Renal Journal Club

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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 ✉, Elena Frolova, Wesley A Romney

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OXFORD ACADEMIC

ndt NEPHROLOGY DIALYSIS TRANSPLANTATION

ORIGINAL ARTICLE

[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

Background

- There is no ideal lock solution
- Two major Complications:
  - Catheter-related thrombosis (CRT) and
  - catheter-related bloodstream infection (CRBSI)
- Catheter loss is associated with increased hospitalization and high inpatient costs.

- 42% of catheter-related dysfunction is attributable to CRT
- 35% probability of developing bacteremia within 3 months of catheter insertion
- Antibiotic locks demonstrated a reduction in CRBSI → antibiotic resistance
- Undertook this study for three reasons.
  1. US Food and Drug Administration issued an urgent warning that citrate-containing tricitrasol **may cause death** when infused into patients
  2. High-concentration (5000 or 10 000 U/mL) heparin-containing catheter locking solution is associated with **major bleeding complications** after tunneled HD catheter placement
  3. Low-concentration (1000 U/mL) heparin catheter lock solution is associated with **greater tissue plasmin alteplase use**

- Sodium bicarbonate ($NaHCO_3$) demonstrates
  - anti-infective and
  - anticoagulation properties
  - with a good safety profile, making it an ideal lock solution development target.
- NaHCO3 has been shown to
  - inhibit bacterial proliferation by
    - decreasing bacterial adherence and
    - preventing biofilm formation
- Bicarbonate-mediated chelation of calcium ions indirectly inhibited the conversion of fibrinogen to fibrin, leading to decreased clotting

- This group previous clinical study →
  - 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
  - Also found no CRBSI in the group using SBCLS.
    - not be statistically validated because the sample size was not large enough.
    - Based on the extensive literature review, hypothesized that sodium bicarbonate (NaHCO3) can play an important role in preventing catheter loss due to CRBSI by multiple anti-infective mechanisms.

Trial Objectives

- 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

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
- 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.
  - The NSCLS contained 0.9% sodium chloride at a pH of 4.5–7.0 and was used to lock NSCLS group catheters.
- 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

- 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.
- 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

- A total of **451 patients**
- 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.
- Intraluminal SBCLS or NSCLS lock solution was removed before connecting the HD catheter to a dialysis machine prior to any treatment.
- 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.

- Patients who had clotted catheters, → catheter replacement

Primary Outcome Measures

1. Lumen Clot Formation [Time Frame: Approximately 18 months]Catheter Loss Due to Lumen Clot Formation

2. Catheter Related Infection [Time Frame: Approximately 18 months]Catheter Loss Due to Catheter Related Infection

3. Malfunction [Time Frame: Approximately 18 months]Catheter Loss Due to Malfunction

4. Overall Cause [Time Frame: Approximately 18 months]Catheter Loss Due to All Causes

- **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.

- National Kidney Foundation guidelines,
  - **catheter dysfunction** was defined when extracorporeal blood flow was ≤300 mL/min or the prepump arterial pressure was ≥−250 mmHg [40].

- **Catheter loss** due to CRT was defined as
  - persistent catheter malfunctioning, irreversible difficulty with line aspiration or infusion despite repositioning before or during HD

