Original Article

Use of Ethanol Lock for Primary Prevention of Catheter Related Blood Stream Infection in Pediatric Surgical Patients

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Background: Catheter related blood stream infection (CRBSI) is one of the most serious complications of the central venous catheterization and can lead to severe sepsis, catheter loss, and death. The ethanol lock (EL) is now widely used as a second line therapy and secondary prevention of CRBSI especially in patients with intestinal failure.

Objective: The present study's objective was to evaluate the effectiveness of EL as the primary prevention of CRBSI in pediatric surgical patients.

Materials and Methods: The present study was an experimental study that used EL in all pediatric surgical patients with central venous catheter (CVC) hospitalized between February 2020 and January 2021.The EL was done by indwelling the CVC with 70% ethanol for at least four hours per day, then the ethanol was aspirated from the catheter before routine using of the catheter. Data collection included demographics, catheter days, complication of CVC, and EL were collected. Statistical analysis was done using SPSS statistics program.

Results: All 13 patients enrolled in the present study had intestinal failure or other gastrointestinal conditions that required a long-term CVC. The results showed no CRBSI in all patients. After using the EL for 1,930 catheter days, the incidence rate of CRBSI was 0 per 1,000 catheter days. The EL group was 1.29 times more likely not to develop CRBSI (RR 1.29, 95% CI 1.10 to 1.52). The authors' CRBSI rates have declined from 3.84 per 1,000 catheter days in 2019 to 0 per 1,000 catheter days after using EL. One patient had central line removal due to mechanical breakage of the line while returning home.

Conclusion: EL prevents CRBSI effectively in pediatric surgical patients especially in tunneled catheter usage.

Keywords: Ethanol lock; Catheter related blood stream infection; Central venous catheter

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The central venous catheter (CVC) is one of the important tools to facilitate treatment for pediatric surgical patients. It is used for fluid resuscitation in critically ill patients and is used as a long-term access to deliver medication or parenteral nutrition to specialized patients. Catheter related blood stream infection (CRBSI) is one of the most serious complications of the central venous catheterization. It can lead to severe sepsis, catheter loss, and death. In addition, economically wise, CRSBI will prolong hospital stay with additional cost of broad-spectrum antibiotics. Some patients require intensive care treatment and the replacement of the CVC. These all increase the health care cost.

Prophylactic antimicrobial lock is recommended for patients with long-term CVC who have history of multiple CRBSI despite optimal aseptic technique for CVC care[1]. After the CVC is inserted and during a CRBSI, biofilm-containing bacteria or fungus is formed by human protein covering the luminal surface of the catheter[2]. Therefore, it makes the bacteria or fungus resistant to treatment or may need higher generation of board spectrum antibiotics to eradicate it. Ethanol lock (EL) is wildly used as a second line therapy and secondary prevention of CRBSI especially in patients with intestinal failure[1,3-5]. Ethanol solution is a commonly used antimicrobial agent. It is cheap and has no drug resistance.

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Furthermore, ethanol itself has thrombolytic effect without altering the catheter's integrity after long-term exposure[6]. All these qualities make ethanol an ideal locking solution for CVCs.

The main objective of the present study was to evaluate the effectiveness of EL as the primary prevention of CRBSI in pediatric surgical patients who never had CRBSI. Secondly, to study other factors that may associate with CRBSI and the complication of CVC and EL.

Materials and Methods

The present study was approved by the Office of Research Ethics, Queen Sirikit National Institute of Child Health (EC 62-052). The present experimental research was a clinical trial with historical control. Data collection were from the Department of Surgery and 70% ethanol solution was prepared by the Manufacturing Unit, Pharmacy Department and Ethic approval from the Ethic committee of QSNICH.

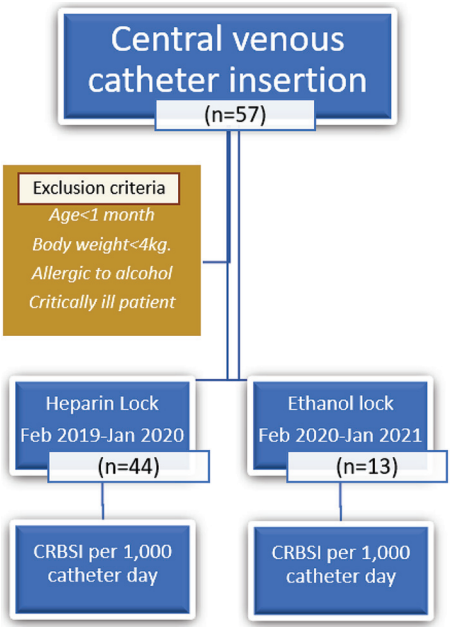

Figure 1. Diagram of the study design.

