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ORIGINAL RESEARCH

Ethanol lock therapy increases mechanical catheter complications in a pediatric intestinal failure population: A retrospective cohort study

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Abstract

Background: Ethanol lock therapy (ELT) decreases central line–associated bloodstream infections; however, the effect on mechanical catheter complications is unclear. In recent years, ELT has become unavailable for many patients, often resulting in high-risk patients switching back to heparin locks. We investigated the impact of ELT on mechanical catheter complications during this period.

Methods: We performed a retrospective cohort study of the Boston Children's Hospital intestinal rehabilitation program from January 1, 2018, to December 31, 2020. Pediatric patients with a central venous catheter requiring parenteral support for 3 months were included. The primary outcome was the composite rate of mechanical catheter complications (repairs and replacements).

Results: The pediatric intestinal failure cohort consisted of 122 patients. Forty-four percent received ELT for the entirety of the study period, 29% used only heparin locks, and 27% used ELT and heparin locks at different periods. During ELT use, there was 1.65 times the risk of mechanical catheter complications (composite outcome of repairs and replacements) compared with heparin locks (adjusted incidence rate ratio [aIRR] = 1.65, 95% CI = 1.18–2.31). Current ELT use was associated with 2.3 times the risk of catheter repairs (aIRR = 2.30, 95% CI = 1.36–3.89) but no significant increase in catheter replacement risk (aIRR = 1.41, 95% CI = 0.91–2.20).

Conclusion: In the largest pediatric intestinal failure cohort evaluated to date, the use of ELT, compared with heparin locks, increased the risk of mechanical catheter complications. Mechanical complications carry morbidity requiring urgent clinic or emergency department visits and additional procedures. The investigation of alternative lock solutions is warranted.

KEYWORDS

bacteremia, catheter-related infections, ethanol/adverse effects, intestinal failure, parenteral nutrition, pediatrics

CLINICAL RELEVANCY STATEMENT

Complications from long-term central venous catheters are a major source of morbidity in patients with intestinal failure. Ethanol lock therapy (ELT) is often used in high-risk patients to decrease the rate of central line–associated bloodstream infections, but the impact on mechanical catheter complications is poorly understood. Here, we find that ELT increases mechanical catheter complications requiring repair or replacement. New catheter lock solutions are urgently needed to prevent infections and mechanical catheter complications in the intestinal failure population.

INTRODUCTION

Patients with intestinal failure receiving parenteral support require long-term central venous catheters (CVCs). Central line–associated bloodstream infections (CLABSIs) are a key source of morbidity and mortality. CLABSIs require hospitalization, contribute to the progression of intestinal failure–associated liver disease, and may result in severe sepsis and death.[1] Recent North American guidelines have recommended that pediatric patients with intestinal failure at high risk for CLABSI, or with at least one previous CLABSI episode, receive prophylactic lock solution with ethanol lock therapy (ELT) or another nonantibiotic lock solution.[2] In contrast, European guidelines recommend using taurolidine locks to prevent CLABSI; however, taurolidine is not available in the United States.[3] Thus, most pediatric intestinal rehabilitation programs in the United States use ELT for high-risk patients.[4]

Ethanol is bactericidal and fungicidal against a broad range of microorganisms and prevents biofilm formation.[5,6] A recent meta-analysis in pediatric patients with intestinal failure found that ELT reduces the rate of CLABSIs by 63%.[7] Despite the benefit of ELT on CLABSI prevention, the impact on mechanical catheter complications is unclear. Mechanical catheter complications often require frequent catheter repairs and replacements. Frequent vascular procedures increase the risk of the loss of central vein access, ultimately requiring referral for intestinal or multivisceral transplant.[8]

Recent changes in ELT price and availability have caused many high-risk patients with intestinal failure to switch from ELT back to heparin locks, both at our institution and nationally.[4] This has provided a unique window to study the effects of ELT on mechanical catheter complications in a large pediatric population with intestinal failure. We hypothesized that the rate of mechanical catheter complications in pediatric patients with intestinal failure would be higher during time periods using ELT compared with time periods using heparin locks.

