Nephrol Dial Transplant (2019) 34: 1739–1745
doi: 10.1093/ndt/gfy388
Advance Access publication 21 January 2019

ndt
Nephrology Dialysis Transplantation

ORIGINAL ARTICLE

Sodium bicarbonate catheter lock solution reduces hemodialysis catheter loss due to catheter-related thrombosis and blood stream infection: an open-label clinical trial

Adel S. El-Hennawy[1], Elena Frolova[1] and Wesley A. Romney[2]

[1]Department of Nephrology, NYC Health + Hospitals/Coney Island, Brooklyn, NY, USA and [2]Department of Medicine, NYC Health + Hospitals/Coney Island, Brooklyn, NY, USA

Correspondence and offprint requests to: Adel S. El-Hennawy; E-mail: adel7@yahoo.com; Twitter handle: @Adelhennawy

ABSTRACT

Background. There is no ideal lock solution that prevents hemodialysis (HD) catheter loss due to catheter-related thrombosis (CRT) and catheter-related bloodstream infection (CRBSI). Catheter loss is associated with increased hospitalization and high inpatient costs. Sodium bicarbonate ($NaHCO_3$) demonstrates anti-infective and anticoagulation properties with a good safety profile, making it an ideal lock solution development target.

The objective of this study was to determine the safety and efficacy of using sodium bicarbonate catheter lock solution (SBCLS) as a means of preventing HD catheter loss due to CRT and CRBSI.

Methods. The study took place in a community hospital in Brooklyn, NY, USA. All admitted patients ≥18 years of age who needed HD treatment through CVC were included in the study. 451 patients included in the study were provided SBCLS or NSCLS post-dialysis. Catheter loss due to CRT or CRBSI was evaluated over a period of 546 days.

Results. A total of 452 patients met the criteria; 1 outlier was excluded, 226 were in the NSCLS group and 225 were in the SBCLS group. There were no significant differences between groups in comorbidities at the outset. The NSCLS group had CRT and CRBSI rates of 4.1 and 2.6/1000 catheter days (CD), respectively, compared with 0.17/1000 CD for both outcomes in the SBCLS group. SBCLS patients had a significantly reduced catheter loss rate due to CRT ($P < 0.0001$) and CRBSI ($P = 0.0004$). NSCLS patients had higher odds of losing their catheter due to CRT {odds ratio [OR] 26.6 [95% confidence interval (CI) 3.57–198.52]} and CRBSI [OR 15.9 (95% CI 2.09–121.61)] during the study period.

Conclusion. The novel approach of using SBCLS was found to be safe and was statistically superior to normal saline in preventing HD catheter loss due to CRT and CRBSI. $NaHCO_3$ solution is inexpensive, readily available in various settings and holds the potential to decrease hospitalization, length of stay and dialysis-related costs.

Trial registration. Maimonides Medical Center Investigational Review Board, Study IRB 2015-06-25-CIH. ClinicalTrials.gov identifier: NCT03627884.

Keywords: catheter lock, catheter-related blood stream infection, catheter-related thrombosis, ESRD, sodium bicarbonate

INTRODUCTION

Central venous catheters (CVCs), originally introduced for short-term dialysis, have become an acceptable form of permanent vascular access [1–3]. CVCs evolved as a bridge to optimal management in hemodialysis (HD) patients who await arteriovenous fistula (AVF) maturation as well as a solution for patients who have no alternate access [2, 4]. Despite great advances, two major causes of catheter loss continue to plague sustained effective HD treatment: catheter-related thrombosis (CRT) and catheter-related bloodstream infection (CRBSI) [5, 6].

A report suggests that up to 42% of catheter-related dysfunction is attributable to CRT, and a prospective study suggested that catheter-dependent HD patients have a 35% probability of developing bacteremia within 3 months of catheter insertion [2, 7]. Given the high percentage of dialysis patients who develop CRT and CRBSI, management that mitigates these rates may prove itself invaluable.

Multiple studies have assessed the role of catheter lock solutions for the prevention of CRT and CRBSI. Antibiotic locks demonstrated a reduction in CRBSI; however, there is growing concern that their overuse enables the development of antibiotic resistance [6, 8–13]. Furthermore, Landry and Braden [14] concluded that no ideal catheter lock solution existed that could prevent catheter loss due to CRT and CRBSI.

In reviewing the long history of developing an ideal lock solution, Wong *et al.* [15] and Wong [16] studied the effects of bicarbonate on blood coagulation. They suggested that removing bicarbonate chelated calcium ions from the coagulation pathway required calcium as a cofactor. In doing so, the bicarbonate-mediated chelation of calcium ions indirectly inhibited the conversion of fibrinogen to fibrin, leading to decreased clotting [15, 16].

Building upon this work, in our previous clinical study we demonstrated the novel approach of using sodium bicarbonate catheter lock solution (SBCLS) as an inexpensive, safe and effective method in preventing HD catheter loss due to clot formation [17]. We also found no CRBSI in the group using SBCLS. However, this finding could not be statistically validated because the sample size was not large enough. Based on the extensive literature review, we hypothesized that sodium bicarbonate (NaHCO3) can play an important role in preventing catheter loss due to CRBSI by multiple anti-infective mechanisms.

