

Efficacy and Antimicrobial Properties of Different Locking Solutions in Hemodialysis Patients to Prevent Catheter-Related Bloodstream Infection

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ABSTRACT

Background: Dialysis and infection remain challenging despite ongoing updates to measures, approaches, and preventive protocols. Particularly, vascular access-related infections, which are associated with catheters that are often unavoidable due to late referrals or patients' poor vascular condition. Bloodstream infections and related complications continue to be the second leading cause of morbidity and mortality among hemodialysis patients. Antimicrobial locking solutions have been proposed to reduce the risk of infection, but data from Georgia remain limited.

Objectives: To evaluate the effectiveness of different catheter locking solutions—including unfractionated heparin, sodium bicarbonate, and gentamicin/citrate—in reducing the incidence of catheter-related bloodstream infections (CRBSIs) and catheter removal in hemodialysis patients with long-term tunneled central venous catheters in Georgia.

Methods: We performed a retrospective study at a high-volume HD center in Tbilisi, Georgia, including adult patients with long-term tunneled CVCs. Two study periods were compared: the Pre-Lock Period (2019–2020; n = 80) when unfractionated heparin (UFH) was the only locking solution, and the Lock Period (2022–2024; n = 241) when three different agents were used: UFH (5000 U/mL), sodium bicarbonate (8.4%), and gentamicin/citrate (0.5 mg gentamicin in 2.2% citrate). CRBSIs were defined according to the KDOQI-2019 criteria, with incidence rates expressed per 1,000 catheter days. Pathogens were identified and tested for antimicrobial susceptibility using VITEK 2 and EUCAST standards.

Results: The CRBSI incidence declined from 3.53 per 1,000 catheter-days in the Pre-Lock Period to 0.80 per 1,000 catheter-days in the Lock Period. Among locking solutions, sodium bicarbonate showed the lowest incidence (0.56), followed by gentamicin/citrate (0.72) and UFH (1.2). Catheter removals due to infection were also reduced (11.11/1,000 catheter-days with UFH vs. 3.89, 2.38, and 4.49 for sodium bicarbonate, gentamicin/citrate, and UFH during the Lock Period). Gram-positive bacteria predominated (59–64%), especially *Staphylococcus aureus*, while gram-negatives (36–37%) included *Klebsiella pneumoniae* and *Escherichia coli*. No MRSA, ESBL, or gentamicin resistance was observed.

Conclusions: Antimicrobial locking solutions were more effective than UFH in preventing CRBSIs and reducing catheter removal. Sodium bicarbonate was the most effective agent. These findings support the adoption of antimicrobial locks for CVC maintenance in HD patients, with future studies needed to directly assess biofilm colonization.

Keywords: Bloodstream Infection; catheter lock solutions; central venous catheter; gentamicin/citrate; hemodialysis; sodium bicarbonate.

BACKGROUND

Patients with Kidney Failure (KF) on hemodialysis face a significantly higher risk of life-threatening infections compared to those with normal kidney function. Most bloodstream infections are linked to vascular access, with 70% attributed to the use of central venous catheters.^{1,2} Hemodialysis catheter use is associated with an eightfold higher rate of catheter-related bloodstream infections (CRBSI) compared to an arteriovenous fistula.³ Infection is the second leading cause of death among patients on hemodialysis.⁴

CRBSI is defined as the identification of the same microorganism in blood samples collected from a hemodialysis catheter (or dialysis circuit) and a peripheral vein in patients showing clinical signs of infection, after ruling out other sources.⁵ CRBSI can be measured either by the time to an event or by the incidence per population and duration at risk (e.g., CRBSIs per 1000 catheter days).⁶ Literature indicates that the

incidence of hemodialysis CRBSIs averages between 5 and 6.6 cases per 1000 catheter days.^{7–11}