METHODS

Study design, setting, participants

We performed a single-center, retrospective cohort study of the intestinal rehabilitation program at Boston Children's Hospital, a free-standing academic children's hospital. This study was determined to be exempt by the Boston Children's Hospital Institutional Review Board. We included all pediatric patients (3 months to 18 years) with a long-term CVC for parenteral support who were followed primarily by our intestinal rehabilitation program for at ≥3 months from January 1, 2018, to December 31, 2020. At our institution, heparin is the initial lock solution for all new pediatric patients with intestinal failure. Following a single CLABSI event, patients are switched to daily 70% ELT in agreement with guidelines for high-risk patients (ie, for secondary prophylaxis). The dose of ELT used is based upon the measured catheter fill volume. ELT is used between infusions, with a minimum dwell time of 2 h, although typically for substantially longer (depending on the time between infusions, which is specific to the patient). If daily ELT is not possible because of availability or insurance coverage, ELT is provided three times per week. ELT is only used in silicone catheters.

Variables and exposure

Demographic and medical history information were collected both from chart review and from a prospectively maintained CLABSI quality improvement database. The exposure of interest was use of ELT as determined by medical notes and prescription records. The comparator was the use of heparin locks. The initial lock solution was determined and specific dates of switching between lock solutions (ie, ELT to heparin locks or heparin locks to ELT) were recorded to identify the time periods when a given patient was exposed to a given lock solution.

Catheter complications, including occlusions requiring thrombolysis, repairs, and replacements, were recorded and the indication for repair or replacement was noted. Catheter replacements were not counted as an event of interest if the indication was catheter malpositioning (eg, because of patient growth leading to the catheter tip in a more proximal location) or accidental catheter trauma (eg, cutting the catheter during a dressing change or pulling out the catheter).

Outcomes

The primary outcome was a composite outcome of mechanical catheter complications, defined as the number of repairs plus the number of replacements for a mechanical indication. This outcome was prespecified, as repairs and replacements are clinically relevant complications that typically require emergency department visits and additional procedures. Using a composite primary outcome increases the power to detect a statistically significant difference with a relatively small population size. We hypothesized that the rate of mechanical catheter complications in pediatric patients with intestinal failure would be higher during time periods receiving ELT compared with time periods receiving

heparin locks. Secondary outcomes included the rate of CLABSIs, catheter occlusions, catheter repairs, catheter replacements for a mechanical indication, and catheter replacements for a CLABSI.

Statistical methods

Patient characteristics were summarized by median (range) when continuous and by frequency (percentage) when categorical. Two types of analysis were used to examine these data, including comparison of event rates and comparison of the time to the event. Event rates were compared between the time receiving ELT and the time receiving heparin, expressed as the number of events per 1000 CVC days. Outcomes that represent counts over time are right-skewed and exposure time among patients are not necessarily equal, rendering unequal opportunity for events across patients. Negative binomial regression, an alternate form of regression analysis that accounts for the unique properties of count data, was used for this analysis. Because some patients received more than one lock solution during the study period, a mixed effects model was required to account for both the fixed effect covariates (age, sex, and short bowel syndrome diagnosis) and the random effect of lock solution. The random effect prevents a patient receiving two solutions from being treated as two unique patients, each receiving two different solutions. Failure to account for this would artificially increase the sample size and lead to possible spurious results because of increased Type I error. The second type of analysis was a time-to-event comparison performed by the Kaplan-Meier method. Additional details for both approaches are herein described.