NaHCO3 has been shown to inhibit bacterial proliferation by decreasing bacterial adherence and preventing biofilm formation [18, 19]. 'Biofilms are gelatinous masses of microorganisms capable of attaching to virtually any surface. They glom onto medical devices where they are deadly or difficult to eradicate' [20]. According to the National Institues of Health, they factor into nearly 80% of all bacterial infections and are inherently resistant to antibiotics [21]. Biofilms plague hospitals and contribute greatly to our health care burden, and approaches that minimize biofilm formation are good targets for antimicrobial research [20, 22].

Staphylococci are biofilm-forming pathogens commonly associated with serious foreign body and catheter-related infections across settings [20, 23]. Ní Eidhin *et al.* [24] found a subfamily of adhesins, microbial surface components that recognize adhesive matrix molecules, promoted *Staphylococcus aureus* adherence to HD tubing by targeting extracellular matrix components such as fibrinogen [24]. Adhesins found in similar bacteria were able to confer virulence based on this approach, and it is evident that adhesins contribute greatly to biofilm formation [25]. Alkaline solutions, such as those containing NaHCO3, have been observed to interfere with staphylococci adherence and prevent biofilm formation [23].

Additional evidence from other studies suggested that NaHCO3 served as an abundant ionic factor that stimulated global changes in bacterial structure, gene expression and membrane permeability [18, 19, 23, 26–30]. These changes corresponded to the increased susceptibility of microbes to human cationic antimicrobial peptides [18, 19, 23, 26–30]. NaHCO3 was also found to inhibit the growth of bacteria and yeast in agar media [31]. Morphologic examinations by transmission electron microscopy of microorganisms exposed to $NaHCO_3$ solution demonstrated cytoplasmic shrinkage and fibrillary condensation [28]. These cellular changes rendered susceptible bacteria less viable through hindered proliferation [28]. Although these are just a few examples, the evidence of NaHCO3's antimicrobial properties continues to accumulate.

It is clear that pathogens encountering NaHCO3 must devise facultative qualities to survive an environment that interferes with surface adhesion, biofilm formation and enzymatic processes vital for proliferation [18, 19, 23, 26–30, 32]. In contrast to the inhibitory effects of NaHCO3, equimolar sodium chloride had no effect on growth, ruling out any osmotic or sodium-mediated mechanisms of inhibition [31].

In addition to these antimicrobial properties, an advantage of using SBCLS over other antimicrobial agents is its safety, availability and low cost that is comparable to normal saline catheter lock solution (NSCLS) [28]. The low cost and numerous benefits make NaHCO3 an ideal candidate for development as a locking solution. In this trial we tested the translation of this evidence into the potential clinical use of NaHCO3 as a microbial deterrent for CRBSI in HD patients.

MATERIALS AND METHODS

CVCs used in the study varied according to the patient's needs and consisted of either Mahurkar acute dual lumen catheters, made of polyurethane, or Palindrome chronic catheters, made of urethane. The exposure of polyurethane and urethane catheters to NaHCO3 is considered extremely safe based on the chemical compatibility data and regular clinical use [33, 34].

Mahurkar catheters were not tunneled and Palindrome catheters were tunneled beneath the skin. All CVCs were inserted by an expert operator under strict aseptic protocol. Catheter care was performed by trained dialysis staff according to our hospital's Administrative Policy and Procedure Manual. At the end of dialysis, all catheters were flushed and locked with one of the two solutions. SBCLS contained 7.5 or 8.4% NaHCO3 at a pH of 7.0–8.5 and was used to lock SBCLS group catheters. An 8.4% SBCLS was used primarily, except for 1 week when our hospital had a shortage of 8.4% SBCLS. During that single week we used 7.5% SBCLS to lock SBCLS group catheters. The NSCLS contained 0.9% sodium chloride at a pH of 4.5–7.0 and was used to lock NSCLS group catheters. All solutions used were sterile nonpyrogenic solutions. Dialysis was performed only on Fresenius model 4008K2 dialysis machines using Advanced Fresenius Polysulfone Optiflux F180NR dialyzers (Fresenius, Bad Homburg vor der Höhe, Germany).

Study design and patients

We conducted a prospective cohort, clinical open-label trial at Coney Island Hospital, in Brooklyn, NY, USA. The study period was between 1 October 2016 and 30 March 2018, a total of 546 days. All patients provided written informed consent before enrollment. The trial protocol was approved by the Maimonides Medical Center Investigational Review Board (Study 2015-06-25-CIH). Patients >18 years of age requiring HD via CVCs were eligible. One patient was excluded due to a poor venous system with inadequate blood flow for appropriate HD. No other patient was excluded from the study.

A total of 451 patients undergoing HD with CVCs were included in the study. Patients had tunneled internal jugular vein (IJV) catheters, nontunneled IJV catheters and nontunneled femoral vein catheters. All patients were randomly assigned based on the simple sequential order into one of the two groups: NSCLS ($n = 226$) and SBCLS ($n = 225$). NSCLS patients were assigned between 1 October 2016 and 30 June 2017. SBCLS patients were assigned between 1 July 2017 and 30 March 2018. Recruitment ended based on the similar number of enrolled participants between groups. A primary or coinvestigator enrolled the participant into the trial and assigned the participant to the intervention at the time of presentation. Both groups received heparin-free HD treatment. Before each HD treatment, catheters and connections were inspected for leaks, evidence of damage, exit-site infection and tunnel infection. Intraluminal SBCLS or NSCLS lock solution was removed before connecting the HD catheter to a dialysis machine prior to any treatment.

