorhexidine end-caps ('chlorhexidine group') as well as a group using standard needlefree connectors ('standard group'). An initial assessment found that a substantial CLABSI rate reduction was seen with use of chlorhexidine-coated end caps; therefore, most patients were switched to chlorhexidine by February 2019 and data continued to be collected till June 2019. The second study period spanned 9 months from October 2018 to June 2019.

Results: Across 13 dialysis centers, anonymized health records of 5934 patients who were dialyzed via CVCs between May 2018 and June 2019 were analyzed. The mean age was 61.3 and 47.1% of all patients were female. Study period one included 967 patients with chlorhexidine and 1044 patients with standard end caps, while there were 3647 chlorhexidine and 276 standard patients in the second period. The combined CLABSI rate in the chlorhexidine group was 0.09/1000 CVC days versus 0.63/1000 CVC days in the standard group ($p < 0.0001$).

Conclusion: Chlorhexidine-coated CVC caps may provide a therapeutic improvement in CVC hemodialysis management.

Keywords: catheter-related infection, renal dialysis, quality improvement, infection control, chronic kidney failure, chlorhexidine-coated CVC caps

Introduction

A bloodstream infection (BSI) is the presence of one or more viable pathogens in systemic circulation confirmed by positive microbiological blood culture(s). BSIs can elicit a life-threatening systemic inflammatory response characterized by fever, chills and/or hypotension. Indwelling devices, namely central venous catheters (CVCs), are common sources of secondary BSIs in outpatient hemodialysis settings where vascular access is essential in carrying out a hemodialysis procedure.^{1,2} In fact, central line-associated bloodstream infections (CLABSIs) are the second leading cause of death in hemodialysis patients, with an attributable mortality rate ranging between 12% and 25% and estimated

Correspondence: Steven Weiss
Quality and Support Services, Atlantic
Dialysis Management Services, 385 Seneca
Ave, Ridgewood, NY, 11385, USA
Tel +1 347-512-9090
Fax +1 718-366-2936
Email sweiss@atlanticdialysis.com

costs of 45,000 USD per event.^{3,4} Approximately 500,000 patients receive hemodialysis for end-stage renal disease annually in the United States, and are susceptible to BSIs arising from frequent hospitalizations and weakened immune systems.^{3,5} Over 80% of these patients initiate hemodialysis via CVCs, a modality associated with a higher risk of vascular access-related bloodstream infection (VRBSI), sepsis, and mortality compared to patients dialyzed via arteriovenous fistulas (AVFs) or arteriovenous grafts (AVGs).⁶ According to the Center for Disease Control's National Healthcare Safety Network (NHSN), 69.8% of VRBSIs in the United States can be attributed to CVCs.⁵ Specifically, the CLABSI rate per thousand CVC days is reported as 0.71 for CVCs, which is significantly higher than 0.09 for AVFs, and 0.13 for AVGs.⁵

Recent advances in CVC technology such as needleless connectors and disinfecting caps have been identified as effective strategies to reduce CLABSI incidence.⁷ National Kidney Foundation's Kidney Disease Outcomes Quality Initiative (KDOQI) has also emphasized the importance of preventing CVC dysfunction in the latest Clinical Practice Guidelines for Vascular Access, and recommends the use of antimicrobial barrier caps to help reduce catheter-related bloodstream infections in high-risk patients or facilities.⁸ To this notion, a novel CVC cap with antimicrobial coated rods featuring the broad-spectrum biocide chlorhexidine, has demonstrated lower rates for CLABSI and positive blood cultures in CVC hemodialysis patients in two randomized clinical trials.^{9,10} Herein, findings are reported from a multi-center quality improvement assessment conducted at a US-based outpatient dialysis network to evaluate CLABSI rates following the use of these novel chlorhexidine-coated CVC end caps.

