Comparison of Tetrasodium EDTA 4% with Sodium Citrate 4% as Line-Locking Solutions at 2 Tertiary Hemodialysis Centres

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ABSTRACT

Background: The patency of central venous catheters (CVCs) in patients undergoing hemodialysis (HD) is maintained by instilling sodium citrate 4% (SC 4%) locking solution. Alteplase, a thrombolytic agent, is administered to restore function if patency is lost.

Objective: To compare SC 4% with a new line-locking solution, ethylenediaminetetraacetic acid 4% (EDTA 4%), in terms of CVC patency and alteplase use.

Methods: This retrospective chart review included all HD patients who were switched from SC 4% to EDTA 4% locking solution at 2 tertiary HD centres between June and December 2021. Patients were switched to EDTA 4% if they had high usage of alteplase (receiving ≥ 2 doses of alteplase in a 2-week period). For each line-locking agent, HD pump speeds and alteplase use were analyzed over 2 consecutive 12-week periods. Mean serum calcium and ionized calcium values were recorded during each period. A cost analysis was also performed.

Results: A total of 37 HD patients were switched to EDTA 4% during the study period. There was no difference in mean HD pump speed between SC 4% and EDTA 4% (307.7 vs 305.1 mL/min, $p = 0.48$). The number of catheter-use-days on which alteplase was required declined significantly, from 313 days with SC 4% to 94 days with EDTA 4% ($p < 0.001$), with an overall cost reduction of 34% ($13 183.21). The decrease in alteplase usage was primarily driven by 1 of the 2 sites. A statistically significant decrease in mean ionized calcium at site 2 (from 1.12 to 1.1 mmol/L, $p = 0.037$) was noted. As well, an intraluminal interaction between EDTA 4% and serum calcium caused 6 cases of low serum calcium.

Conclusions: This study showed that use of EDTA 4% as a line-locking agent reduced alteplase usage in the CVCs of HD patients while maintaining adequate pump speed (i.e., ≥ 300 mL/min).

Keywords: hemodialysis, ethylenediaminetetraacetic acid (EDTA), catheter, locking solution

RÉSUMÉ

Contexte : La perméabilité des cathéters veineux centraux (CVC) chez les patients hémodialysés (HD) est maintenue en instillant une solution de verrouillage de citrate de sodium à 4 % (CS 4 %). L'alteplase, un agent thrombolytique, est administré pour rétablir la fonction en cas de perte de perméabilité.

Objectif : Comparer la solution de CS 4 % et une nouvelle solution de verrouillage, l'acide éthylènediaminetétraacétique 4 % (EDTA 4 %), en termes de perméabilité du CVC et d'utilisation de l'alteplase.

Méthodes : Cet examen rétrospectif des dossiers a été réalisé pour tous les patients HD qui sont passés de la solution de verrouillage de CS 4 % à la solution d'EDTA 4 % dans 2 centres d'hémodialyse tertiaires au cours de la période de juin à décembre 2021. Les patients sont passés à l'EDTA 4 % en cas d'utilisation élevée de l'alteplase (≥ 2 doses d'alteplase reçues sur une période de 2 semaines). Pour chaque agent de verrouillage, les vitesses de la pompe d'hémodialyse et l'utilisation de l'alteplase ont été analysées sur 2 périodes consécutives de 12 semaines. Les valeurs moyennes de calcium sérique et de calcium ionisé ont été enregistrées au cours de chaque période. Une analyse des coûts a également été réalisée.

Résultats : Au total, 37 patients HD sont passés à l'EDTA 4 % au cours de la période de l'étude. Aucune différence dans la vitesse moyenne de la pompe d'hémodialyse n'a été constatée en cas d'utilisation de la solution de CS 4 % ou d'EDTA 4 % (307,7 c. 305,1 mL/min, $p = 0,48$). Le nombre de jours d'utilisation du cathéter qui ont nécessité l'utilisation de l'alteplase a diminué de manière significative, passant de 313 jours avec la solution de CS 4 % à 94 jours avec l'EDTA 4 % ($p < 0,001$); la réduction globale des coûts se montait à 34 % (économies de 13 183,21 $). L'utilisation moins importante de l'alteplase était principalement due à 1 des 2 sites. Une diminution significative du calcium ionisé moyen (1,12 c. 1,1 mmol/L, $p = 0,037$) a été observée au deuxième site. De plus, une interaction intraluminale entre l'EDTA 4 % et le calcium sérique a provoqué 6 cas d'hypocalcémie.