During each treatment, patients were monitored for complications and standard care was provided to every patient. After each treatment, blood was rinsed from the dialysis lines with normal saline solution back to the patient. Upon the conclusion of treatment, each port of all two-port catheters was flushed and locked with 10 mL of NSCLS or SBCLS, respective of the patient's group. Approximately 2 mL of the injected solution remained locked within the catheter. Catheter exit-site dressing changes occurred after each HD treatment.

We undertook this study for three reasons. First, the US Food and Drug Administration issued an urgent warning to all hospital pharmacies and HD units that citrate-containing tricitrasol may cause death when infused into patients [35]. Second, high-concentration (5000 or 10 000 U/mL) heparin-containing catheter locking solution is associated with major bleeding complications after tunneled HD catheter placement [36]. Third, low-concentration (1000 U/mL) heparin catheter lock solution is associated with greater tissue plasmin alteplase use, which further increases bleeding risk and costs [37].

For this last reason, in patients who had clotted catheters, thrombolytic therapy was not instituted. Risk assessment performed by our hospital's risk management department determined that the net risk of thrombolytic use in their opinion was greater than the net risk of catheter replacement by our qualified operators.

Outcome variables

The primary outcome measured the removal of catheters due to CRBSI, CRT and malfunction. Based on the CDC definitions, CRBSI was diagnosed when clinical sepsis symptoms (clinical manifestations) and empirical evidence of an infection related to the catheter were present [38].

Acceptable empirical evidence of CRBSI was defined as two peripheral venous blood samples drawn from the patient producing positive quantitative (>1000 CFU/segment) culture results. Alternatively, one positive blood culture obtained from a peripheral vein and one catheter culture with a positive semiquantitative (>15 CFU/segment) result was acceptable. Comparison cultures must have grown the same microorganism, identified by its species and antibiogram, and must have resulted within 2 h of each other. Although this contrasts from practice suggested by Pelletier *et al.* [39], our institution does not find the evidence compelling to depart from the CDC guidelines at this time.

In concordance with National Kidney Foundation guidelines, catheter dysfunction was defined when extracorporeal blood flow was $\leq$300 mL/min or the prepump arterial pressure was ≥ -250 mmHg [40]. Malfunctioning catheters were recorded when the catheter showed a visible kink or repositioning maneuvers such as ipsilateral arm raising, sitting, standing or rolling the patient onto one side led to catheter dysfunction reversibility. Catheter loss due to CRT was defined as persistent catheter malfunctioning, irreversible difficulty with line aspiration or infusion despite repositioning before or during HD.

Statistical analysis

The assumption of normality for continuous variables was assessed using skewness and kurtosis statistics. Frequency and cross-tabulation statistics were run on categorical variables. The NSCLS and SBCLS groups were compared on baseline demographic and clinical variables using between-group comparisons and all statistical assumptions (normality and homogeneity) were analyzed before interpreting the results. Results are expressed as sample mean (standard deviation) or as a percentage.

Independent sample *t*-tests were used to compare the groups on normal continuous outcomes. Mann–Whitney U-tests were utilized for between-subject comparisons when statistical assumptions were violated. Chi-square and Fisher's exact tests were used for testing categorical associations. Unadjusted odds ratios (ORs) with 95% confidence intervals (CIs) were used to compare the rates of catheter adverse events between the NSCLS and SBCLS groups. Statistical significance was assumed at an α-value of 0.05 and all analyses were conducted using SPSS Version 22 (IBM, Armonk, NY, USA).

RESULTS

A total of 451 patients were included in the sample. Of the participants, 226/451 (50.1%) were in the NSCLS group and 225/451 (49.9%) in the SBCLS group. There were no significant differences between groups on outset demographics or exposure, except for serum albumin level ($P = 0.006$) (Table 1). The NSCLS group patients underwent a combined 2480 treatments corresponding to 5787 catheter days (CD). SBCLS group patients underwent a combined 2474 treatments corresponding to 5773 CD.

Primary outcome variables demonstrated statistically significant between-group differences. In the NSCLS group, 24/226 (10.6%) patients lost catheters due to CRT, 15/226 (6.6%) due to CRBSI and 5/226 (2.2%) due to other malfunctions not attributable to CRT or CRBSI for a total of 44/226 (19.5%) due to all causes. This corresponds to 4.1 CRT and 2.6 CRBSI/1000 CD in the NSCLS group. In the SBCLS group, 1/225 (0.4%) patient lost a catheter due to CRT, 1/225 (0.4%) due to CRBSI and 5/225 (2.2%) due to other malfunctions not attributable to CRT or CRBSI for a total of 7/225 (3.1%) due to all causes. This corresponds to 0.17 CRT and 0.17 CRBSI/1000 CD in the SBCLS

group. Malfunction occurred in 0.86/1000 CD in the NSCLS group and 0.87/1000 CD in the SBCLS group (Figure 1).