Event rates were compared with negative binomial regression with log (CVC days) used as an offset to account for differential lengths of observation time. Poisson regression was not used because of the overdispersion of the variance parameter relative to the mean. The model was adjusted for age at the initial central venous line placement (or January 1, 2018, if placed prior to this date), sex, and short bowel syndrome diagnosis (yes/no) to account for imbalances across the three comparison groups. Modeling was performed with the SAS GLIMMIX procedure with maximum likelihood estimation and a logarithmic link function. A random effect for residual error with an unstructured covariance matrix was included to account for within-subject correlation among patients receiving more than one lock solution. Because of model convergence failure, the convergence criterion was increased from the default 10^{-8} to 10^{-7}, and the number of optimizations increased from 20 to 500.[9] Empirical SEs based on the sandwich estimator were reported. The results were summarized as mean ± SE and compared across groups by the incidence rate ratio (IRR) with 95% CI. The time-to-event analysis was performed under three scenarios. The time to first repair was assessed by the Kaplan-Meier method among patients without a mechanical catheter complication in the preceding 12 months (ie, a compromised catheter). Because the curves crossed, the log-rank test loses power and the Renyi test statistic was used instead.[10] The time from the first mechanical catheter complication to the second, among those with a first event, was assessed by log-rank statistic. The assessment of all recurrent (repeated) times to event was made by the semiparametric marginal means method.[11] All tests of significance were two-sided with $\alpha = 0.05$ and performed with SAS version 9.4 (SAS Institute Inc).

RESULTS

One-hundred twenty-two patients were eligible for study inclusion (Table 1). Forty-four percent of patients ($n = 54$) received ELT for the entirety of the study period, 29% ($n = 35$) used only heparin locks, and 27% ($n = 33$) used ELT and heparin locks at different periods during the study period. Patients who used both ELT and heparin locks were referred to as "switchers." The total days of ELT exposure was 64,678 days, compared with 43,061 days of heparin locks exposure. Figure 1 demonstrates the catheter types and location of placement for initial and subsequent catheter placements. A total of 89% ($n = 108$) of initial catheters and 87% ($n = 129$) of subsequent catheters were tunneled CVCs. A total of 86% ($n = 102$) of initial catheters and 91% ($n = 135$) of subsequent catheters were placed in either the internal jugular or subclavian veins.

During periods receiving ELT, there were 130 catheter repairs, 53 catheter replacements for mechanical complication, 113 occlusions requiring intervention, and 55 CLABSIs. While receiving heparin locks, there were 48 catheter repairs, 24 catheter replacements for mechanical complication, 51 occlusions requiring intervention, and 32 CLABSIs. Based on exploratory investigation with negative binomial regression, the rate of mechanical catheter complications while receiving a particular lock solution was not influenced by whether an individual patient switched between the lock solutions. However, the rate of CLABSIs was influenced by whether a patient was a "switcher." As patients are typically switched to ELT after the first CLABSI, the risk for CLABSI was found to be inherently lower in the heparin-only population (as a patient could typically only remain in it without CLABSIs). Thus, the outcomes of CLABSI incidence and catheter replacement for CLABSIs were evaluated only in patients who received both ELT and heparin locks at different periods during the study period.

Primary outcome

During periods of ELT, compared with heparin locks, there was 1.65 times the risk of mechanical catheter complications, defined as the composite of catheter repairs and replacements for a non-CLABSI mechanical indication (adjusted IRR [aIRR]=1.65, 95% CI=1.18–2.31) (Table 2). Figure 2 demonstrates spaghetti plots of mechanical complications over time for individual patients.

TABLE 1 Patient characteristics (*N* = 122).

Characteristics	ELT only (*n* = 54)	Heparin only (*n* = 35)	ELT + heparin (*n* = 33)
Age at first HPN visit, median (range)	9.9 mo (2.3 mo–12.9 y)	9.0 mo (3.5 mo–14.1 y)	9.9 mo (3.8 mo–9.1 y)
Age at most recent CVC placement as of study initiation, median (range), y	3.9 (0.1–12.9)	4.5 (0.1–14.7)	1.6 (0.1–17.8)
Male sex, *n* (%)	32 (59)	19 (54)	24 (73)
Short bowel syndrome diagnosis, *n* (%)	47 (87)	26 (74)	27 (82)
Etiology of intestinal failure, *n* (%)[a]			
Gastroschisis	16 (30)	4 (11)	11 (33)
Midgut volvulus	10 (19)	8 (23)	7 (21)
Necrotizing enterocolitis	9 (17)	7 (20)	9 (27)
Intestinal atresia	13 (24)	6 (17)	3 (9)
Intestinal dysmotility (pseudo-obstruction)	2 (4)	8 (23)	5 (15)
Hirshsprung's disease	5 (9)	2 (6)	2 (6)
Omphalocele	3 (6)	1 (3)	0 (0)
Microvillus inclusion diagnosis	1 (2)	0 (0)	1 (3)
Traumatic resection	0 (0)	1 (3)	0 (0)
Other malabsorptive diagnosis	1 (2)	0 (0)	0 (0)
Tunneled CVC, *n* (%)	49 (91)	28 (80)	30 (91)
Current catheter age before January 1, 2018, median (range), d[b]	207 (0–2854)	46 (0–2208)	68 (0–1509)

