THE IMPACT OF TAUROLIDINE-BASED CATHETER LOCK REGIMEN VERSUS HEPARIN LOCK FOR TUNNELED HEMODIALYSIS CATHETERS IN NEPHROLOGY &UROLOGY MINIA UNIVERSITY HOSPITAL

Basma Fathy[1], Mohamed Sharawy[1], Moataz Fatthy[2], Aml Azzam[1], Shimaa Abdelrazeq[1] and Hisham Mostafa Tawfeik[1]

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Abstract

Background: Catheter-related infections (CRIs) and dysfunction are the chief complications of Catheters causing morbidity and mortality in patients on hemodialysis.
Methods: prospective, randomized controlled trial (RCT); two lock regimens using two commercial catheter lock solutions were compared in hemodialysis patients with newly inserted tunneled central catheters. There were two groups of patients. The first received 0.5 mL of Taurolock solution (Taurolidine group), and the other group received 0.5 mL of unfractionated heparin (Heparin group) before the catheter lock. Both groups were compared regarding catheter-related infections (CRI), catheter dysfunction, and hospital admission.
Results: Over one year of catheter insertion, two catheter-related infections occurred in 40 patients in the Taurolidine group (TG), and ten CRIs occurred in 46 patients in the heparin group (HG) (p =0.031*). Catheter dysfunction rates were significantly lower in the TG (p=0.004*), and hospitalization for CRI events was significantly lower in the TG (p-=0.032*).
Conclusion: The use of taurolidine-based catheter lock solutions significantly reduces CRIs, dysfunction, and overall hospitalization rates related to tunneled hemodialysis catheters compared to heparin solution.

Keywords: Tunneled hemodialysis Catheter, catheter-related infections, taurolidine.

[1].Internal Medicine Department, Faculty of Medicine, Minia University, Egypt
[2].Internal Medicine Department, Faculty of Medicine, Cairo University, Egypt
Corresponding Email: Basma.Fathi@mu.adu.eg

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1. Introduction

Infection is the second leading cause of catheter removal, morbidity, and mortality in patients with end-stage renal disease (1). The incidence of CRIs varies per dialysis unit, insertion site, type of catheter inserted, and catheter care adequacy (1). About 20% to 40% of chronic hemodialysis patients depend on tunneled central venous catheters throughout their dialysis dependency (2). Catheter patency is an additional problem with CRIs resulting in decreasing quality of dialysis and more disturbed electrolytes (3). Thus, for preventing catheter dysfunction, prevent CRIs in hemodialysis patients, and select of an appropriate catheter lock solution (CLS) become compulsory option. There are different strategies for maintaining catheter patency, including distributing fluid infusion and using anticoagulants (4). Current guidelines do not recommend Antibiotic lock solutions (e.g., gentamicin) as a routine use, although they reduce the rate of CRIs even in combination with heparin or citrate due to a lack of anticlotting properties (5). High-concentrated trisodium citrate (30% or 46.7%) shows both an antithrombotic and antimicrobial effect, but it needs in many situations to use of thrombolytic therapy (6). therefore, its use is decreasing because of the potential cardiac, embolic, and mortality risks related to an accidental IV Administration of 46.7% citrate, ((7, 8) In contrast, the use of low-concentrated citrate (4%) is safe but has lower antimicrobial efficacy in vitro studies (9). The

administration of heparin is a common and efficient method for preventing catheter occlusion and maintaining its patency, but it can cause some complications, including allergic reaction and Heparin-Induced Thrombocytopenia (HIT) (10). Taurolidine is a nontoxic agent, a non-antibiotic lock alternative that reduces biofilm development, so, no bacterial resistance occurs.no adverse effects happen even when leakage into circulation occurs (11). Recent studies have shown that taurolidine lock decreases central venous catheter infection (12), and heparin addition to taurolidine–citrate has been shown to reinforce its efficacy concerning patency (13). Currently, taurolidine–citrate combinations or 4% citrate are widely used in CLS in dialysis centers (14). We, therefore, studied taurolidine–citrate with heparin versus heparin solution regarding CRIs, catheter patency, and overall hospitalization rates in our trial.