The SBCLS group was found to have a lower rate of catheter loss due to CRT ($P < 0.0001$), whereas the NSCLS group had 26.6 times higher odds (95% CI 3.57–198.52) of losing catheters due to CRT (Table 2). SBCLS patients also had a lower rate of catheter loss due to CRBSI ($P = 0.0004$), whereas NSCLS patients had 15.9 times higher odds (95% CI 2.09–121.61) of losing catheters due to CRBSI (Table 2). No differences between groups were observed for catheter loss due to malfunction ($P = 1$) (Table 2). Overall, SBCLS patients had reduced catheter loss ($P < 0.0001$) and NSCLS patients had 7.5 times higher odds (95% CI 3.31–17.12) of losing their catheter. A comparison of the P-values, rates and ORs (95% CIs) for each primary outcome can be found in Table 2.

Table 3 summarizes the *post hoc* subgroup analysis comparing tunneled and nontunneled catheters used in the internal jugular site. Reductions in catheter loss remained statistically significant for SBCLS patients on primary outcomes, irrespective of catheter type. No deaths or significant adverse events related to HD occurred in any group. Figure 2 visually demonstrates group outcomes via a flow diagram.

Table 1. Baseline characteristics of the NSCLS and SBCLS groups

Characteristic	NSCLS	SBCLS	P-value
Age (years), median (SD)	69.0 (18.0)	69.0 (19.5)	0.84
Weight (kg), mean (SD)	76.5 (23.0)	76.4 (22.0)	0.96
Height (cm), mean (SD)	163.3 (7.1)	163.9 (8.5)	0.44
PT, median (SD)	11.9 (1.2)	12.0 (1.2)	0.76
INR, median (SD)	1.1 (0.2)	1.1 (0.2)	0.59
aPTT, median (SD)	30.1 (4.3)	30.2 (4.2)	0.62
Ca, mean (SD)	8.6 (0.9)	8.5 (0.8)	0.42
Serum albumin, mean (SD)	3.3 (0.8)	3.4 (1.0)	0.006
Phos, mean (SD)	4.0 (1.5)	3.7 (1.4)	0.06
CO_2, mean (SD)	23.3 (3.3)	23.7 (3.1)	0.15
Hemoglobin, mean (SD)	9.3 (1.5)	9.4 (1.4)	0.68
Gender, *n* (%)			
Male	111 (49.1)	119 (52.9)	
Female	115 (50.9)	106 (47.1)	0.42
Race, *n* (%)			
Caucasian	120 (53.1)	122 (54.2)	
African American	31 (13.7)	34 (15.1)	
Asian	16 (7.1)	17 (7.6)	
Hispanic	38 (16.8)	33 (14.7)	
Other	21 (9.3)	19 (8.4)	0.96
HTN, *n* (%)	196 (86.7)	197 (87.6)	0.79
DM, *n* (%)	122 (54.0)	121 (54.3)	0.95
CAD, *n* (%)	131 (58.0)	133 (59.6)	0.72
IJV tunneled, *n* (%)	160 (71.1)	173 (76.9)	0.14
IJV not tunneled, *n* (%)	55 (24.3)	45 (20.0)	0.27
Femoral vein, *n* (%)	11 (4.9)	7 (3.1)	0.34
HD treatments, mean (SD)	11.01 (8.46)	11.00 (8.46)	1.00

PT, prothrombin time; INR, international normalized ratio; aPTT, activated partial thromboplastin time; Ca, calcium; Phos, phosphorus; CO2, carbon dioxide; HTN, hypertension; DM, diabetes mellitus; CAD, coronary artery disease.

DISCUSSION

Infections are common complications among HD patients. Compared with patients with an AVF or graft, HD patients with a CVC have more than double the risk of hospitalization for infection and death [41]. Although nontunneled HD CVCs

Table 2. Catheter loss outcomes by cause

Outcome	NSCLS, *n* (%)	SBCLS, *n* (%)	P-value	OR (95% CI)[a]
Catheter loss due to CRT	24 (10.6)	1 (0.4)	<0.0001*	26.6 (3.57–198.52)
Catheter loss due to CRBSI	15 (6.6)	1 (0.4)	0.0004*	15.9 (2.09–121.61)
Catheter loss due to malfunction	5 (2.2)	5 (2.2)	1	0.996 (0.28–3.49)
All-cause catheter loss	44	1	<0.0001*	7.5 (3.31–17.12)

[a]Unadjusted ORs with 95% CIs.
*Statistical significance $P < 0.05$.

Table 3. Internal jugular subgroup analysis

Outcomes	NSCLS	SBCLS	P-value	OR (95% CI)
Internal jugular tunneled				
Functional	144	173	<0.0001	0.53 (0.35–0.80)
CRT	10	0	0.006	NA[a]
CRBSI	6	0	0.01	NA[a]
Internal jugular non-tunneled				
Functional	30	38	0.0001	0.75 (0.45–1.27)
CRT	12	1	0.005	12.56 (1.62–97.44)
CRBSI	8	1	0.039	8.22 (1.02–66.28)

Femoral catheter subgroup analysis was not done due to insufficient sample size. All subgroups shown here demonstrated statistical significance at $P < 0.05$.
[a]OR was not applied in tunneled catheters, as the sample size did not detect any catheter loss in SBCLS.