Abbreviations: CVC, central venous catheter; ELT, ethanol lock therapy; HPN, home parenteral nutrition.

[a]This may be more than one diagnosis; therefore, the total is >100%.

[b]Approximated as the age (in days) of the most recent CVC at January 1, 2018, or the first home parenteral nutrition clinic visit if later.

Secondary outcomes

Catheter repairs and replacements were also investigated as individual endpoints; only the risk of catheter repairs was significantly increased on ELT. While receiving ELT, compared with heparin locks, patients had 2.3 times the risk of catheter repairs (aIRR = 2.30, 95% CI = 1.36–3.89). There was no statistically significant increase in the risk of catheter replacements for a mechanical indication (aIRR = 1.41, 95% CI = 0.91–2.20) or occlusive events requiring intervention (aIRR=1.40, 95% CI = 0.78–2.53). In patients who received both ELT and heparin locks at different periods during the study period (switchers), the CLABSI risk was 0.45 times lower (but not statistically significant) while receiving ELT compared with heparin locks (aIRR = 0.45, 95% CI = 0.13–1.57). Patients who were switchers experienced 0.06 times the risk of catheter replacements for CLABSI compared with those who received heparin locks (aIRR = 0.06, 95% CI = 0.01–0.32).

Time to first and second catheter repair or replacement

Kaplan-Meier curves were constructed to evaluate the time to the first mechanical catheter complication requiring repair or replacement from the start of the study period and the time to the subsequent mechanical complication following the first (Figure 3). Patients with a mechanical catheter complication in the preceding 12 months (ie, a compromised catheter) were excluded. There was no difference in the time to the first mechanical catheter complication between ELT and heparin locks (median = 371 days for those receiving ELT vs 410 days for those receiving heparin locks; $P = 0.85$ by Renyi test statistic), but there was evidence of a shorter time from the first to the second mechanical catheter complication (median = 270 days for those receiving ELT vs 445 days for those receiving heparin; $P = 0.09$ by log-rank statistic). Considering all successive mechanical catheter complications, there was no evidence of shorter time between events for either lock solution (ELT hazard ratio = 1.16; $P = 0.35$ by semiparametric marginal means model).

DISCUSSION

Pediatric patients with intestinal failure are at particularly high risk for recurrent CLABSIs. Recent guidelines from the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition recommend that ELT or an alternative nonantibiotic lock solution be used in pediatric patients with intestinal failure with a CVC at high risk for CLABSI or with at least one previous CLABSI.[2] Similarly, the Centers for Disease Control

and Prevention recommend the use of antimicrobial lock solutions for patients with long-term CVCs with a history of multiple CLABSIs despite optimal aseptic technique.[12] Accordingly, the majority of patients in our intestinal rehabilitation program receive long-term ELT instead of heparin locks. The recent change in affordability and availability of ELT has provided a unique window to investigate mechanical catheter complications, as many patients who typically received ELT had to switch back to heparin. In the largest investigation of ELT in a pediatric cohort with intestinal failure to date, we found that ELT increased the risk of the composite outcome of mechanical catheter complications requiring repair or replacement. This finding warrants the investigation of alternative lock solutions.