Conclusions : Cette étude a montré que l'utilisation de l'EDTA 4 % comme agent de verrouillage réduisait l'utilisation de l'alteplase dans les CVC des patients HD tout en maintenant une vitesse de pompe adéquate (c'est-à-dire ≥ 300 mL/min).

Mots-clés : hémodialyse, acide éthylènediaminetétraacétique (EDTA), cathéter, solution de blocage, solution de verrouillage

INTRODUCTION

Central venous catheters (CVCs) are a common vascular access option for patients undergoing hemodialysis (HD).[1] Maintaining CVC patency between HD runs involves instilling a line-locking solution into each lumen at the end of a run, which is then withdrawn before initiation of dialysis at the next session. The primary causes for loss of catheter patency are formation of a thrombus within the catheter and formation of an external fibrin sheath.[2] Catheter-related infections are another serious complication.[2] Sodium citrate 4% (SC 4%), a calcium chelator, is currently the preferred line-locking solution for CVCs in HD patients.[3,4] This compound has been shown to be equivalent or superior to heparin in maintaining catheter function and offers the advantage of no bleeding risk.[5-7] If a CVC occlusion does occur, alteplase is used on a one-time basis as the line-locking agent to break down the clot. In some patients, alteplase may be used prophylactically for frequent occlusions.[8] However, alteplase is considerably more expensive than traditional locking agents (see Appendix 1).

In 2018, tetrasodium ethylenediaminetetraacetic acid (EDTA 4%; KiteLock, SterileCare Inc) became available as a line-locking agent. Like SC 4%, EDTA 4% exhibits its anticoagulant effects through chelation of calcium, which is required for activation of calcium-dependent clotting factors in the coagulation cascade.[9] The evidence for efficacy of EDTA 4% relative to SC 4% locking solution is limited. In a small study involving 22 HD patients, reported only in abstract form, EDTA 4% significantly reduced alteplase usage relative to SC 4%.[10] Other studies involving patients receiving parenteral nutrition have also shown significantly lower usage of alteplase with EDTA 4% than with other locking solutions (normal saline, taurolidine, ethanol).[11-13] Conversely, the largest published study involving HD patients compared EDTA 4% with heparin in 117 participants and showed an increase in alteplase usage; however, that study used a different baseline population and focused on catheter colonization.[14]

Given the potential for EDTA 4% to reduce alteplase usage, CVC locking with EDTA 4% was initiated in September 2021 for patients with high alteplase requirements who were receiving dialysis in 2 large outpatient HD units. The purpose of this study was to compare EDTA 4% with SC 4% in terms of efficacy in maintaining CVC patency and reducing alteplase usage, as well as effects on catheter-related infections. A cost analysis was also performed to determine if there was a cost benefit with EDTA 4%.

METHODS

Patient Population

This study was a retrospective chart review conducted at 2 tertiary HD outpatient centres (site 1 and site 2) from June 1 to December 17, 2021. Patients were switched in mid-September 2021 to EDTA 4%. Selection criteria were based on high alteplase usage, which was defined as having received at least 2 separate instillations of alteplase within a 2-week period or receiving prophylactic alteplase lock on a weekly basis. Patients receiving antibiotic lock solutions were not switched to EDTA 4%. In-service sessions were provided to health care staff to describe the various line-locking solutions (SC 4%, EDTA 4%, alteplase), including their mechanisms of action, doses, costs, and administration techniques. All HD patients who were switched to EDTA 4% with a plan for at least 12 weeks of therapy and who had received SC 4% for 12 weeks before the switch were included. Patients were excluded if they did not receive at least 4 weeks of EDTA 4% therapy.

The 2 line-locking solutions, before and after the switch, were administered in the same manner. The total volume of solution instilled into each CVC lumen was the internal lumen volume plus 0.3 mL. Before the next HD session, the locking solution was withdrawn, and each lumen was prepared for dialysis as follows: 5 mL of blood was withdrawn from the catheter and discarded; 3–10 mL of blood was aspirated to assess for clots and then re-instilled as a flush (a step that could be repeated up to 3 times to evaluate lumen flow); and then 20 mL of normal saline was forcefully flushed through the lumen.