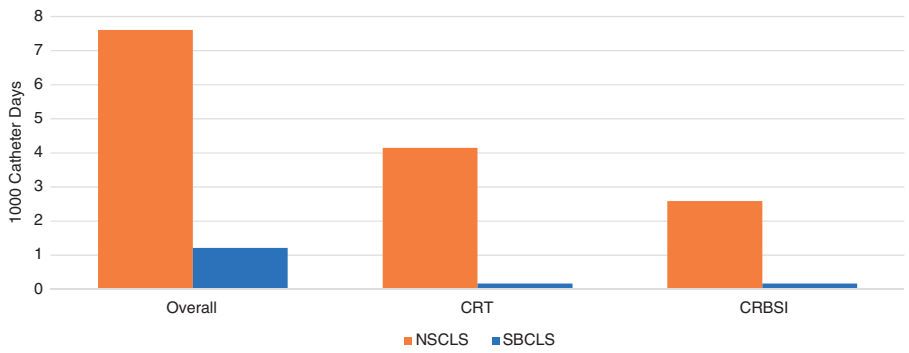

FIGURE 1: NSCLS versus SBCLS catheter loss rate.

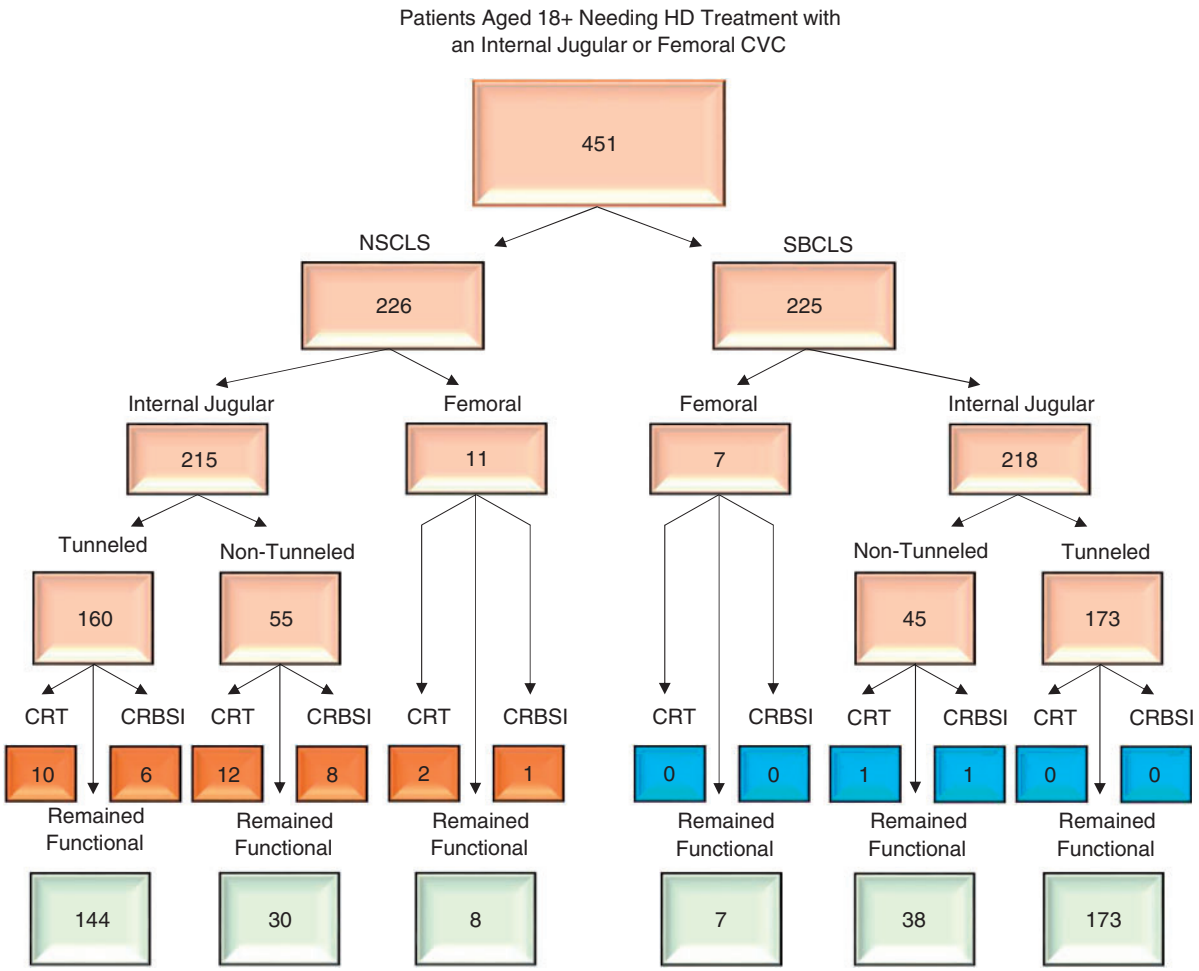

FIGURE 2: Groups and outcomes.

remain the preferred means of immediate access, bacteremia is the primary complication that limits their use [42].