Few previous studies have investigated the impact of ELT on mechanical catheter complications. A meta-analysis by Rahhal et al. found only three studies (combined $n = 52$) that evaluated catheter repair rates, with the estimated overall effect demonstrating fewer catheter repairs in heparin locks compared with ELT (−1.67 repairs per 1000 catheter days, 95% CI = −2.30 to −1.05).[7] Seven studies were included that investigated catheter replacements (total $n = 79$). Heparin locks were associated with increased catheter replacements compared with ELT (estimated mean

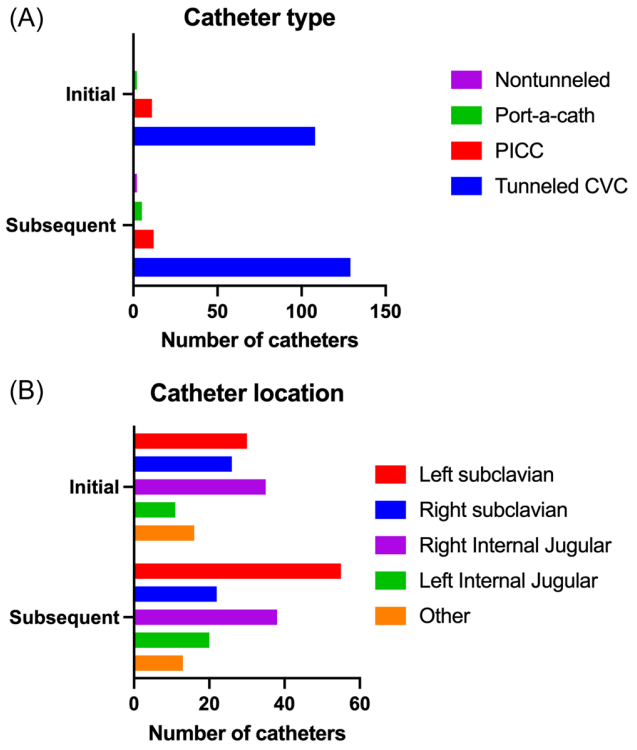

FIGURE 1 Catheter type (A) and location of placement (B) for initial and subsequent central venous catheter placements in the pediatric intestinal failure cohort. CVC, central venous catheter; PICC, peripherally inserted central catheter.

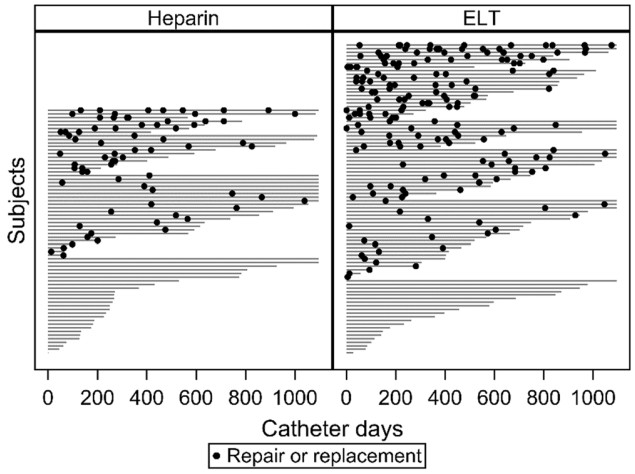

FIGURE 2 Spaghetti plots of mechanical catheter complications over time. Each line indicates the consecutive period of time that an individual patient received a given lock solution, and dots (●) indicate a repair or replacement. Individual patients are sorted (top to bottom) by the number of mechanical complications followed by the length of time on the given lock solution. ELT, ethanol lock therapy.

TABLE 2 Central venous catheter complication rates by lock solution.