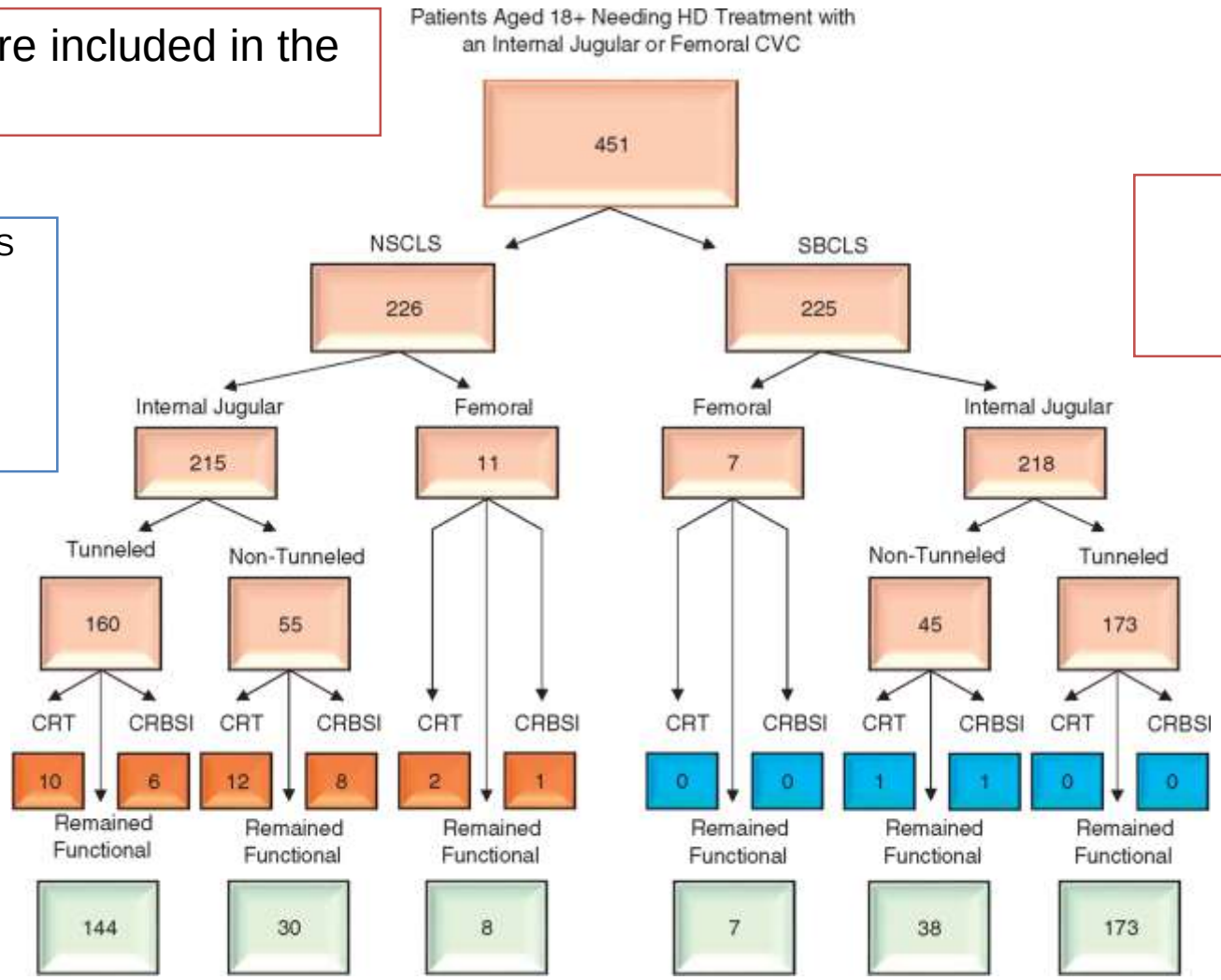
Results

FIGURE 2: Groups and outcomes.

A total of 451 patients were included in the sample

•226/451 (50.1%) were in the NSCLS group
•underwent a combined 2480 treatments corresponding to 5787 catheter days

•225/451 (49.9%) in the SBCLS group.
•underwent a combined 2474 treatments corresponding to 5773 CD.



Nephrology Dialysis Transplantation, 21 January 2019, gfy388, https://doi.org/10.1093/ndt/gfy388

Characteristics of the Patients at Baseline

- There were no significant differences between groups on outset demographics or exposure, except for serum albumin level (P = 0.006)

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.

Primary outcome variables

Table 2.