Previous studies successfully curbed infection rates using antibiotic lock solutions, but the liberal use of antibiotics entails potential adverse consequences to patients and communities [43, 44]. With an annual incidence of 1 million cases, and 200 000 deaths in the USA alone, the emergence and prevalence of antibiotic-resistant bacteria as an increasing cause of death worldwide should bear significant weight on the choice of a standard lock solution [44]. Antibiotic resistance has resulted in a global 'call to action' to avoid receding into an era lacking effective antibiotics [18]. For antibiotic locks, significant costs and catastrophic adverse effects on the community outweigh the benefit of reduced infections for a few patients [26, 43, 44]. Consequently, using antibiotics to regularly reduce CRBSI in a population leads to a poor cost–benefit profile. Antibiotic lock solutions also fail to address catheter loss due to CRT. Exchanging NSCLS, a benign solution, for an antibiotic lock solution is thus impractical and a poor approach to minimize adverse outcomes [31].

In our prior study we challenged the standard NSCLS by demonstrating the effective reduction of CRT using SBCLS, yet the study left us without conclusive results regarding the effects on CRBSIs [17]. Accordingly, the current goal was to evaluate the efficacy of SBCLS in mitigating the CRBSI rate at our community hospital. We considered the known antibacterial properties of NaHCO3 and the favorable cost–benefit profile [18, 27, 43]. The rate of catheter loss due to CRBSI was found to be dramatically lower in the SBCLS group (Figure 1). Only one patient lost a catheter due to CRT, and only one catheter was lost due to CRBSI in the SBCLS group. No patients had any evidence of adverse effects related to the locking solutions, which attests to an equivalent safety profile. Overall, SBCLS patients demonstrated significantly lower catheter loss rates when compared with NSCLS patients for all causes. This is especially striking as the overall 19.5% NSCLS catheter loss rate is below reported average catheter loss rates for similar catheters, 21–46%, implying a strong external validity for our study [45, 46]. Additionally, Napalkov *et al.* [47] reported that complication by CRBSI had an incidence rate of '0.46 to 30 per 1000 CD or approximately 4.3% to 26% of placed catheters' [47]. They also reported that the CRT incidence was between '0.06 to 21 per 1000 CD or 0.6% to 33% of placed catheters' [47]. The NSCLS group rates in our study comparatively fall within the lower range of both categories. This suggests that the rates of CRT and CRBSI events in the control group are not exceptionally high. Furthermore, in 2008, Moran *et al.* [48] described that their rate of 'flow-related catheter exchange', almost equivalent to

catheter thrombosis, was 4.1/1000 CD in its heparin lock group. This suggests that the use of heparin may not have significantly decreased the rate of thrombosis compared with NSCLS. The evidence supports our hesitance in using heparin as a strategy to decrease thrombosis at our institution given the limited potential benefit compared with the harms and costs associated with its regular use.

We also considered if the statistically significant difference in mean albumin level between groups could have altered the results, yet a difference of only 0.1 mg/dL is not clinically significant and not consistent with affecting the results pertinent to this study [49].

Despite no statistically significant difference between the groups of catheters used, we considered the potential difference of catheters used within groups, and the collected data were further analyzed. *Post hoc* subgroup analysis applying the available data continued to demonstrate statistically significant differences between groups even when correcting for catheter type and tunneling as demonstrated in Table 3. These findings suggest that SBCLS is better than NSCLS at CRT and CRBSI prevention, regardless of the type of HD catheter used. SBCLS proved to be a superior lock solution that decreased the likelihood of CRT and CRBSI.

Our findings uphold the growing evidence that NaHCO3 is an overlooked ally of host immunity in the defense against pathogens and may be a solution to some of medicine's most urgent needs. The unique mechanism of action of bicarbonate has far-reaching effects on the activity of innate immune components and the effectiveness of antibiotics [36]. Furthermore, bicarbonate has remarkable power as an antibiotic adjuvant, suggesting that there is great potential to exploit this activity in the discovery and development of new antibacterial drugs [18, 23].

CONCLUSIONS

Using a standard NaHCO3 solution for locking CVCs will safely lead to a decreased incidence of HD catheter loss due to both CRT and CRBSI. The significance of this finding is self-evident. This solution is readily available in multiple care settings. The implementation of our protocol using SBCLS will be easy among these settings as there is otherwise no change to standard care. All facilities that provide HD and all patients with HD CVCs will greatly benefit from the reduced cost of treatment due to avoidance of expensive thrombolytics, catheter replacements and hospitalizations for CRBSI. This is a step forward in the improvement of HD patient care and possibly the care of patients with other venous catheter types.

ACKNOWLEDGEMENTS

We offer a very warm and special thanks to Robert Eric Heidel, PhD, Associate Professor of Biostatistics, Department of Surgery, University of Tennessee Graduate School of Medicine, for the many hours he assisted us with our statistics, and the dialysis team at Coney Island Hospital for the hard work, dedication and endurance they provided to make this study possible. We would also like to acknowledge the Medical Library staff and their Director, Laraine Tursi, MLS for their work on our literature review.

CONFLICT OF INTEREST STATEMENT

Patent number US 9,789,227B1, 17 October 2017, 'Lock solution for venous catheters using sodium bicarbonate'.