Several studies have examined the bacterial organisms involved in CRBSI among dialysis patients. As summarized by Charmaine E Lok et al., 52% of CRBSIs are caused by Gram-positive bacteria.¹² *Staphylococcus aureus* accounts for 21–43% of these infections, with methicillin-resistant *S. aureus* (MRSA) responsible for approximately 12–38%. Gram-negative bacteria are found in 27–36% of cases, while fungal isolates are less common, making up 10% or fewer. Farrington Crystal A et al. also reported that among hemodialysis patients with a single-organism CRBSI, the infecting organism was *S. aureus* in 34%, *S. epidermidis* in 38%, another Gram-positive coccus in 7%, and Gram-negative bacteria in 20%.¹³

Despite the implementation of CDC-recommended core interventions, which have reduced infection rates by 20–50%, CRBSIs continue to be a significant clinical problem.^{14,15} One



strategy is the use of catheter-locking solutions with antimicrobial and anticoagulant properties to inhibit biofilm formation. Evidence, including a Cochrane review, suggests that antimicrobial lock solutions reduce the risk of CRBSI compared with standard heparin locks. However, antibiotic locks are generally reserved for high-risk patients due to concerns about the development of resistance.^{16,17}

In Georgia, the “fistula first” policy failed several years ago due to a significant increase in demand for public resources.^{18,19} According to published data, nearly 90% of patients in Georgia use catheters when starting hemodialysis.¹⁹ Notably, these data closely align with US Medicare statistics, which indicate that 80% of patients begin hemodialysis treatment with a central venous catheter.²⁰

No precise statistical data are available on the types of bacterial infections causing CRBSI in hemodialysis patients in Georgia. Along with local epidemiological recommendations for infection control in hemodialysis centers, there is no universal protocol for the use of catheter locking solutions. To explore the potential benefits of catheter locking solutions in preventing catheter-related bloodstream infections (CRBSIs) and to assess the possible association between infection-causing organisms and the type of locking solution used, we analyzed data from adult patients with Kidney Failure undergoing chronic hemodialysis (HD) via long-term tunneled central venous catheters (CVCs) during two distinct periods. First, the Pre-Lock Period occurred before the implementation of catheter locking solutions to prevent catheter-related bloodstream infections. Second, the Lock Period involved three groups of hemodialysis patients. Each group utilized a different locking solution: unfractionated heparin (5000 U/mL), 8.4% sodium bicarbonate (NaHCO_3), and gentamicin in a 2.2% sodium citrate dextrose solution. This comparison aimed to evaluate the efficacy of alternative locking agents in reducing CRBSI incidence and to identify any potential differences in the microbiological profiles of infections across the groups.

METHODS

We conducted a retrospective study to compare the incidence of catheter-related bloodstream infections (CRBSIs) and the distribution of infectious agents among adult patients with kidney failure undergoing chronic hemodialysis (HD) via permanent central venous catheters (CVCs) during two distinct periods.

The Pre-Lock Period (September 1, 2019–October 1, 2020) spanned 13 months and included 80 patients, during which

conventional unfractionated heparin (5000 U/mL) was used exclusively as the catheter locking solution.

The Lock Period (2022–2024; 36 months, including a 6-month extension) encompassed a post hoc evaluation of the prior study, Impact of Sodium Bicarbonate Locking Solution on Catheter-Related Bloodstream Infection in Hemodialysis Patients: Comparative Effectiveness of Three Locks.²¹ It involved 241 patients allocated into three groups based on the locking solution used: unfractionated heparin (5000 U/mL), 8.4% sodium bicarbonate (NaHCO_3), or a gentamicin/citrate solution (acid citrate dextrose A solution containing 2.2% sodium citrate/gentamicin 0.5 mg).

Data were collected at a high-volume, hospital-based dialysis center in Tbilisi, Georgia, affiliated with Tbilisi State Medical University and Ingorokva High Medical Technology University Clinic, which provides care to over 400 HD patients annually. All patients were dialyzed via long-term, dual-lumen, tunneled CVCs of varying lengths, selected based on individual clinical requirements.