Study design

There were two groups of patients. For the EL group, all pediatric surgical patients in the authors' department who had CVC, had never been diagnosed with CRBSI, and consented to using EL between February 2020 and January 2021. For the control group, a retrospective chart review of all pediatric surgical patients in the authors' department who had CVC using standard heparin lock (HL) between February 2019 and January 2020. Demographic data, catheter days, complication of CVC, HL, and EL were collected (Figure 1).

Exclusion criteria

Patients who are under one month of age.

Patients who have body weight under four kilograms.

Patients who have history of allergic to alcohol.

Patients who are critically ill.

Definitions and procedure

CRBSI: CRBSI is a clinical definition when blood stream infection occurs associated with having a CVC. The infection must be confirmed by laboratory testing and being treated[1].

In the present study, clinical suspected of CRBSI began when the patients have two or more of Pediatric Systemic Inflammatory Response Syndrome (SIRS) criteria while having the CVC and at least 48 hours after insertion of the CVC. The diagnosis must be confirmed by positive hemoculture from both of CVC and peripheral vein. After the diagnosis of CRBSI, treatment of at least 14 days of intravenous antibiotics would be given to all patients. If multidrug resistant bacteremia or fungal infection are presented with clinical severe sepsis the attending physician would consider removing the CVC.

Catheter day: In the present study, the catheter days was counted from the first day the CVC was inserted until the day the CVC was removed, despite of the CRBSI.

Ethanol lock: The volume of catheter for each patient was measured and then the actual volume of ethanol was used accordingly. The EL was done under aseptic technique by indwelling the CVC with 70% medical grade ethanol for at least four hours per day to eliminate both bacteria and fungus[2]. Then before the routine use of the CVC, the ethanol solution was aspirated then 0.9% Sodium Chloride 1 mL/kg, with a maximum of 10 mL, was flushed into the CVC[7,8] (Figure 2).

Safety considerations: Although the authors aspirated the ethanol solution before the routine use of the CVC, they were aware of the adverse event that the ethanol may be accidentally flushed into the patient's body. Toxicity level of ethanol is 1 mL/kg/day of 95% ethanol. In the present study, the amount of ethanol used each time per protocol was 0.2% of intoxication level[9,10].

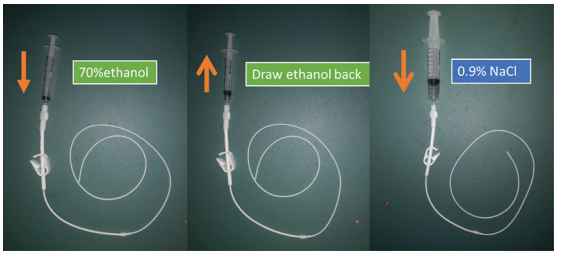

Figure 2. Ethanol lock procedure.

Statistical analysis

The statistical analysis was done using IBM SPSS Statistics, version 25 (IBM Corp., Armonk, NY, USA). The demographic data and factor associated with CRBSI including catheter day, age and body weight were presented and analyzed by Mann-Whitney U test and p-value of less than 0.05 was considered significant. The type of catheter and site of insertion were also presented and analyzed by Fisher's exact test and p-value of less than 0.05 was considered significant. The relative risk of not to develop CRBSI and their 95% confidence interval (CI) were calculated together with risk reduction of CRBSI per 1,000 catheter day. The association of complication and EL usage were also analyzed using Fisher's exact test and p-value of less than 0.05 was considered significant.

Results

In the 12-month period, there were 13 patients in EL group and 44 patients in the HL group, enrolled in the present study (Table 1). There was no missing data in the present study. Regarding the demographics, there was no statistical difference of the body weight between both groups. The median body weight was 10 with a range of 4 to 30 kilograms in HL and 16 with a range of 4 to 40 kilograms in ELs group. However, there were statistical differences in age, catheter days, catheter type, and site of insertion between both groups. The median age was 1.71 years in HL and 4.91 years in EL group (p=0.015). The EL group had longer catheter days than HL group, with a median of 121 and a range of 13 to 341 days and a median of 16 and a range of 1 to 357 days, respectively (p=0.020). The use of non-tunneled to tunneled catheter was also significantly higher in the HL group (p=0.001). As for the site of insertion, mostly were subclavian vein in both groups however, there were statistical significance in the other sites (p=0.015). In HL, there were 11 internal jugular veins, 21 subclavian veins, and 12 femoral veins. In EL, there was 1 internal jugular vein and 12 subclavian veins.