(See related article by Niyyar. Catheter dysfunction and lock solutions: are we there yet? *Nephrol Dial Transplant* 2019; 34: 1626–1628)

REFERENCES

1. Haddad NJ, Van Cleef S, Agarwal AK. Central venous catheters in dialysis: the good, the bad, and the ugly. *Open Urol Nephrol J* 2012; 5(Suppl 1: M3): 12–18
2. Niyyar VD, Chan MR. Interventional nephrology: catheter dysfunction-prevention and troubleshooting. *Clin J Am Soc Nephrol* 2013; 8: 1234–1243
3. Mojibian H, Spector M, Ni N *et al.* Initial clinical experience with a new heparin-coated chronic hemodialysis catheter. *Hemodial Int* 2009; 13: 329–334
4. Hemodialysis Adequacy 2006 Work Group. Clinical practice guidelines for hemodialysis adequacy, update 2006. *Am J Kidney Dis* 2006; 48(Suppl 1): S2–90
5. Oliver MJ, Callery SM, Thorpe KE. Risk of bacteremia from temporary hemodialysis catheters by site of insertion and duration of use: a prospective study. *Kidney Int* 2000; 58: 2543–2545
6. Miller LM, Clark E, Dipchand C *et al.* Hemodialysis tunneled catheter-related infections. *Can J Kidney Health Dis* 2016; 3: 1–11
7. Gahlot R, Nigam C, Kumar V *et al.* Catheter-related bloodstream infections. *Int J Crit Illness Sci* 2014; 4: 162–167
8. James MT, Conley J *et al.* Meta-analysis: antibiotics for prophylaxis against hemodialysis catheter-related infections. *Ann Intern Med* 2008; 148: 596–605
9. Jaffer Y, Selby NM, Taal MW *et al.* A meta-analysis of hemodialysis catheter locking solutions in the prevention of catheter-related infection. *Am J Kidney Dis* 2008; 51: 233–241
10. Labriola L, Crott R, Jadoul M *et al.* Preventing haemodialysis catheter-related bacteraemia with an antimicrobial lock solution: a meta-analysis of prospective randomized trials. *Nephrol Dial Transplant* 2008; 23: 1666–1672
11. Yahav D, Rozen-Zvi B, Gafter-Gvili A *et al.* Antimicrobial lock solutions for the prevention of infections associated with intravascular catheters in patients undergoing hemodialysis: systematic review and meta-analysis of randomized, controlled trials. *Clin Infect Dis* 2008; 47: 83–93
12. Rabindranath KS, Bansal T, Adams J *et al.* Systematic review of antimicrobials for the prevention of haemodialysis catheter-related infections. *Nephrol Dial Transplant* 2009; 24: 3763–3774
13. Snaterse M, Rüger W, Scholte Op Reimer WJM *et al.* Antibiotic-based catheter lock solutions for prevention of catheter-related bloodstream infection: a systematic review of randomized controlled trials. *J Hosp Infect* 2010; 75: 1–11
14. Landry D, Braden G. Reducing catheter-related infections in hemodialysis patients. *Clin J Am Soc Nephrol* 2014; 9: 1156–1159
15. Wong DW, Mishkin FS *et al.* The effects of bicarbonate on blood coagulation. *JAMA* 1980; 244: 61–62
16. Wong DW. Effect of sodium bicarbonate on in vitro conversion of fibrinogen to fibrin. *J Pharm Sci* 1980; 69: 978–980
17. El-Hennawy AS, Frolova E, Pollack E. First time sodium bicarbonate catheter lock solution is found to be a safe and effective lock method in preventing hemodialysis catheter loss due to lumen clot formation. *J Clin Nephrol Res* 2017; 4: 1078–1082
18. Farha MA, French S, Stokes JM *et al.* Bicarbonate alters bacterial susceptibility to antibiotics by targeting the proton motive force. *ACS Infect Dis* 2018; 4: 382–390