The data extracted from the database included the following variables: patient ID, date of birth, catheter lock type, CVC placement date, CRBSI date, pathogens causing CRBSI, and the catheter locking agent. CRBSI was verified according to the 2019 KDOQI guidelines.¹⁷

Blood culture samples (two 10 mL bottles) were inoculated into BACT/ALERT culture media for aerobic and anaerobic cultivation using the Bact/ALERT 3D system (bioMérieux, France).²² Positive growths were Gram-stained and cultured onto blood agar and MacConkey agar. Bacterial identification at the species level and antibiotic susceptibility testing were performed using the VITEK 2 Compact system. Antimicrobial panels were selected according to the guidelines of the European Committee on Antimicrobial Susceptibility Testing (EUCAST, v. 13).²³ Bacteria causing CRBSIs were classified as Gram-negative or Gram-positive. Antibiotic susceptibility was reported as susceptible, intermediate, or resistant. The catheter care protocol was identical during both study periods.

Descriptive statistics were used to summarize the data: categorical variables were expressed as percentages. In contrast, continuous variables were presented as means with standard deviations (SD) and medians with interquartile ranges (IQR), as appropriate. All statistical analyses were performed using STATA version 18, a widely accepted and reliable statistical software.

To calculate the catheter-related bloodstream infection (CRBSI) incidence rate, only the first infection event per patient during the study period was considered in the numerator. The

denominator consisted of the total cumulative number of days at risk (i.e., patient-days). The incidence rate was expressed as the number of infections per 1000 catheter-days. The incidence rate of catheter removal due to infection was calculated as the number of catheters removed for confirmed CRBSI divided by the total number of catheter-days, multiplied by 1,000. Microbiological testing and pathogen identification were performed using the VITEK 2 Compact system, ensuring accurate, standardized results.

RESULTS

A total of 80 patients with permanent central venous catheters (CVCs) were registered in the electronic database during the Pre-Lock Period. The cohort comprised 48.8% men ($n = 39$) and 51.2% women ($n = 41$). The mean age at catheter implantation was 58.89 years ($SD = 17.63$), ranging from 18 to 89 years, with a median age of 62 years (IQR: 54.25–70.0). Over these 13 months, during which only unfractionated heparin (5000 IU/mL) was used as the catheter locking solution, 48 catheter-related bloodstream infections (CRBSIs) were documented, yielding an incidence rate of 3.53 cases per 1,000 catheter-days (Tab.1). Gram-positive pathogens accounted for 64% of infections, while gram-negative pathogens comprised 36%. Detailed pathogen distribution is provided in Table 2.

During the Lock Period, 241 patients with CVCs were registered in the electronic database. The sex distribution was 55.2% men ($n = 133$) and 44.8% women ($n = 108$). The mean age was 62 years ($SD = 14$), ranging from 18 to 95 years, with a median age of 64 years (IQR: 55–71). Three types of catheter locking solutions were used, and patients were stratified into three cohorts based on the locking solution they received: unfractionated heparin, sodium bicarbonate, or gentamicin/citrate. A total of 61 CRBSI cases were identified. Among them, 12 cases (19.7%) occurred in the sodium bicarbonate cohort ($n=68$), 22 cases (36.1%) in the gentamicin/citrate cohort ($n=80$), and 27 cases (44.3%) in the heparin cohort ($n=93$). CRBSI incidence rates ranged from 0.56 to 1.2 cases per 1,000 catheter-days, with an overall rate of 0.8 cases per 1,000 catheter-days. Specifically, the incidence rates were 0.56 for Sodium Bicarbonate, 0.72 for gentamicin/citrate, and 1.2 for heparin (Tab.1).