2. Methods

This prospective RCT compared a taurolidine-based catheter-lock regimen versus heparin on the occurrence of CRIs, catheter malfunctions, and hospitalization events in patients who had a newly inserted tunneled hemodialysis catheter. The study was incompletely blinded as patients, laboratory staff, and study evaluators were blinded, while physicians and nurses on duty were not. The study was performed at the Nephrology unit/ Nephrology & Urology Minia University Hospital starting in September 2021 until August 2022. Adult hemodialysis patients were suitable to join this study after the implantation of a tunneled dialysis catheter in the central venous system, allowing adequate blood flow (300 ml/min) after the first session of dialysis. The patients were on a dialysis regimen with three treatments per week. The patients on the study were classified into two groups, A and B. Group A (Heparin group); 46 patients, each of them received 0.5 mL of unfractionated heparin (5000 units/mL) before the catheter gets locked. Group B (Taurolidine group); 40 patients of them received 0.5 mL Taurolock solution (containing cyclo-taurolidine, Citrate 4%, and heparin 500 IU/mL) before the catheter gets locked. Patients <18 years received systemic anticoagulant therapy, bacteremia in the previous 21 days that lead to current use of antibiotic therapy, major bleeding or intracranial hemorrhage in the preceding three months, pregnancy, and known allergies or contraindications to the CLS used were the Exclusion criteria for study patients. All participants were subjected to introduction of tunneled double-lumen silicone catheter without side holes in the right internal jugular vein when possible, at the operating room. When CRIs occurred which defined as a positive blood culture withdrawn from a symptomatic patient with a tunneled line without other source of infection to emphasis the uniformity of diagnostic procedures (15). based on culture results, the treatment was described after that (16).if an insufficient response to antibiotic therapy or recurrence of a CRI occur, the catheter was removed, and the observation period was stopped. Catheter dysfunction was defined as insufficient blood flow during dialysis (blood flow <200 ml/min or >30% fewer than the average of the preceding ten sessions), and if existing before or during dialysis session, repositioning of patient or catheter lines reversal was done (17). If unsuccessful, flush the catheter with 10 ml saline, then 2.5 ml of Urokinase was instilled per lumen with a 60-minute dwell time, then remove the solution before the dialysis session as a release. If no response after repeated use of Urokinase, the catheter was removed. All laboratory parameters were determined at the laboratory of the same hospital.

Outcomes:

The primary outcome was the number of CRIs in each group. Secondary outcomes were defined for episodes of antibiotic therapy, hospitalization events for a catheter-related infection, or for mechanical cause) and for patency (catheter dysfunction, release with Urokinase). catheter removal due to infectious and mechanical complications were considered as Additional secondary outcomes Some Important strengths of this study include a randomized controlled trial, inclusion of patients showing comparable comorbidity and basic characteristics and with only newly inserted tunneled catheters, complete aseptic conditions during catheter insertion, and strict follow-up care (18), specific objective outcome and the data analyzed by blinded evaluators for study.

Statistical analyses

The categorized data was presented as absolute counts and relative frequencies. Continuous data are presented as means, SD. To compare randomization success, treatment groups were compared qualitatively and the chi-square test or the Fisher exact test were used for categorized variables. We used SPSS version 28 for data management and analysis. When the p-value of 0.05 or less, the results were considered statistically significant

Approval and registration

The Ethics Committee of Minia University has approved the study protocol. All study participants provided written informed consent.

3. Results

We assessed 105 patients for the suitability, 19 of whom were excluded due to refusal to participate. The remaining 86 patients underwent randomization; 46 patients were assigned to receive 0.5ml Heparin (HG), and 40 were assigned to the taurolidine-based lock solution (TG).

Table (1): Statisticaldistribution of the baseline characteristics of the Patients

Patient characteristics	Group Heparin (n= 46)	Taurolidine Group (no= 40)	P -value
Age (mean±SD) Range	46.4 ± 16 (22-76)	51.6 ± 13.8 (22-67)	0.114
Sex: male female	47.8%)(22 24 (52.2%)	20 (50%) 20 (50%)	0.841
Site of insertion: RT.IJV	36	29	0.88
Lt.IJV:	3	2	
Rt. Scv	4	4	
Lt.Scv	2	3	
Rt. Femoral	0	1	
Lt. femoral	1	1	
Hb (g/dl) (mean±SD) Range	8.8 ± 1.3 (6-11)	9.3 ± 1 (6.5-11)	0.051
Platlets (*1000/mm3) (mean±SD) Range	272 ±82.3 (110-415	248.4 ± 98.3 (100-433)	0.21
TLC (*1000/mm3) (mean±SD)	9.1 ± 4.3	8.1 ± 3.3	0.26
Creat.(mg/dl) (mean±SD) Range	8.2 ± 3.2 (4-22)	7.5 ± 2.4 4.5-13)(	0.26
Urea (mg/dl) (mean±SD) Range	142.8 ± 46.5 (44-258)	144.4 ± 45.6 (66-231)	0.87
Clotting Time (mean±SD) Range	4.9 ± 1.5 (2-13)	4.9 ± 0.8 (4-7)	0.97
BleedingTime Median (IQR)	3.3 ± 1	3.1 ±1	0.37
INR (mean±SD) Range	1.1 ± 0.1 1.2 (1-1.3)	1.1 ± 0.1 (1-1.3)	0.31
CRP(Basal)(mean±SD)	1.8 ± 0.4	1.9 ± 0.2	0.06