Data Collection

The following baseline characteristics were collected, based on chart data recorded at the time of initiation of the EDTA 4% phase: primary renal disease, comorbidities, dialysis and CVC vintage, CVC type and location, and concomitant anticoagulant or antiplatelet medication. Laboratory data included mean serum calcium (site 1) or ionized calcium (site 2), measured every 6 weeks, as part of regularly scheduled bloodwork, starting 12 weeks before the switch (SC 4% phase) to 12 weeks after the switch (EDTA 4% phase). To assess for CVC-related infections during the 12-week period for each locking solution, we reviewed all microbiology results relating to the CVC wound, catheter tip, or blood, as well as any relevant antibiotics ordered. Removal and replacement of the CVC line were also recorded.

Alteplase use was characterized as either weekly (i.e., prophylaxis) or as needed. Any deviations from the EDTA 4% protocol during the EDTA 4% phase (e.g., SC 4% used instead of EDTA 4%) were noted. The proportion of catheter-use-days on which alteplase was required was calculated by summing the number of days with alteplase use across all patients and then dividing by the total number of catheter days per patient per phase.

Data relating to catheter patency were recorded from the 2-week period at the end of each phase, specifically mean dialysis pump speed (mL/min), efficiency of dialysis (expressed as K_t/V), and volume (L) of blood processed per

HD session, along with nursing comments regarding line flow (e.g., unable to aspirate, "sluggish" line), appearance of dialyzer, and whether any reversal of lines occurred. Adverse effects at any time during the EDTA 4% phase were also recorded.

Cost analysis was performed by summing all doses of the locking solutions administered during each 12-week phase and multiplying by the cost per unit dose for each medication (Appendix 1).

Outcomes

The primary outcome was the efficacy of EDTA 4% (relative to SC 4%) in terms of its ability to maintain mean HD blood pump speed greater than or equal to 300 mL/min[15] and any change in alteplase usage.

Secondary outcomes were differences in total cost and catheter-related infections between the 2 line-locking agents.

Data Analysis

Categorical variables were summarized as frequencies and percentages. Quantitative variables were summarized using means and standard deviations (SDs) (age, weight, dialysis and catheter vintage, HD pump speed, K_t/V, volume of blood processed) or median with interquartile range (IQR) (alteplase use per patient). Univariate analyses used either a 2-tailed t test to compare quantitative variables or χ^2 test to analyze categorical variables, with p values less than 0.05 considered significant.

The study was approved by the institutional ethics board and research institute.

RESULTS

Of the 42 patients switched to EDTA 4%, 5 patients were excluded for the following reasons: death before receiving 4 weeks of EDTA 4% (n = 3), transfer to another dialysis unit (n = 1), or refusal to receive EDTA 4% (n = 1). The final analysis thus included 37 patients: 18 patients at site 1 and 19 patients at site 2.

Baseline characteristics are presented in Table 1. For all variables, the patients were similar between the 2 sites, with the exception of age and type of catheter used. The patients at site 1 were significantly older than those at site 2 (mean 81 vs 66 years, p = 0.003). At site 1, the Equistream catheter (Bard Access Systems Inc) was used for all patients. At site 2, the Palindrome catheter with Tal VenaTrac insertion stylet (Covidien) was used for most patients (n = 17, 89%), with Equistream and Hemosplit (Bard Access Systems Inc) catheters used for 1 patient each. Approximately 40% of patients at each site were receiving acetylsalicylic acid. Although the difference was not statistically significant, a lower proportion of patients at site 1 than at site 2 were receiving weekly alteplase prophylaxis (39% [n = 7] vs 63% [n = 12], p = 0.14). Weekly prophylactic doses of alteplase also differed between sites: 1 mg per lumen at site 1 (n = 7) and 2 mg per lumen at site 2 (n = 12).