Pathogen distribution across locking solutions during the Lock period showed gram-positive organisms accounted for 63.64%, 63.62%, and 59.3% of infections in the Sodium Bicarbonate, gentamicin/citrate, and heparin groups, respectively. Gram-negative pathogens comprised 36.36%, 36.38%, and 37% in the respective groups. Polymicrobial infections involving *Escherichia coli* and *Staphylococcus aureus*

were observed in 3.7% of the positive cultures in the heparin group (Tab.2).

TABLE 1. Infection rates by catheter lock types

Study period	Number of patients	Number of CRBSI cases	Incidence per 1,000 catheter-days	Notes
Pre-Lock Period (Sep 2019–Oct 2020)	80	48	3.53	Heparin lock only
Lock Period (2022–2024)	241	61	0.80	Heparin, Sodium bicarbonate, and Gentamicin/citrate
Sodium bicarbonate	68	12	0.56	
Gentamicin/citrate	80	22	0.72	
Heparin	93	27	1.20	
Total (All periods)	321	109	—	

Abbreviations: CRBSI, catheter-related bloodstream infection.

The incidence of CRBSIs significantly decreased from 3.53 cases per 1,000 catheter-days in the Pre-Lock Period to 0.80 cases per 1,000 catheter-days overall during the Lock Period. The Sodium Bicarbonate cohort exhibited the lowest incidence rate (0.56 per 1,000 catheter-days), compared to gentamicin/citrate (0.72) and heparin (1.2).

During the Lock Period, 17 catheters were removed due to CRBSIs. The incidence rates of catheter removal due to infection per 1,000 catheter-days were 3.89 for Sodium Bicarbonate, 2.38 for gentamicin/citrate, and 4.49 for heparin. In contrast, during the Pre-Lock Period, 18 catheters were removed due to infection, corresponding to an incidence rate of 11.11 removals per 1,000 catheter-days for heparin lock.

Methicillin-resistant *Staphylococcus aureus* (MRSA) was not detected during either period. No gentamicin resistance was observed, and neither extended-spectrum beta-lactamase (ESBL)-producing bacteria nor carbapenemase-producing *Enterobacterales* (CPE) were identified.

Across all periods and locking agents, gram-positive bacteria accounted for approximately 59% to 64% of CRBSI cases. Among these, *Staphylococcus aureus* was the most prevalent species, accounting for roughly 27–32% of gram-positive infections across the Lock Period groups and 32% during the Pre-Lock Period. Other common gram-positive pathogens included *Staphylococcus capitis* and *Enterococcus faecalis*, though their relative frequencies varied between cohorts. Detailed pathogen distribution is provided in Table 2.

TABLE 2. Pathogens causing catheter-related bloodstream infections according to the locking agent

Bacterial Pathogens	Sodium bicarbonate, % (n=12)	Gentamicin/Citrate, % (n=22)	Heparin lock, % (n=27)	Heparin pre-lock, % (n=48)
<i>S. aureus</i>	63.64	63.62	59.30	64.0
<i>S. capitis</i>	27.27	31.80	29.70	32.0
<i>S. epidermidis</i>	9.10	-	-	-
<i>S. lentus</i>	18.18	22.72	3.70	12.0
<i>S. hominis</i>	9.09	-	-	8.00
<i>S. infantarius</i>	-	-	11.1	-
<i>E. faecalis</i>	-	4.55	-	-
<i>E. faecium</i>	-	-	11.1	-
<i>S. haemolyticus</i>	-	-	3.70	-
<i>C. pseudodiphthericum</i>	-	-	-	8.00
<i>M. luteus</i>	-	4.55	-	4.00
<i>P. stutzeri</i>	36.36	36.38	37.0	36.0
<i>P. fluorescens</i>	9.09	-	-	-
<i>P. pneumoniae</i>	9.09	-	-	-
<i>L. adecarboxylata</i>	9.09	-	-	-
<i>E. coli</i>	9.09	9.09	7.40	8.00
<i>S. ficaria</i>	-	4.55	3.70	-
<i>S. marcescens</i>	-	4.55	-	12.0
<i>P. aeruginosa</i>	-	4.55	-	-
<i>E. cloacae</i>	-	9.09	3.70	-
<i>S. liquefaciens</i>	-	4.55	-	-
<i>A. denitrificans</i>	-	-	3.70	4.00
<i>A. lwoffii</i>	-	-	3.70	4.00
<i>K. oxytoca</i>	-	-	3.70	4.00
<i>M. morganii</i>	-	-	3.70	4.00
<i>E. cloacae</i> complex	-	-	7.40	4.00
<i>E. coli</i> + <i>S. aureus</i>	-	-	3.70	-
Fungal	-	-	-	-