	Number of events per 1000 catheter days		Unadjusted	Adjusted[a]	
Event	ELT Mean ± SE	Heparin Mean ± SE	IRR (95% CI)	aIRR (95% CI)	*P*
Mechanical complication	2.73 ± 0.31	1.63 ± 0.23	1.68 (1.18–2.37)	1.65 (1.18–2.31)	0.004
Catheter repair	2.06 ± 0.23	1.12 ± 0.23	1.84 (1.16–2.92)	2.30 (1.36–3.89)	0.002
Catheter replacement for mechanical indication	0.77 ± 0.12	0.57 ± 0.10	1.37 (0.87–2.15)	1.41 (0.91–2.20)	0.13
Catheter replacement for CLABSI[b]	0.39 ± 0.24	0.83 ± 0.51	0.47 (0.08–2.63)	0.06 (0.01–0.32)	<0.001
Catheter occlusion	1.61 ± 0.28	1.06 ± 0.29	1.52 (0.82–2.84)	1.40 (0.78–2.53)	0.26
CLABSI[b]	1.22 ± 0.57	2.90 ± 0.86	0.42 (0.19–0.94)	0.45 (0.13–1.57)	0.21

Abbreviations: aIRR, adjusted incidence rate ratio; CLABSI, central line–associated bloodstream infections; ELT, ethanol lock therapy; IRR, incidence rate ratio.

[a]Adjusted for age at the initial central venous line placement (or January 1, 2018, if placed before this date), sex, and short bowel syndrome diagnosis (yes or no). The results are from a negative binomial regression with a random effect to account for patients receiving more than one solution over time.

[b]An analysis of catheter replacement for CLABSI and CLABSI events conducted in the "switcher" population only (ie, patients who received both heparin and ELT at different times during the study period).

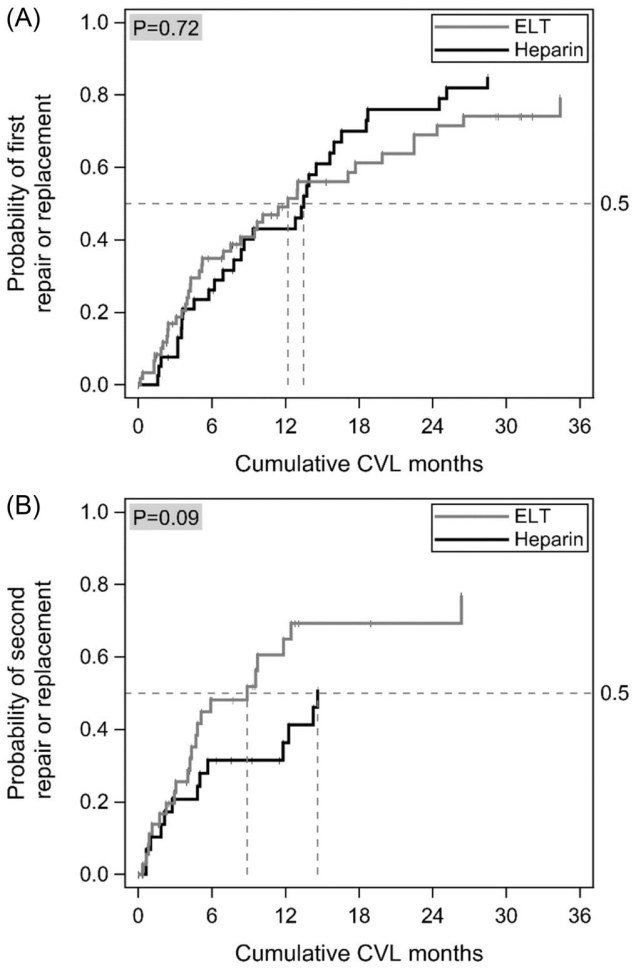

FIGURE 3 Kaplan-Meier curves were constructed for the time to mechanical complication requiring repair or replacement, with patients censored for a switch in lock solution, catheter replacement for a nonmechanical complication, or the end of follow-up. Patients receiving ELT compared with heparin have a similar time to first catheter repair or replacement (A) but a trend towards decreased time from the first to the second catheter repair or replacement (B). ELT, ethanol lock therapy.

effect size, 4.56 replacements/1000 catheter days; 95% CI = 2.68–6.43). Critically, this analysis included catheter replacements for all indications (eg, CLABSIs), not only mechanical complications. Our results are consistent with those of Mokha et al. which found that catheter replacements for CLABSI were decreased with ELT, whereas catheter replacements for mechanical indications were actually increased.[13]