Primary Outcome

HD pump speeds of at least 300 mL/min were maintained in both phases of the study (307.7 mL/min with SC 4% vs 305.1 mL/min with EDTA 4%) (p = 0.48) (Table 2). There were no significant differences in mean dialysis efficiency (K_t/V) or mean volume (L) processed per run. In the SC 4% phase, 3 patients at site 1 had missing data during the specified period, and information from 2 weeks before the intended data collection period was used instead. During the EDTA 4% phase, SC 4% was administered in 20 (1.6%) of the 1264 HD sessions for which EDTA 4% should have been used, primarily because the patients had been admitted to hospital.

Total alteplase administered declined from 1084 mg during the SC 4% phase to 342 mg in the EDTA 4% phase. The number of catheter-use-days when alteplase was required was significantly reduced, from 313 days in the SC 4% phase to 94 days in the EDTA 4% phase (p < 0.001). This decrease was driven primarily by site 2 (Table 3). More

TABLE 1. Patient Characteristics

Characteristic	No. (%) of Patients[a] (n = 37)
Age (years) (mean ± SD)	73.6 ± 14
Weight (kg) (mean ± SD)	67.6 ± 19.3
Gender, male	22 (59)
Dialysis vintage (months) (mean ± SD)	47.5 ± 50.8
Central venous catheter	
HD catheter location	
Right internal jugular	27 (73)
Other	10 (27)
Catheter type	
Equistream (Bard Access Systems Inc)	19 (51)
Palindrome (Covidien)	17 (46)
Hemosplit (Bard Access Systems Inc)	1 (3)
Catheter vintage (months) (mean ± SD)	13.2 ± 14.5
Comorbidities	
Hypertension	33 (89)
Diabetes mellitus	18 (49)
Heart failure	16 (43)
Antiplatelet/anticoagulation	
ASA	14 (38)
Clopidogrel	3 (8)
Warfarin	2 (5)
Alteplase regimen before EDTA 4%	
Weekly	19 (51)
As needed	18 (49)

ASA = acetylsalicylic acid, EDTA = ethylenediaminetetraacetic acid, HD = hemodialysis, SD = standard deviation.
[a]Except where indicated otherwise.

specifically, the reduction in alteplase administration (in terms of catheter-use-days) was 94% at site 2 compared with 48% at site 1. In the EDTA 4% phase, there were 13 patients (35%) who no longer required alteplase (1 patient at site 1 and 12 patients at site 2). Overall, only 1 patient returned to weekly prophylaxis with alteplase during the EDTA 4% phase.

Secondary Outcomes

There were no differences in CVC line infections or line removal/replacement between phases of the study (Table 2) or between sites. During the SC 4% phase, there were 2 cases of CVC line–related bacteremia (due to methicillin-sensitive *Staphylococcus aureus* and methicillin-resistant *S. aureus*, respectively), both necessitating line removal. There was

TABLE 2. Outcomes

Outcome	SC 4% Phase (n = 37)	EDTA 4% Phase (n = 37)	p Value
Dialysis efficiency[a]			
Blood pump speed (mL/min) (mean ± SD)	307.7 ± 20.6	305.1 ± 24.6	0.48
K_t/V (mean ± SD)	1.5 ± 0.34	1.48 ± 0.4	0.83
Volume (L) processed per run (mean ± SD)	73.2 ± 12.7	72.5 ± 17.8	0.82
Alteplase usage			
Total amount used (mg)	1084	342	
Use per patient (mg) (median and IQR)	26 (16-42)	4 (0-12)	
No. (%) of total catheter-use-days requiring alteplase	313/3108 (10.1)	94/2967 (3.2)	< 0.001
No. (%) of patients requiring any alteplase	37 (100)	24 (65)	< 0.001
Once weekly	19 (51)	1 (4)	
As needed	18 (49)	23 (96)	
Locking solution cost per 12-week period ($)[b]	38 862.61	25 679.40	
CVC issues (no.)			NA
Infections[c]	3	3	
Line removal and replacement	7	5	
Nursing comments[a] (no.)			0.22
Line reversal	23	24	
Unable to aspirate	2	5	
Sluggish line	39	47	

CVC = central venous catheter, EDTA 4% = ethylenediaminetetraacetic acid 4%, IQR = interquartile range, K_t/V = measure of efficiency of dialysis (where K = clearance, t = time, V = volume), NA = not applicable, SC 4% = sodium citrate 4%, SD = standard deviation.
[a]Data derived from the last 2 weeks of each line-locking solution period, except for 3 patients at site 1, for whom the closest 2 weeks of data available near the end of the period were used.
[b]See Appendix 1 for costs.
[c]With sodium citrate 4%: CVC line infection (n = 2), exit site infection (n = 1). With EDTA 4%: CVC line infection (n = 1); exit site infection (n = 2).