Abbreviations: *A. denitrificans*, *Achromobacter denitrificans*; *A. lwoffii*, *Acinetobacter lwoffii*; *C. pseudodiphthericum*, *Corynebacterium pseudodiphthericum*; *E. cloacae* complex; *E. cloacae*, *Enterobacter cloacae*; *E. coli*, *Escherichia coli*; *E. faecalis*, *Enterococcus faecalis*; *E. faecium*, *Enterococcus faecium*; *Enterobacter cloacae* complex; *K. oxytoca*, *Klebsiella oxytoca*; *L. adecarboxylata*, *Leclercia adecarboxylata*; *M. luteus*, *Micrococcus luteus*; *M. morganii*, *Morganella morganii*; *P. aeruginosa*, *Pseudomonas aeruginosa*; *P. fluorescens*, *Pseudomonas fluorescens*; *P. stutzeri*, *Pseudomonas stutzeri*; *S. aureus*, *Staphylococcus aureus*; *S. capitis*, *Staphylococcus capitis*; *S. epidermidis*, *Staphylococcus epidermidis*; *S. ficaria*, *Serratia ficaria*; *S. haemolyticus*, *Staphylococcus haemolyticus*; *S. hominis*, *Staphylococcus hominis*; *S. infantarius*, *Streptococcus infantarius*; *S. lentus*, *Staphylococcus lentus*; *S. liquefaciens*, *Serratia liquefaciens*; *S. marcescens*, *Serratia marcescens*.

Gram-negative bacteria accounted for about 36% of CRBSI cases across all groups, with *Klebsiella pneumoniae*, *Escherichia coli*, *Pseudomonas spp.*, and *Enterobacter cloacae* among the most frequently isolated species. Notably, *Klebsiella pneumoniae* was more prominent in the Sodium bicarbonate group (9.09%) than in others, while *Escherichia coli* and *Enterobacter cloacae* had higher representation in the gentamicin/citrate and heparin cohorts. Detailed pathogen distribution is provided in Table 2.

Polymicrobial infections involving both *Escherichia coli* and *Staphylococcus aureus* were observed exclusively in the heparin cohort during the Lock Period, albeit at a low rate (3.7%).

Compared with the Pre-Lock Period, the overall pathogen profiles were similar during the Lock Period. However, the presence of specific life-threatening gram-negative pathogens such as *Enterobacter cloacae* and *Escherichia coli* was more frequent in the heparin and gentamicin/citrate groups than in the Sodium Bicarbonate group.

No fungal infections or multidrug-resistant organisms, including MRSA, ESBL-producing bacteria, and carbapenem-resistant *Enterobacter*, were detected across all groups.

DISCUSSION

Our study revealed a significant reduction in catheter-related bloodstream infections (CRBSIs) when antimicrobial locking solutions were used compared with unfractionated heparin (UFH) alone. The CRBSI rate decreased from 3.53 infections per 1,000 catheter-days during the Pre-Lock Period (heparin-only) to 0.80 infections per 1,000 catheter-days during the Lock Period, which involved antimicrobial locks.