Ethanol lock solutions likely do not substantially impact silicone catheter material integrity. In vitro, silicone catheter exposure to 70% ethanol for 10 weeks does not alter force-at-break or other mechanical parameters (except for a mild decrease in elasticity).[14] However, ethanol solutions induce plasma protein precipitation, which may lead to intraluminal catheter occlusion and higher required flush pressures—ultimately leading to catheter breakage. In vitro, plasma added to ≥28% ethanol solutions results in plasma protein precipitation.[15] In addition, catheters "locked" with ethanol demonstrate an influx of plasma into the catheter tip when placed in a simulated recumbent/head-down position.[15] Because of laminar flow, 20%–25% of the lock solution is systemically injected at nominal fill volumes.[16] Many ethanol lock protocols also recommend the aspiration of ethanol from the catheter. In clinical use, these factors all lead to unavoidable ethanol and plasma protein interaction in the catheter. An unexpected finding from our study was a similar time to the first mechanical complication between ELT and heparin but a decreased time to the second mechanical complication. This may suggest that compromised catheters (ie, those with repairs) are particularly susceptible to ELT-related catheter complications, potentially because of the introduction of a "weak" point exposed to the potentially higher flush/infusion pressures necessitated by plasma protein precipitation.

Most CVCs used in this study were tunneled CVCs, although a small minority of peripherally inserted central catheters (PICCs) were used. PICCs are typically used in the patient with difficult vascular access and placed by interventional radiology preferentially into small extremity veins.[17] PICCs may have an increased risk of venous injury (stenosis or thrombosis) as well as catheter malposition or dislodgement.[18] Inconsistent and limited literature has investigated the impact of PICCs on CLABSI rates.[2] Given the small sample size of patients receiving PICCs in this study, the effect of ELT on catheter type-specific complications cannot be ascertained.

The potential benefits of ELT on CLABSI prophylaxis in pediatric patients with intestinal failure may outweigh the increased risk of mechanical catheter complications when the alternative is heparin locks, especially in high-risk patients. Some evidence suggests that heparin may even contribute to biofilm formation and *Staphylococcus aureus* growth.[19] Although not statistically significant, our data are consistent in magnitude with previous studies demonstrating that ELT reduces CLABSIs. Rahhal et al. conducted a meta-analysis of ELT versus heparin locks in pediatric patients with intestinal failure, demonstrating a 63% reduction in the CLABSI rate across nine included observational studies (−6.27 CLABSIs per 1000 catheter days, 95% CI = −4.89 to −7.66).[7] The benefit of CLABSI prophylaxis may be lower in our population because of our lower baseline CLABSI rate in patients receiving heparin locks (2.90 ± 0.86 CLABSIs per 1000 catheter days). We also found that ELT essentially eliminated catheter replacements for CLABSI, although our baseline catheter replacement rate for CLABSI in the heparin lock group is also relatively low (approximately one catheter replacement every 2 years). This likely highlights a combination of successful CLABSI prevention (aside from ELT) as well as successful catheter salvage when CLABSI occurs.

Nonethanol lock solutions for CLABSI prophylaxis are under active investigation. Antibiotic locks (eg, vancomycin and gentamicin) are effective at preventing CLABSIs in long-term tunneled catheters but are often avoided because of the development of antibiotic resistance.[20,21] Some guidelines recommend antibiotic lock use in patients with multiple CLABSIs.[12,22] A promising nonantibiotic antimicrobial agent approved in Europe is taurolidine.[22] Taurolidine has broad-spectrum bactericidal activity and acts by inhibiting microbial adhesion to biological surfaces, thus preventing biofilm formation.[23,24] The European Society for Clinical Nutrition and Metabolism has recommended adjunctive use of

taurolidine to prevent CLABSIs.[3] A meta-analysis found a 51% reduction in CLABSIs across 34 studies, although most included studies were in adults, had small sample sizes, and had heterogenous populations that limit generalizability.[25] Unfortunately, few studies evaluated the mechanical complications. In a recent retrospective review of pediatric patients with intestinal failure who were receiving ELT and then were switched to taurolidine, there were lower rates of mechanical complications when receiving taurolidine.[26] A well-designed randomized controlled trial in the pediatric population with intestinal failure, especially with ethanol as a comparator, would be valuable.