19. Dorschner RA, Lopez-Garcia B, Peschel A *et al.* The mammalian ionic environment dictates microbial susceptibility to antimicrobial defense peptides. *FASEB J* 2006; 20: 35–42
20. Paharik AE, Horswill AR. The staphylococcal biofilm: adhesins, regulation, and host response. *Microbiol Spectrum* 2016; 4: 1–27
21. Schachter B. Slimy Business-the biotechnology of biofilms. *Nat Biotechnol* 2003; 21: 361–365
22. Hall-Stoodley L, Costerton JW, Stoodley P. Bacterial Biofilm: from the natural environment to infectious disease. *Nat Rev Microbiol* 2004; 2: 95–108
23. Nostro A, Cellini L, Di Giulio M *et al.* Effect of alkaline pH on staphylococcal biofilm formation. *APMIS* 2012; 120: 733–742
24. Ní Eidhin D, Perkins S *et al.* Clumping factor B (ClfB), a new surface-located fibrinogen-binding adhesin of *Staphylococcus aureus*. *Mol Microbiol* 1998; 30: 245–257
25. Davis SL, Gurusiddappa S, McCrea KW *et al.* SdrG, a fibrinogen-binding bacterial adhesin of the microbial surface components recognizing adhesive matrix molecules subfamily from *Staphylococcus epidermidis*, targets the thrombin cleavage site in the bβ chain. *J Biol Chem* 2001; 276: 27799–27805
26. Drake D. Antibacterial activity of baking soda. *Compend Contin Educ Dent Suppl* 1997; 17: S17–S21
27. Selvi C, Ersoy A *et al.* Correcting a fundamental flaw in the paradigm for antimicrobial susceptibility testing. *BioMedicine* 2017; 20: 173–181
28. Newbrun E, Hoover C, Ryder M. Bactericidal action of bicarbonate ion on selected periodontal pathogenic microorganisms. *J Periodontol* 1984; 55: 658–667
29. Cheung HY, So CW, Sun SQ. Interfering mechanism of sodium bicarbonate on spore germination of bacillus stearothermophilus. *J Appl Microbiol* 1998; 84: 619–626
30. Dinerstein C. *A Spoonful of Baking Soda Helps the Antibiotics Go Down*. American Council on Science and Health. 2018. https://www.acsh.org/news/2018/01/11/spoonful-baking-soda-helps-antibiotics-go-down-12387 (18 April 2018, date last accessed)
31. Corral LG, Post LS, Montiville TJ. Antimicrobial activity of sodium bicarbonate. *J Food Sci* 1988; 1365–2621
32. Higashibata A, Fujiwara T, Fukumori Y. Studies on the respiratory system in alkaliphilic Bacillus; a proposed new respiratory mechanism. *Extremophiles* 1998; 2: 83–92
33. Chemical Compatibility Database. *Cole-Parmer*. https://www.coleparmer.com/Chemical-Resistance. (accessed 18 April 2018)
34. Chemical Compatibility Guide. *GRACO*. July 2013. http://www.graco.com/content/dam/graco/ipd/literature/misc/chemical-compatibility-guide/Graco_ChemCompGuideEN-B.pdf. (accessed 18 April 2018)
35. US Food and Drug Administration. *Warning on Tricitrasol Dialysis Catheter Anticoagulant*. FDA Talk paper (Apr) 16, 14 April 2000
36. Yevzlin AS, Sanchez RJ, Hiatt JG *et al.* Concentrated heparin lock is associated with major bleeding complications after tunneled hemodialysis catheter placement. *Semin Dial* 2007; 20: 351 4
37. Thomas CM, Zhang J, Lim TH *et al.* Concentration of heparin-locking solution and risk of central venous hemodialysis catheter malfunction. *ASAIO J* 2007; 53: 485–488
38. O'Grady NP, Alexander M, Dellinger EP *et al.* Guideline for the prevention of intravascular catheter-related infections. *Clin Infect Dis* 2002; 35: 1281–1307
39. Pelletier FQ, Joarder M, Poutanen SM *et al.* Evaluating approaches for the diagnosis of hemodialysis catheter–related bloodstream infections. *Clin J Am Soc Nephrol* 2016; 11: 847–854
40. Daugirdas JT, Goldstein S, Ing TS *et al.* National Kidney Foundation. KDOQI clinical practice guidelines and clinical practice recommendations for 2006 Updates: Hemodialysis adequacy, peritoneal dialysis adequacy and vascular access. *Am J Kidney Dis* 2006; 48: S1–S322, (suppl 1): 227–241
41. Krishnasami Z, Carlton D, Bimbo L *et al.* Management of hemodialysis catheter-related bacteremia with an adjunctive antibiotic lock solution. *Kidney Int* 2002; 61: 1136–1142
42. Dhingra RK, Young EW, Hulbert-Shearon TE *et al.* Type of vascular access and mortality in US hemodialysis patients. *Kidney Int* 2001; 60: 1443–1451
43. Poole CV, Carlton D, Bimbo L *et al.* Treatment of catheter-related bacteraemia with an antibiotic lock protocol: effect of bacterial pathogen. *Nephrol Dial Transplant* 2004; 19: 1237–1244
44. Deutschman C, Tracey K. Sepsis: current dogma and new perspectives. *Immunity* 2014; 40: 463–475
45. Parienti JJ, Thirion M *et al.* Femoral vs jugular venous catheterization and risk of nosocomial events in adults requiring acute renal replacement therapy: a randomized controlled trial. *JAMA* 2008; 299: 2413–2422
46. Hwang HS, Kang SH, Choi SR *et al.* Comparison of the palindrome vs. step-tip tunneled hemodialysis catheter: a prospective randomized trial. *Semin Dial* 2012; 25: 587–589
47. Napalkov P, Felici DM, Chu LK *et al.* Incidence of catheter-related complications in patients with central venous or hemodialysis catheters: a health care claims database analysis. *BMC Cardiovasc Disord* 2013; 13: 86
48. Moran JE, Ash SR; ASDIN Clinical Practice Committee. Locking solutions for hemodialysis catheters; heparin and citrate–a position paper by ASDIN. *Semin Dial* 2008; 21: 490–2
49. Bharadwaj S, Ginoya S, Tandon P *et al.* Malnutrition: laboratory markers vs nutritional assessment. *Gastroenterol Rep (Oxf)* 2016; 4: 272–280

Received: 1.8.2018; Editorial decision: 19.11.2018