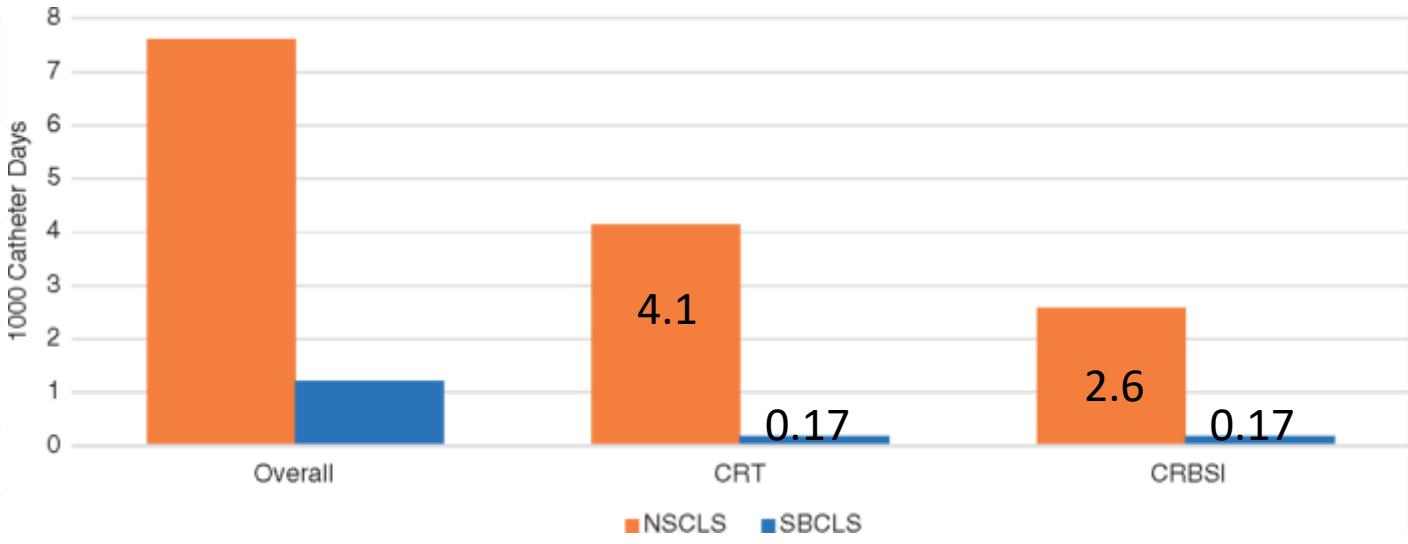
Catheter loss outcomes by cause

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	7	<0.0001*	7.5 (3.31–17.12)

a Unadjusted ORs with 95% CIs.

* Statistical significance P < 0.05.

Catheter loss rate:



No deaths or significant adverse events related to HD occurred in any group.

Comparing tunneled and nontunneled catheters used in the internal jugular site

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.

Caveats

Outcomes of the Use of Sodium Bicarbonate (8.4%) Solution as a Catheter Lock Solution to Prevent Hemodialysis Catheter Loss Due to Lumen Clot Formation

ClinicalTrials.gov Identifier: NCT03627884

Recruitment Status : Completed
First Posted : August 14, 2018
Last Update Posted : August 14, 2018

Sponsor:
Coney Island Hospital, Brooklyn, NY

Information provided by (Responsible Party):
Adel S EL-Hennawy, Coney Island Hospital, Brooklyn, NY

Study Design

Go to

Study Type :	Interventional (Clinical Trial)
Actual Enrollment :	451 participants
Allocation:	Randomized
Intervention Model:	Parallel Assignment
Masking:	None (Open Label)
Primary Purpose:	Prevention
Official Title:	Outcomes of the Use of Sodium Bicarbonate (8.4%) Solution as a Catheter Lock Solution as a Catheter Lock Solution to Prevent Hemodialysis Catheter Loss Due to Lumen Clot Formation
Actual Study Start Date :	October 1, 2016
Actual Primary Completion Date :	March 30, 2018
Actual Study Completion Date :	March 30, 2018

Detailed Description:

A randomized, comparative clinical, open-label trial at Coney Island Hospital, in Brooklyn, NY. The study period was between October 1, 2016 and March 30, 2018, a total of 546 days. All patients provided written informed consent before enrollment. The trial protocol was approved by Maimonides Medical Center Investigational Review Board: Study #2015-06-25-CIH. Patients presenting over the age of 18 requiring hemodialysis via CVCs were eligible. One patient was excluded due to having 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, non-tunneled IJV catheters, and non-tunneled femoral vein catheters. All patients were randomly assigned based on simple sequential order into one of two groups: NSCLS (n = 226) and SBCLS (n = 225). NSCLS patients were assigned between October 1, 2016 and June 30, 2017. SBCLS patients were assigned between July 1 2017 and March 30, 2018. Recruitment ended based on the similar number of enrolled participants between groups. A primary or co-investigator 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.