Patients and Methods

Project Design and Setting

This study is a retrospective analysis of data collected from a quality improvement assessment conducted at 13

outpatient dialysis clinics across New York, USA (New York City and Long Island), all of which are members of a regional dialysis network (Atlantic Dialysis Management Services, NY, USA). The Atlantic Dialysis Quality and Support Services and Research Department provided ethical approval and oversight, and the 13 respective participating dialysis clinics' governing bodies also approved this retrospective data analysis. Patient consent was not required since this was a retrospective assessment of a quality improvement project. Additionally, all patient data was de-identified, and confidentiality of data was maintained throughout the course of the study.

Patients dialyzed via CVCs represent approximately 19% of the 2400 patients served by the clinics. CVC use and CLABSI incidence data from a 5-month period (May to September 2018) was used for an initial assessment. Given the substantial CLABSI rate reduction with the group who received hemodialysis with chlorhexidine-coated end caps ("chlorhexidine group"), almost all patients were switched to the chlorhexidine-coated end caps by February 2019 and follow-up data collection concluded in June 2019.

Materials and Procedures

The chlorhexidine-coated CVC caps used were ClearGuard HD Antimicrobial Barrier Caps (ICU Medical, San Clemente, CA, USA), which are equipped with chlorhexidine-coated cap threads and a chlorhexidine-coated rod that extends into the hemodialysis catheter hub (Figure 1). Therefore, attaching the cap to the dialysis catheter hub results in the local dissolution of concentrated chlorhexidine within the lock solution between the tubing clamp and the cap. The chlorhexidine-coated CVC cap was removed from the catheter at the time of dialysis and discarded. The dialysis catheter hub was then cleaned with an alcohol wipe. The lock solution was aspirated until 5 mL of



Figure 1 Antimicrobial barrier cap (ClearGuard™ HD) used in the chlorhexidine group.

blood returned into the syringe, and dialysis was initiated. At the completion of dialysis, the catheter was flushed and locked with saline, the hub was cleaned with an alcohol wipe, and a new chlorhexidine-coated CVC cap was applied.

The standard end cap group ("standard group") underwent hemodialysis with the components and procedures previously used at the dialysis network. The catheters were capped by needlefree connectors (Tego, ICU Medical, San Clemente, CA, USA), which remained on the catheter during and after dialysis. The aspiration, flush and locking procedures were identical to those in the chlorhexidine group. However, in the standard group, the connector itself was not additionally capped and was typically discarded and replaced after three dialysis sessions. At the time of connector replacement, the CVC hub was also scrubbed with commercial disinfectant (Alcavis 50, Alcavis Intl., Gaithersburg, MD, USA).

Analysis

CVC patients and days per study group were estimated from the total number of CVC patients per month. CLABSI counts were recorded by month, and rates were reported as CLABSI/1000 CVC days. Chi-squared tests assessed significance of CLABSI/1000 CVC days between the chlorhexidine and standard groups. Data were collected with Microsoft Excel (Microsoft Corporation, Redmond, WA, USA) and statistical analyses were performed using SAS 9.4 (SAS Institute, Cary, NC, USA).

Results

Across 13 dialysis centers, de-identified health records of 5934 patients who were dialyzed via CVCs between May 2018 and June 2019 were analyzed. The mean age was 61.3 and 47.1% of all patients were female. In the first

5-month study period, 967 patients and 1044 patients were identified in the chlorhexidine and standard groups, respectively. One patient was excluded based on physical incompatibility of CVC with chlorhexidine-coated CVC caps, and no patients were excluded based upon allergy-informed contraindications to chlorhexidine. CLABSI rates during the first study period (Table 1) were significantly lower in the chlorhexidine group (0.03, $p<0.0001$) relative to the standard group (0.70). The second study period included 3647 and 276 patients in the chlorhexidine and standard groups, respectively. Monthly CLABSI rates remained low in the chlorhexidine group despite increasing CVC days due to conversion (Figure 2, Table 2). Combined results (both study periods) showed CLABSI rates of 0.63 in the standard group and 0.09 ($p<0.0001$) in the chlorhexidine group (Table 1). Additionally, no increase in thrombosis was reported in clinics converting to the chlorhexidine-coated CVC caps while using saline as the standard locking solution.