TABLE 3. Primary Outcomes by Site

	Site 1 (n = 18)		Site 2 (n = 19)	
Variable	SC 4%	EDTA 4%	SC 4%	EDTA 4%
Pump speed (mL/min) (mean ± SD)[a]	305.1 ± 13.3	301.0 ± 19.8	310.1 ± 26.4	308.9 (29)
Alteplase usage				
Total amount used (mg)	474	308	610	34
Use per patient (mg) (median and IQR)	24 (16.5–27.5)	14 (6–22)	40 (14–48)	0 (0–4)
No. (%) of total catheter-use-days requiring alteplase	163/1512 (10.8)	85/1512[c] (5.6)	150/1596 (9.4)	9/1455[c] (0.6)
No. (%) of patients requiring any alteplase	18 (100)	17 (94)	19 (100)	7[c] (37)
Locking solution cost per 12-week period ($)[b]	17 065.17	17 182.51	21 797.44	8496.89

EDTA 4% = ethylenediaminetetraacetic acid 4%, IQR = interquartile range, SC 4% = sodium citrate 4%, SD = standard deviation.
[a]Values determined from the last 2 weeks of each line-locking solution period, except for 3 patients at site 1, for whom the closest 2 weeks of data available near the end of the period was used.
[b]See Appendix 1 for the cost of each line-locking solution.
[c]Significantly different from SC 4% at the same site (p < 0.001).

also 1 exit site infection (due to coagulase-negative *Staphylococcus*). During the EDTA 4% phase, there was 1 case of CVC line–related bacteremia (due to methicillin-sensitive *S. aureus)* for which line removal was required, and 2 exit site infections (due to methicillin-resistant *S. aureus* and *Staphylococcus epidermidis*, respectively), neither of which required line removal. The remainder of line removals (n = 5 in the SC 4% phase, n = 4 in the EDTA 4% phase) were due to catheter dysfunction issues. The number of nursing chart comments in the last 2 weeks of each phase (line reversal, unable to aspirate, sluggish line) were also similar in both phases and at both sites.

At site 1, mean serum calcium did not differ significantly between the 2 phases (2.16 [SD 0.2] mmol/L vs 2.13 [SD 0.1] mmol/L, $p = 0.57$). However, the latter value, for the EDTA 4% phase, excludes 6 erroneous serum calcium values that arose secondary to an interaction between EDTA 4% and the calcium within the catheter lumen (Table 4). In these cases, repeat serum calcium and ionized calcium values based on samples drawn at the next dialysis session were within the expected ranges. For site 2, a statistically significant decrease in ionized calcium was observed, from 1.12 mmol/L in the SC 4% phase to 1.10 mmol/L in the EDTA 4% phase ($p = 0.037$).

Cost Analysis

The overall cost of all locking solutions (SC 4%, EDTA 4%, alteplase) was reduced by $13 183.21 (34%) at study end (Table 3). This reduction in cost was due to savings achieved at site 2 (costs increased slightly at site 1).

DISCUSSION

To our knowledge, this is the first published study to specifically assess the effect of EDTA 4% on CVC patency as a primary outcome in HD patients. This retrospective 24-week study of 37 HD patients provides evidence suggesting that switching patients with high alteplase usage from SC 4% to EDTA 4% improves catheter patency, as indicated by a reduction in alteplase usage. Catheter-use-days on which alteplase was required declined from 313 days (10.1% of total catheter-use-days) in the SC 4% phase to 94 days (3.2%) in the EDTA 4% phase ($p < 0.001$). Furthermore, the quality of dialysis during the EDTA 4% phase was maintained, as shown by similar HD pump speeds of at least 300 mL/min, dialysis efficiency (K_t/V), and volume processed per HD run. The improvement in catheter patency with EDTA 4% may be attributed to several factors, including increased potency of EDTA 4% as a calcium chelator relative to SC 4%, leading to an increase in anticoagulation effects,[16] and reduction in biofilm formation, which has previously been associated with increased risk of thrombus development.[17,18]