Table 1. Demographic data

	Heparin Lock	Ethanol lock	p-value
Age (years)			0.015*
Median	1.71	4.91	
Range	0.08 to 9.00	0.33 to 12.00	
Body weight (kg)			0.189
Median	10	16	
Range	4 to 30	4 to 40	
Type of catheter; n (%)			0.001*
Non-tunneled catheter	35 (79.52)	2 (15.38)	
Tunneled catheter	9 (20.48)	11 (84.62)	
Site of insertion; n			0.015*
Internal jugular vein	11 (91.67)	1 (8.33)	
Subclavian vein	21 (63.63)	12 (36.36)	
Femoral vein	12 (100)	0 (0.00)	
Catheter days (days)			0.020*
Median	16	121	
Range	1 to 356	13 to 341	

SD=standard deviation
* Statistically significant

Table 2. Factors associated with CRBSI

	No CRBSI	CRBSI	p-value
Catheter days (days)			0.007*
Median	18	162	
Range	1 to 341	13 to 356	
Age (years)			0.449
Median	1.83	4	
Range	0.08 to 12	1.68 to 0.41	
Body weight (kg)			0.338
Median	10	13.50	
Range	4 to 40	6.00 to 18.00	
Type of catheter; n			0.493
Non-tunneled	32	5	
Tunneled	15	5	
Site of insertion; n			0.601
Internal jugular vein	26	7	
Subclavian vein	11	1	
Femoral vein	10	2	

CRBSI=catheter related blood stream infection; SD=standard deviation
* Statistically significant

Regarding the primary outcome of CRBSI, there was no incidence of CRBSI in the EL group with the total of 1,930 catheter days, compared to the CRBSI of 10 of 44 patients in the HL group with the total of 2,748 catheter days. Regarding the factors associated with CRBSI (Table 2), the catheter days were significantly longer in CRBSI patients

Table 3. Rate of CRBSI in HL and EL group

	Heparin lock; n (%)	Ethanol lock; n (%)	RR	95% CI	p-value
CRBSI					
All patients (n=57)	10/44 (22.73)	0/13 (0.00)	1.29	1.10 to 1.52*	0.002*
Non-tunneled catheter usage (n=37)	5/35 (14.29)	0/2 (0.00)	1.17	1.02 to 1.34*	0.026*
Tunneled catheter usage (n=20)	5/9 (55.56)	0/11 (0.00)	2.25	1.08 to 4.67*	0.030*
CRBSI/1,000 catheter days	3.84	0.00	-	-	

CRBSI=catheter related blood stream infection; RR=relative risk; CI=confidence interval

* Statistically significant

Table 4. Microorganisms detected and antibiotics used in CRBSI

Microorganism	Antibiotics
Staphylococcus hominis (MDR)	Vancomycin
Staphylococcus haemolyticus (non-MDR)	Gentamycin
Acinetobacter bambini (MDR)	Sulperazone
Acinetobacter ursingii (non-MDR)	Amikacin
Streptococcus viridan (MDR)	Vancomycin
Acinetobacter junii (MDR)	Fosfomycin
Candida albican	Amphotericin B
Acinetobacter ursingii (non-MDR)	Amikacin
Candida albican	Amphotericin B
Acinetobacter bambini (MDR)	Meropenam

MDR=multidrug resistant

Table 5. Complication

	Heparin lock (n=44); n (%)	Ethanol lock (n=13); n (%)	p-value
Thrombosis	6 (13.63)	0 (0.00)	0.492
Line breakage	0 (0.00)	1 (7.69)	0.228

compared to patients without CRBSI, with a median of 162 and a range of 13 to 356 days and a median of 18 with a range of 1 to 341 days, respectively (p=0.007). Other factors such as age, body weight, type of catheter, and site of insertion had no statistical association with CRBSI. It was noted in prior studies that longer catheter days and non-tunneled catheter were associated with CRBSI. Therefore, a subgroup analysis for confounding factors was done. However, despite the longer catheter days in the EL group, there was no CRBSI, so the authors did not consider it as a confounding factor. From subgroup analysis for factors associate with CRBSI (Table 3), despite the type of catheter usage, the EL group was more likely not to develop CRBSI.