Taurolidine group (TG). There were no significant differences between treatment groups at randomization time in baseline characteristics as shown in Table 1. No patients were lost during follow-up evaluation period. The main results are shown in Table (2).

Table (2): clinical outcome of patients' study sample

	Total (n= 86)	Group Heparin (n= 46)	Taurolidine Group (no= 40)	p-Value
Outcome of infection:				
Catheter related infection	12	10	2	0.031*
Episodes of antibiotic therapy	12	10	2	0.031*
Hospitalization for catheter related infection	5	4	1	0.032*
Outcome for catheter patency:				
Catheter Dysfunction	12	11	1	0.004*
Need for urokinase	5	3	2	0.76
Additional secondary outcomes:				

Catheter removal for infection	5	5	0	0.032*
Catheter removal for mechanical complications	8	7	1	0.043*

Catheter-related infections

A total of 2 CRIs occurred in 2 of 40 patients receiving the taurolidine-based regimen, and 10 CRIs occurred in 10 of 46 patients receiving heparin (p value=0.031*). The episodes of antibiotic therapy rate were significantly lower in the TG (p-value=0.031*). Hospitalization days for CRI events were significantly lower in the TG (p-value=0.032*). The total catheter dysfunctions rate was lower in the TG significantly (P =0.004*). The use of Urokinase as management of the tunneled catheter dysfunction was not significantly different between the 2 groups (P =0.76). Catheter removal for infectious causes was significantly lower in TG (p=0.032*), and removal for mechanical complications also occurred less in the TG (P=0.043*). No patients died due to infection-related complications.

Table (3) blood culture

	Group Heparin (n= 46)	**Taurolidine Group (no= 40)**	**P value**
Gram positive bacteria	6	1	0.75
Gram negative **bacteria**	1	1	0.92
fungi	3	0	0.1
Staph. aureus	4	1	0.22
MRSA	2	0	0.18
Pseudomonas	1	1	0.9
Candida	3	0	0.1

No difference was seen for gram-positive organisms, gram-negative, or fungi between the two groups (p =0.75, 0.92, and 0.1, respectively). Microorganisms detected in blood cultures are shown in Table (3).

4. Discussion

Total CRIs rates were moderately low in our study (14 %), which may be due to the CLS used and our compliance with standards concerning insertion and catheter care according to infection control criteria (18). we found that the incidence of CRIs was significantly lower in the TG (p=0.031*) which was in agreement with a study by O'Grady, et al.(19). Furthermore, it was consistent with findings by other investigators (20,21) . The blood culture withdrawn was not significantly different between the two groups, which was not consistent with Winnicki et al., (22). The rate of catheter dysfunction was significantly lower in TG (p value=0.004*), which agrees with a study by Winnick, et al. (22) which compared taurolidine lock solution and citrate 4%. Catheter dysfunction was in need in some cases for urokinase use as a fibrinolytic, which was determined by some studies (22,23). Improved catheter patency in all cases of catheter dysfunction in the two groups was observed after the use of Urokinase (taurolock you), which might be due to the destruction of Fibrin sheath or small blood clots by fibrinolytic (19,23). There was no significant difference in reversal of catheter dysfunction by use of Urokinase between the two groups (p=0.76). The catheter removal rate was very low in our study in both groups (15.1%) due to strict insertion and standard care. The rates of removal due to infectious or mechanical causes were significantly lower in TG (P-value=0.032*, 0.043*, respectively). Lastly, Hospitalization for catheter-related infection was significantly lower in TG also (P-value=0.032*). It was worth noting that we extended the follow-up duration for each patient in TG by 14% more than HG due to a reduction in catheter-based complications in TG.

5. Conclusion

Our study shows clear benefits of the taurolidine-based regimen compared with heparin solution regarding CRIs, catheter patency, removal for infectious or mechanical complications, and all-cause of Hospitalization. Thus, this catheter lock regimen may be favorable regarding complication rates and morbidity of dialysis patients with central lines.

Disclosure

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