The reduction in alteplase usage during the EDTA 4% phase was most notable at site 2, which had a 94% drop in usage (150 vs 9 catheter-use-days), whereas site 1 had a 48% reduction (163 vs 85 catheter-use-days). The number of orders for alteplase declined at site 2 despite similar frequency of nursing comments in the charts suggesting CVC dysfunction during the 2 phases. One possible reason for decreased alteplase usage could be improved prescriber awareness (through in-service sessions) of the costs of the various locking solutions. As well, all weekly alteplase prophylaxis was given as 2 mg per lumen at site 2, as opposed to the guideline-recommended 1 mg per lumen used at site 1.[19] During the EDTA 4% phase, no patients at site 2 went back to receiving weekly alteplase administration, which suggests that periodic evaluation of alteplase prophylaxis is required. At site 1, there were also 3 patients who consistently had poor line function requiring multiple doses of alteplase, which might have skewed the results. These 3 patients accounted for 34% of all alteplase usage at site 1 in the SC 4% phase and 43% of usage during the EDTA 4% phase. Removal of these outliers from the analysis yielded total cost savings with the use of EDTA 4% of $281.36 at site 1. Similar outliers were

TABLE 4. Low Serum Calcium Measurements during Administration of EDTA 4% (Site 1)

Patient	Initial Serum Calcium (mmol/L)	Repeat Serum Calcium[a] (mmol/L)	Repeat Ionized Calcium[a] (mmol/L)
Normal range	2.1–2.55	2.1–2.55	1.1–1.3
1[b]	1.69	2.13	1.12
1[b]	1.44	–	1.18
2	1.69	–	1.19
3	1.77	2.15	1.04
4	< 1.25	1.88	0.99
5	< 1.25	2.28	1.19

EDTA = ethylenediaminetetraacetic acid.
[a]Measured at next hemodialysis session (48 hours later).
[b]Same patient at different draw times.

not present at site 2. Finally, the Equistream catheter was used for all patients at site 1 and the Palindrome for most patients at site 2; it is unclear whether catheter type may have contributed to outcome differences between the sites.

We performed a post hoc quality assurance analysis for 2 consecutive 12-week periods after the EDTA 4% phase (first period, $n = 36$ patients; second period, $n = 32$ patients) to determine whether the reduction in alteplase usage was sustained. We found that the number of catheter-use-days on which alteplase was required rose slightly from 94 during the EDTA 4% phase of the study to 116 and 106 days, respectively, for the 2 subsequent periods, but was still significantly less than the initial 313 alteplase catheter-use-days in the SC 4% phase ($p < 0.001$ for each post hoc period). At site 1, there was an increase to 6 patients requiring weekly alteplase in this post hoc analysis, compared with 1 patient during the EDTA 4% phase. No patients at site 2 were restarted on weekly alteplase during or after the switch to EDTA 4%.

The article by Kanaa and others[14] is the only previously published trial evaluating EDTA 4% in HD patients. This prospective randomized, nonblinded trial compared EDTA 4% and heparin 5000 units per lumen as line-locking solutions. All 117 HD patients were switched to EDTA 4%, with monitoring over a period of 8 months. The primary outcome was incidence of catheter colonization, and the secondary outcome was requirement for use of thrombolytics to restore patency. These authors found significantly increased use of alteplase line locks in the EDTA 4% phase (23 vs 64 locks, $p < 0.001$). The major difference between that study and ours was the use of heparin as the line-locking comparator, although trials have shown similar efficacy in terms of catheter patency between heparin and SC 4%.[5-7] As well, all patients in the Kanaa trial[14] were switched to EDTA 4%, whereas we used a more targeted approach, focusing on patients with high usage of alteplase. Contrariwise, in a recent abstract, Ouellet reported a mean reduction of 1.68 sessions/month requiring alteplase among 22 patients after being switched from SC 4% to EDTA 4% (based on 3 months of data for each period).[10] However, that study was a retrospective review and was limited by its small sample size.