Chelators are another type of lock solution with anticoagulant and antimicrobial properties; the two most commonly studied chelators are citrate and ethylenediaminetetraacetic acid (EDTA).[27] Chelators bind calcium (a necessary cofactor in the coagulation cascade) and other essential metal irons necessary for bacterial growth.[27] Citrate lock solutions have been evaluated at a range of concentrations, with 4% solutions sufficient for anticoagulant activity but concentrations over 15% needed for antimicrobial activity.[27] Higher concentrations of citrate with inadvertent systemic exposure may result in life-threatening cardiac toxicity.[28] Thus, low concentration citrate is often combined with a variety of antimicrobial agents (including taurolidine) for lock solutions.[29] EDTA also has antimicrobial activity against common biofilm-forming organisms.[30] Tetrasodium EDTA, approved in Canada as a lock solution, decreased CLABSIs and catheter occlusions in two small retrospective studies of populations receiving home parenteral nutrition.[31,32] We have initiated a compassionate use program for tetrasodium EDTA at our institution for high-risk patients who have lost access to ELT. Similar to citrate, EDTA is often combined with antimicrobial agents for improved CLABSI prophylaxis (often minocycline).[33] Unfortunately, few studies have investigated these alternative lock solutions in pediatric populations with intestinal failure.

Several limitations must be considered when interpreting this work. This was a retrospective cohort study evaluating a specific time period of increased switching between lock solutions because of changing access to ELT. Although this study reports the largest pediatric cohort with intestinal failure receiving ELT in the literature, the sample size remains relatively small and this limits the statistical power. Point estimates may be influenced substantially by random error, although the reported point estimates are generally in agreement with existing literature. Although most patients who received ELT received a 70% ethanol solution instilled 7 days per week, some patients decreased their rate of ethanol usage to as infrequently as three times per week based on ELT availability. However, this would likely underestimate of the effects of ELT on both mechanical complications and CLABSI-related complications because of less frequent catheter exposure to ethanol. As the primary purpose of this study was to investigate mechanical catheter complications, we believe that our results remain robust. This study has several strengths, including the use of accurate endpoints, the presence of procedure notes in the medical record for catheter repairs and replacements, and the collection of CLABSIs in a prospectively maintained database. However, catheter occlusions that are treated successfully with alteplase, often at home, are poorly documented in the medical record and may be unreliable.

CONCLUSION

In the largest pediatric cohort with intestinal failure evaluated to date, the use of ELT, compared with heparin locks, increased the rate of mechanical complications requiring catheter repair or replacement. A multicenter study should be conducted to validate these findings, as mechanical catheter complications carry substantial morbidity. These findings underscore the urgent need to investigate alternative nonantibiotic lock solutions for the prevention of CLABSIs and mechanical catheter complications.

AUTHOR CONTRIBUTIONS

Scott C. Fligor, Kathleen M. Gura, and Mark Puder contributed to the conception of the study; Scott C. Fligor, Paul D. Mitchell, Jennifer McClelland, Alexandra Carey, Kathleen M. Gura, and Mark Puder contributed to the methodology design of the study; Scott C. Fligor, Thomas I. Hirsch, Savas T. Tsikis, Malachi M. Joiner, Sarah Carbeau, Jennifer McClelland, and Alexandra Carey contributed to the research and investigation; Paul D. Mitchell designed and visualized the formal statistical analysis; Kathleen M. Gura and Mark Puder supervised the study; and Scott C. Fligor and Sarah Carbeau drafted the manuscript. All authors agree to be fully accountable for ensuring the integrity and accuracy of the work. All authors read and approved the final manuscript.

CONFLICTS OF INTEREST STATEMENT

Mark Puder and Kathleen M. Gura are investigators of a compassionate use protocol utilizing tetrasodium EDTA for high-risk patients who lost access to ethanol lock therapy.

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