The patients in the EL group are 1.29 times more likely not to develop CRBSI with statistical significance (relative risk 1.29, 95% CI 1.10 to 1.52; p=0.002). In non-tunneled catheter usage patients, the EL group was 1.17 times more likely not to develop CRBSI with statistical significance (relative risk 1.17, 95% CI 1.02 to 1.34; p=0.026). In addition, in tunneled catheter usage patients, the EL group was also 2.25 times more likely not to develop CRBSI with statistical significance (relative risk 2.25, 95% CI 1.08 to 4.67; p=0.030). The CRBSI per 1,000 catheter day were 3.84 and 0 per 1,000 catheter day, respectively. The risk reduction of CRBSI after using the EL was 3.84.

From the 10 cases of CRBSI, the microorganism detected was classified into multidrug resistant/fungal infection group (MDR/fungus) and non-multidrug resistant (non-MDR) group, which 7 of 10 (70%) cases were MDR/fungus. The microorganism that was found were different in each of the 10 patient (Table 4). The antibiotics used were vancomycin, gentamycin, sulperazone, amikacin, fosfomycin, meropenem, and amphotericin B.

Regarding complications, there was no statistical differences between both groups (Table 5). There were six catheter thrombosis occurred in HL group and single line breakage in EL group. This line breakage occurred while the patient was visiting home, which was due to mechanical force on the line.

Cost effectiveness

The total medical cost per patient with CVC in the authors' department for 14 days were 29,202.16 Baht using HL, and 29,776.97 Baht using EL. This cost included all expenses related to the CVC, which are the device itself, the CVC insertion procedure under ultrasound or fluoroscopic guided, daily nursing care including HL or EL procedure, and local wound care at CVC exit site. However, in the HL group that had CRBSI non-MDR microorganism, the medical cost will increase to 32,588.42 Baht due to the cost of antibiotics and more attentive medical care. In addition, the medical cost would increase to 46,603.86 Baht if the CRBSI were MDR microorganism or fungus and the replacement of the CVC was needed.

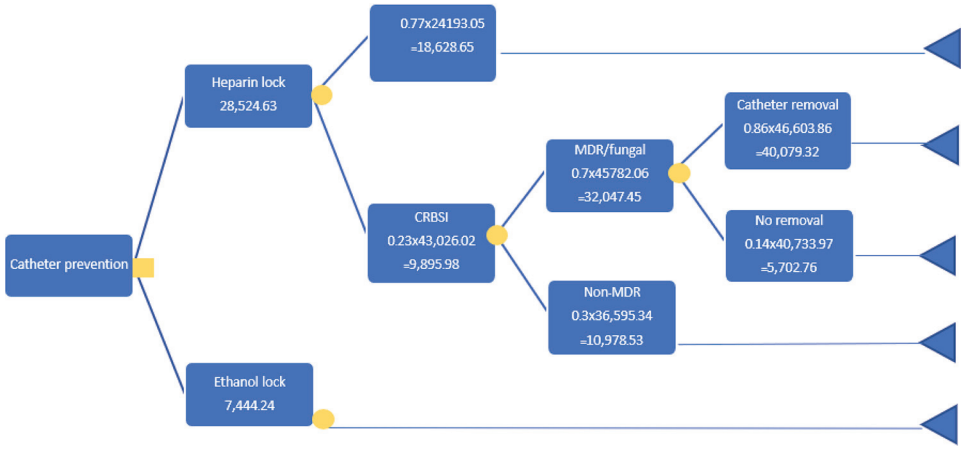

Figure 3. The decision tree model is the incremental cost effectiveness ratio (ICER) is –91,653.87.

The incremental cost effectiveness ratio (ICER) was –91,653.87, which meant that the EL prevents CRBSI compared to HL with the reduction of health care cost for 91,653.87 in 14 days (Figure 3).

Discussion

EL is a valuable procedure both for prevention and treatment of CRBSI in different pediatric population groups such as intestinal failure patients, oncologic patients, and even patients in intensive care unit[3-5,7,8,11]. The present study is the first study about the effectiveness of EL in pediatric surgical patients in Thailand. The authors aimed for the primary prevention of CRBSI instead of secondary prevention of CRBSI in previously infected patients, since the authors acknowledge that primary is much better than secondary prevention in most areas of medicine. Therefore, EL is the new modality for primary prevention of CRBSI.