A total of 38 CLABSIs with 42 isolates were identified in this analysis: 34 CLABSIs were monomicrobial and 4 CLABSIs were polymicrobial (Table 3). Out of the 42 isolates, 59.5% were gram-positive organisms, the most common of which were coagulase-negative staphylococci (26.2%, $n=11$), followed by methicillin-resistant *Staphylococcus aureus* (11.9%, $n=5$). Gram-negative organisms accounted for 40.5% of all identified isolates, with *Acinetobacter baumannii* being the most common organism in this group (9.5%, $n=4$).

Discussion

Prior to the two study periods used for this analysis, the CVC CLABSI rate across all 13 dialysis network clinics paralleled the national average for outpatient dialysis facilities.⁵ After period one, dialysis clinics utilizing chlorhexidine-coated CVC caps reported significantly lower CLABSI rates, while clinics using standard needlefree connectors continued

Table 1 Comparison of CLABSI Rates by Study Group

Study Group	Total Number of Patients (N)	CVC Days	CLABSI	CLABSI/1000 CVC Days	p-value
First Study Period					
Chlorhexidine	967	29,010	1	0.03	<0.0001
Standard Therapy	1044	31,320	22	0.70	
First + Second Study Periods					
Chlorhexidine	4614	138,420	13	0.09	<0.0001
Standard Therapy	1320	39,600	25	0.63	

Abbreviations: CLABSI, central line-associated bloodstream infection; CVC, central venous catheter.

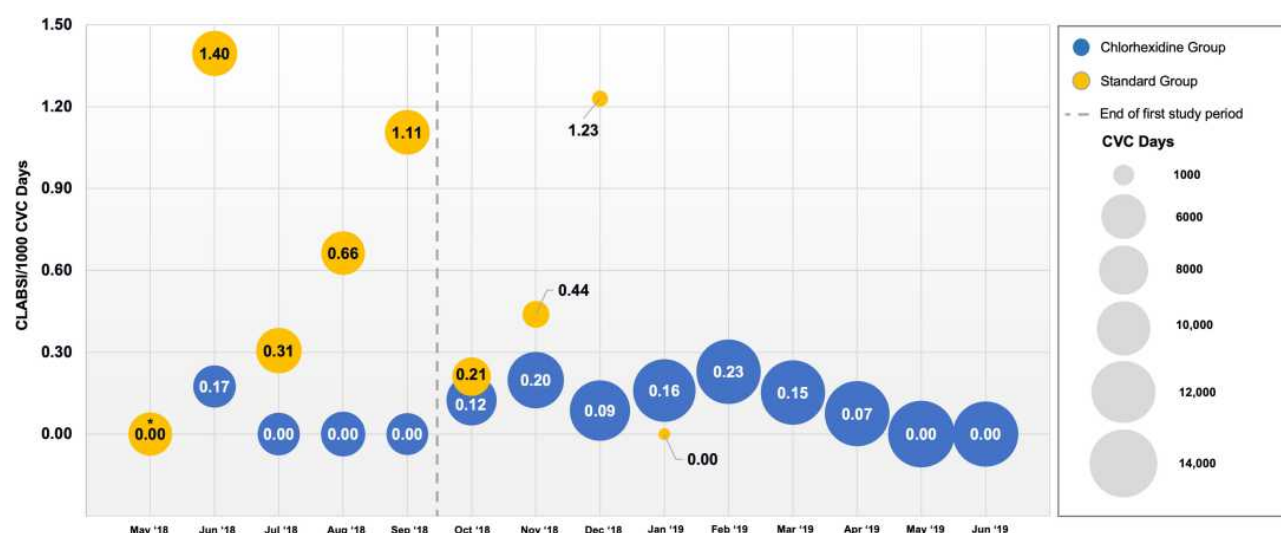


Figure 2 CLABSI/1000 CVC days by study group.