Currently, SC 4% represents the least expensive of the line-locking options. Despite the approximately 6 times higher cost of EDTA 4% relative to SC 4% (see Appendix 1), our study showed an overall cost savings of $13 183.21 when 37 patients with high alteplase usage were switched to EDTA 4%. In terms of overall costs, our study showed that a reduction of more than 50% in alteplase usage (expressed as catheter-use-days), relative to usage with SC 4%, is needed to achieve a cost benefit with EDTA 4%. More specifically, to offset the increased cost of EDTA 4%, for every 7 dialysis sessions in which EDTA 4% is used in place of SC 4%, there must be a reduction of 1 session during which alteplase is administered. Other potential cost savings associated with prevention of line occlusion (e.g., radiology, personnel, line replacement) were not quantified, as they were beyond the scope of this study.

We found no difference between the SC 4% and EDTA 4% phases with respect to the number of CVC-related infections, although our sample size was likely too small and the duration of EDTA 4% use too short to fully elucidate any appreciable difference. Kanaa and others,[14] in their study of 117 HD patients, found a clinically significant decrease in CVC colonization per 1000 catheter-days. In a small study of 22 patients receiving parenteral nutrition, there was also a significant reduction in catheter-associated bloodstream infections.[13]

In our study, we also evaluated the effects of EDTA 4% on serum and ionized calcium values. At site 1, there was no significant difference in mean serum calcium between the 2 line-locking phases, but there were 5 patients who, on a total of 6 occasions, initially had erroneously low serum calcium results (Table 4). In all cases, repeat measurements of both serum and ionized calcium at the next HD session were within the expected range. The initial low calcium values were thought to be due to an interaction within the catheter between EDTA 4%, a strong calcium chelator, and serum calcium. Nurses were reminded of proper flushing technique, which likely resulted in more accurate blood level measurements on the next HD run. Interestingly, at site 2, there was a statistically significant decrease in mean ionized calcium in the EDTA 4% phase (1.12 vs 1.10 mmol/L; $p = 0.037$). Although this difference is likely not clinically relevant, proper catheter flushing technique was also reviewed at site 2.

This study had several limitations. It was a retrospective chart review and therefore reliant on the accuracy of previously recorded data. For 3 patients at site 1, data were missing for the 2-week period before the switch to EDTA 4%, and data from the 2-week period closest to the switch date were used instead. In the EDTA 4% phase, patients erroneously received SC 4% in 20 (1.6%) of the 1264 HD sessions. The small sample size allowed for outliers with disproportionately high usage of alteplase to potentially skew results. As well, the study was likely underpowered to test for statistical significance. There may also have been performance bias, given that prescribers and nurses were aware that the patients were receiving EDTA 4%, which may have influenced their decision to opt for alteplase. Similarly, education provided before the switch to EDTA 4%, which included information about the high cost of alteplase, may have affected prescribers' decisions to minimize alteplase prescribing.

CONCLUSION

This retrospective study of 37 patients undergoing dialysis in 2 HD units showed a decrease in the requirement for

alteplase to maintain catheter patency in patients switched from SC 4% to EDTA 4% lock solution over a 12-week period, while maintaining a similar quality of dialysis. The decrease in usage of alteplase and overall cost savings were primarily driven by 1 of the 2 HD sites. Future studies with longer duration and larger sample sizes would help to further elucidate the impact of switching to EDTA 4%. Proper flushing technique of CVCs is critical when using EDTA 4% to ensure the accuracy of serum and ionized calcium values.

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APPENDIX 1. Cost of each line-locking solution.

Line-Locking Agent	Unit Cost ($)	Price for 2 Lumens ($)
Sodium citrate 4% prefilled syringe (3 mL)[a]	0.91	1.83
Heparin 5000 units/0.5 mL[a]	2.22	4.44
EDTA 4% (Kitelock)[b]	6.00	12.00
Alteplase 2 mg/2 mL[a]	68.26	68.26–136.52 (1–2 mg/lumen)

EDTA = ethylenediaminetetraacetic acid.
[a]Based on BC Provincial Hospital Authority contract price, July 2021.
[b]Based on manufacturer information, July 2021.