During the Lock Period, 17 catheters were removed due to CRBSIs, with catheter removal rates per 1,000 catheter-days of 3.89 for sodium bicarbonate, 2.38 for gentamicin/citrate, and 4.49 for heparin. In contrast, during the Pre-Lock Period, 18 catheters were removed due to infection, corresponding to an incidence rate of 11.11 per 1,000 catheter-days for heparin lock. This highlights the clinical importance of antimicrobial lock solutions in prolonging catheter survival and reducing the need for invasive interventions.^{15-17,24}

Pathogen distribution across locking solutions demonstrated that gram-positive organisms accounted for approximately 59–64% of infections—63.64%, 63.62%, and 59.3% in the sodium bicarbonate, gentamicin/citrate, and heparin groups, respectively—aligning with earlier reports on CRBSI epidemiology.^{6,13,15,25} Gram-negative pathogens comprised 36–37% across all groups.

Notably, polymicrobial infections involving *Escherichia coli* and *Staphylococcus aureus* were observed exclusively in the heparin group, and *E. coli* and *Enterobacter cloacae* were more frequently isolated in the heparin group than in other antimicrobial lock groups. Similar patterns have been reported, with non-antimicrobial locks associated with higher rates of gram-negative infections.^{12,16,24,25} No methicillin-resistant *Staphylococcus aureus* (MRSA) or multidrug-resistant organisms, including ESBL-producing or carbapenem-producing *Enterobacter*, were detected. Importantly, gentamicin was used at a very low concentration in our protocol, which may explain the absence of gentamicin resistance.²⁶

Among gram-positive organisms, *S. aureus* was most prevalent, representing 27–32% of infections during the Lock Period and 32% during the Pre-Lock Period, consistent with previous studies on CRBSI microbiology.^{8,13,15}

Catheter loss due to infection was higher in the heparin group compared to other antimicrobial lock groups, supporting previous evidence that antimicrobial lock solutions—through their bactericidal activity and biofilm inhibition—can prolong catheter survival.^{15-17,25,27} Reducing catheter loss is clinically crucial because catheter replacement is invasive, costly, and increases the risk of morbidity.^{1,2,6}

This study has several limitations. As a retrospective, single-center analysis, the findings may not be fully generalizable. We did not directly assess bacterial colonization or biofilm formation on catheter surfaces, which could have provided more insight into the pathogenesis of CRBSI and the risk of biofilm-related infections.^{16,25} Additionally, we did not account for unmeasured confounders, such as prior antibiotic use and hospitalization. Moreover, catheter lock protocols were not randomized, and the Pre-Lock and Lock periods differed in duration, which could have influenced incidence rate comparisons despite adjustment per 1,000 catheter-days.

Nonetheless, this study has notable strengths. It provides one of the first comparative evaluations of three locking solutions in a large hemodialysis cohort in Georgia, with systematic microbiological testing performed according to standardized EUCAST protocols. Clinical outcomes, including infection rates and catheter removal rates, were assessed, thereby enhancing the clinical relevance of the findings. Importantly, the results offer valuable real-world evidence with public health implications, contributing to the limited epidemiological data on catheter-related infections in the region.

CONCLUSIONS

With the growing burden of CRBSIs in HD patients, selecting an effective catheter-locking solution is essential. While heparin is an anticoagulant, it lacks antimicrobial properties and may promote biofilm formation. Our findings demonstrate that antimicrobial lock solutions are superior to unfractionated heparin in reducing CRBSI incidence, lowering catheter removal rates due to infection, and decreasing the prevalence of specific gram-negative pathogens, such as *E. coli* and *Enterobacter cloacae*. The use of very low-dose gentamicin in our protocol likely contributed to the absence of gentamicin resistance. Given their antimicrobial effects and ability to prevent biofilm formation, antimicrobial locks should be preferred over heparin for CVC maintenance in hemodialysis

patients. We did not directly assess bacterial colonization, which should be addressed in future studies to understand infection mechanisms and optimize lock-solution strategies.

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