Will this be a *retrospective* study, a *prospective* study, or will it be both *retrospective* and *prospective?*

You may choose more than one answer, if applicable.

A proposed research project is generally either *retrospective, prospective,* or both.

Retrospective

The IRB will need to know whether the data collection is retrospective and/or prospective to determine if certain exemptions or waivers can be applied to the research.

***Retrospective** means the data already exits; however, please also select **"retrospective"** if requesting a **prospective** chart review of medical records if they do not exist at the time of the study proposal, but will be reviewed **retrospectively** at the time that the research is conducted and at a time when the patients are not available (e.g., patients would not be in the hospital while the study is being conducted and will not be available for follow-up).*

***Prospective** means that the data does not yet exist.*

Maimonides Medical Center
IRB/Research Committee

View xForm - IRB Application

This "IRB Application" xForm must be used when submitting a new study to the IRB. NOTE: This xForm must also be used for Maimonides research that will be overseen by an external IRB, so that the Maimonides IRB can assess other institutional requirements. (Version 9.2; Published 09.28.2015)

Application Data Entry
- Submitted 6/12/2017 2:58:29 PM ET by EL-Hennawy, Adel MD

Amendment Information

Study #

2015-06-25

Describe where the research data will reside and who will have access to hold or maintain the data?

The PI and co-investigator will have access to the study data. All research data will be kept in a password-protected computer in the Nephrology Department at Coney Island Hospital.

Fully describe any data repository, data warehouse, file server, or database, including the location and institution and the expected duration of the storage.

Describe who will manage the data and any rules for how data can be released to others.

If coded data are stored, the specific details regarding coding agreements or who will have access to the code should be described.

Note: The informed consent or information sheet, when applicable, should describe the the protections in place for the research participants.

Describe the study design and methods.

Methods:
This quality improvement study.

Retrospectively, we will review medical records of patients who were admitted to Coney Island Hospital (CIH) in Brooklyn, New York that need dialysis via catheter over a six month period.

We will review the medical records of patients who were admitted during the study period at CIH to identify those who meet the inclusion criteria.

We will look at patients that were given sodium bicarbonate as a catheter lock solution admitted with a diagnosis of renal failure (acute or chronic failure) and requires hemodialysis treatment using a hemodialysis catheter (tunneled or non-tunneled catheter). Upon completion of hemodialysis treatment, each lumen of the catheter will be flushed with 17.5 mL of $NaHCO_3$ 8.4 % and locked with the 2.5 mL of locking solution. The catheters are monitored for thrombosis at each hemodialysis treatment. Thrombosis will be evaluated by resistance or complete occlusion to inflow or outflow of catheter ports before initiation of heparin free hemodialysis or during hemodialysis treatment if blood flow is less than 200 ml/min. Data will be collected from patients' EMR, nursing notes and Interventional radiologist reports and placed onto the data collection tool in Excel.

Strength

- Primary outcome relevant to patients
- Topic relevant to daily practice
- Clear definitions
- No overlap
- Population: good number

Weakness

- No blinding
- Comparison group not relevant to UK practice
- Wide CI
- Jumbled chronic and acute
- Single centre
- Writer is the patent holder
- Trial protocol document shows it as a retrospective study for NSCLS and prospective for SBCLS
- No clear explanation of randomisation,
- PI had access to data kept on a computer in the nephrology department
- Registered on the trial website after completion of the study

Conclusion

- Bigger, well designed and multicentre study needed
- Too early to change any practice based on this paper

Thank you