Notes: *Standard group had 0 CLABSIs out of 5970 CVC days and chlorhexidine group had 0 CLABSIs out of 5670 CVC days during May 2018.

Abbreviations: CLABSI, central line-associated bloodstream infection; CVC, central venous catheter.

to show rates similar to the national average.⁵ Therefore, the remaining clinics were transitioned to using chlorhexidine-coated CVC caps with minimal disruption to unit workflow and widespread acceptance by clinical staff and patients. Following the second study period, the combined CLABSI rate for the entire 13-clinic network using chlorhexidine-coated CVC caps was 0.09 per thousand CVC days and identical to the NHSN-reported CLABSI rate for hemodialysis via AVFs.⁵

The reduction in CLABSI rates reported from this analysis exceeded the results of previously conducted trials evaluating chlorhexidine-coated CVC caps,^{9,10} and is inclusive of summer months, which have historically demonstrated an upward trend of bacterial infections.¹¹

The significant reduction of CLABSI rates is most likely attributable to the chlorhexidine-coated CVC caps, considering no other systemic changes to infection control or CVC care practices were implemented during this period, and comparable systemic practices were utilized for both groups. Additionally, chlorhexidine has been shown to reduce micro-organism surface adherence and biofilm formation.^{12–15} Chlorhexidine-coated end caps likely impeded contamination and biofilm formation since attaching the cap to the dialysis catheter hub results in the local dissolution of concentrated chlorhexidine within the lock solution between the tubing clamp and the cap, which is removed prior to dialysis (Figure 1). Comparatively, standard needlefree connectors lack inherent antimicrobial properties and promote safe intravenous access by maintaining a closed lumen when not

engaged by mating luer.¹⁶ The commercial disinfectant used in the standard group to clean the catheter hub was specifically developed for antimicrobial effect in hemodialysis catheter applications and, therefore, unlikely to contribute to the higher rates of CLABSI.¹⁷

In accordance with the latest Clinical Practice Guidelines for Vascular Access from KDOQI,⁸ this study showed that the use of an antimicrobial barrier cap was associated with significant reductions in CLABSI incidence among patients hemodialyzed via CVCs and further suggests that antimicrobial barrier cap use is an effective strategy in preventing CVC dysfunction.

Despite presenting significant reductions in CLABSI rates with the use of chlorhexidine-coated CVC end caps, there are several limitations to the inferences from this study. Since this was a retrospective analysis of a quality improvement initiative, it was not possible to match data from the chlorhexidine and standard groups because detailed patient demographics and medical history were limited. Therefore, direct comparison was not possible, hindering the generalizability of this study's results to a larger outpatient hemodialysis patient population. Multi-center studies with larger and geographically diverse cohorts may provide further evidence regarding the real-world benefits of using chlorhexidine-coated caps in CVC hemodialysis.

Conclusions

Patients hemodialyzed via CVCs are at increased risk of bloodstream infections. Based on the reduction in CLABSI

Table 2 Comparison of CLABSI by Study Month and Study Group

2018–2019	Total Number of Patients (N)		CVC Days		CLABSI		CLABSI/1000 CVC Days		
	Chlorhexidine	Standard	Chlorhexidine	Standard	Chlorhexidine	Standard	Chlorhexidine	Standard	p-value
First Study Period									
May	189	199	5670	5970	0	0	0	0.00	
June	191	215	5730	6450	1	9	0.17	1.40	
July	190	218	5700	6540	0	2	0	0.31	
August	209	201	6270	6030	0	4	0	0.66	
September	188	211	5640	6330	0	7	0	1.11	
Subtotal^a	967	1044	29,010	31,320	1	22	0.03	0.70	<0.0001
Second Study Period									
October	268	158	8040	4740	1	1	0.12	0.21	
November	337	76	10,110	2280	2	1	0.20	0.44	
December	386	27	11,580	810	1	1	0.09	1.23	
January	417	15	12,510	450	2	0	0.16	0.00	
February	437	0	13,110	0	3	0	0.23	-	
March	438	0	13,140	0	2	0	0.15	-	
April	447	0	13,410	0	1	0	0.07	-	
May 2019	465	0	13,950	0	0	0	0.00	-	
June 2019	452	0	13,560	0	0	0	0.00	-	
Total^b	4614	1320	138,420	39,600	13	25	0.09	0.63	<0.0001