Since the present study required at least four hours of ethanol indwelling time, all the patients enrolled in EL group required long-term parenteral nutrition without critical condition. The authors paid special consideration on those patients with tunneled catheter usage since it is frequently chosen as the device of choice in long-term parenteral nutrition patients, whom assuming to be the most suitable for EL, so the authors performed the subgroup analysis in those specific patients.

The results of using EL are satisfactory especially in tunneled catheter usage, with zero CRBSI in 12 months, high safety, and with great cost effectiveness compared to the prior HL. Although heparin is cheaper than ethanol, EL reduced the rate of CRBSI compared to HL. Therefore, the cost effectiveness of ethanol indicates that it provides high value for money, which is excellent for the present economic situation. Previous systematic review and meta-analysis about EL in 2018 also showed similar effect of reduction rate of CRBSI for 6.27 per 1,000 catheter day (95% CI 4.89 to 7.66) in intestinal failure patient[8]. The authors' further goal is to promote the EL as standard care of CVC instead of the heparin lock.

However, the present study has limitation of small sample size and the statistically differences of demographic data between the control HL group and the EL group. The number of patients enrolled in both groups were also different. This difference is because of the data in the EL group was collected during 2020 with the COVID-19 pandemic, which affect the admission criteria in the present hospital.

Conclusion

The EL is safe and effective for primary prevention of CRBSI in pediatric surgical patients especially with tunneled catheter usage. Further RCT study with larger population group is recommended to demonstrate more obvious outcome.

What is already known on this topic?

The EL is used for secondary prevention of CRBSI and as second line therapy for CRBSI. There was no report of its usage and effectiveness in Thailand.

What this study adds?

This study is the first study about the effectiveness and cost-effectiveness of EL to prevent CRBSI compared to prior standard of Heparin lock.

The excellent results changed the standard of

care especially in tunneled catheter usage patients.

Conflicts of interest

The authors declare no conflict of interest.

References

1. O'Grady NP, Alexander M, Dellinger EP, Gerberding JL, Heard SO, Maki DG, et al. Guidelines for the prevention of intravascular catheter-related infections. Centers for Disease Control and Prevention. MMWR Recomm Rep 2002;51:1-29.
2. Chambers ST, Peddie B, Pithie A. Ethanol disinfection of plastic-adherent micro-organisms. J Hosp Infect 2006;63:193-6.
3. Broom J, Woods M, Allworth A, McCarthy J, Faoagali J, Macdonald S, et al. Ethanol lock therapy to treat tunnelled central venous catheter-associated blood stream infections: results from a prospective trial. Scand J Infect Dis 2008;40:399-406.
4. Valentine KM. Ethanol lock therapy for catheter-associated blood stream infections in a pediatric intensive care unit. Pediatr Crit Care Med 2011;12:e292-6.
5. Norris LB, Kablaoui F, Brilhart MK, Bookstaver PB. Systematic review of antimicrobial lock therapy for prevention of central-line-associated bloodstream infections in adult and pediatric cancer patients. Int J Antimicrob Agents 2017;50:308-17.
6. Crnich CJ, Halfmann JA, Crone WC, Maki DG. The effects of prolonged ethanol exposure on the mechanical properties of polyurethane and silicone catheters used for intravascular access. Infect Control Hosp Epidemiol 2005;26:708-14.
7. Lopes BC, Borges P, Gallindo RM, Tenório TBS, Machado LB, de Orange FA. Ethanol lock therapy for the prevention of nontunneled catheter-related bloodstream infection in pediatric patients. JPEN J Parenter Enteral Nutr 2019;43:1044-52.
8. Rahhal R, Abu-El-Haija MA, Fei L, Ebach D, Orkin S, Kiscaden E, et al. Systematic review and meta-analysis of the utilization of ethanol locks in pediatric patients with intestinal failure. JPEN J Parenter Enteral Nutr 2018;42:690-701.
9. Wong GA, Armstrong DC, Robertson JM. Cardiovascular collapse during ethanol sclerotherapy in a pediatric patient. Paediatr Anaesth 2006;16:343-6.
10. Hammer FD, Boon LM, Mathurin P, Vanwijck RR. Ethanol sclerotherapy of venous malformations: evaluation of systemic ethanol contamination. J Vasc Interv Radiol 2001;12:595-600.
11. Opilla MT, Kirby DF, Edmond MB. Use of ethanol lock therapy to reduce the incidence of catheter-related bloodstream infections in home parenteral nutrition patients. JPEN J Parenter Enteral Nutr 2007;31:302-5.