Notes: ^aFirst study period subtotal. ^bFirst and second study period total.

Abbreviations: CLABSI, central line-associated bloodstream infection; CVC, central venous catheter.

Table 3 Causative Organisms Isolated from Central-Line Associated Bloodstream Infections Among Patients Dialyzed via Central Venous Catheters

Isolates (N=42)	n (%)
Gram-positive organism	25 (59.5)
Coagulase-negative <i>Staphylococcus</i> Species (CoNS)	11 (26.2)
Methicillin-resistant <i>Staphylococcus aureus</i> (MRSA)	5 (11.9)
<i>Staphylococcus epidermidis</i>	3 (7.1)
<i>Staphylococcus aureus</i>	2 (4.8)
<i>Staphylococcus capitis</i>	1 (2.4)
<i>Enterococcus faecalis</i>	1 (2.4)
Vancomycin-resistant <i>Enterococcus faecalis</i>	1 (2.4)
<i>Streptococcus salivarius</i>	1 (2.4)
Gram-negative organism	17 (40.5)
<i>Acinetobacter baumannii</i>	4 (9.5)
<i>Enterobacter cloacae</i>	3 (7.1)
<i>Pantoea agglomerans</i>	2 (4.8)
<i>Escherichia coli</i>	2 (4.8)
<i>Klebsiella pneumoniae</i>	2 (4.8)
<i>Serratia marcescens</i>	1 (2.4)
<i>Stenotrophomonas maltophilia</i>	1 (2.4)
<i>Raoultella planticola</i>	1 (2.4)
<i>Citrobacter freundii</i>	1 (2.4)

Notes: 38 central line-associated bloodstream infections (CLABSIs) with 42 isolates were identified among patients dialyzed via central venous catheters; 34 CLABSIs were monomicrobial; 4 CLABSIs were polymicrobial.

rates, findings from this quality improvement report indicate that using chlorhexidine-coated CVC caps may provide a therapeutic improvement. Additional potential benefits of this conversion include improvement in a facility's Quality Incentive Program (QIP) score and reduced costs of treating infections with medications that are not billable outside of the Medicare bundled reimbursement rate. Reduced infection rates also have the potential to decrease hospitalization rates and increase patient satisfaction, both of which may increase unit revenue. Finally, given that every infection carries mortality risk, this analysis suggests that chlorhexidine-coated CVC caps also have the potential to decrease a dialysis unit's mortality rate.

Abbreviations

AVF, arteriovenous fistulas; AVG, arteriovenous grafts; BSI, bloodstream infection; CLABSI, central line-associated bloodstream infection; CVC, central venous catheter; KDOQI, Kidney Disease Outcomes Quality Initiative; NHSN, National Healthcare Safety Network; QIP, Quality Incentive Program; VRBSI, vascular access-related bloodstream infection.

Ethics Statement

The Atlantic Dialysis Quality and Support Services and Research Department provided ethical approval and oversight, and the 13 respective participating dialysis clinics' governing bodies also approved this retrospective data analysis. Patient consent was not required since this was a retrospective assessment of a quality improvement project. Additionally, all patient data was de-identified, and confidentiality of data was maintained throughout the course of the study.

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Disclosure

The authors declare no competing financial interests and no conflicts of interest in this work.

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