Comparison Between Vancomycin Lock and Taurolock Solution for the Prevention of Catheter- related Infections in Hemodialysis Patients, A Multicenter Study

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Introduction. Central venous catheters, frequently used in patients undergoing hemodialysis, place the patients at high risk of catheter-related infections. Therefore, it is essential to select the optimal prevention protocol for these infections. This study aims to compare the efficacy of the Taurolock solution and antibiotic lock in preventing tunneled catheter (permcath) related infections.
Methods. This multicenter study was conducted between June 2020 and July 2021 on 86 hemodialysis patients with a central venous catheter from four dialysis centers in Tehran, Iran. The patients were randomly assigned into two groups. The first group received Taurolock, and the second group received antibiotic lock (a combination of vancomycin and heparin) at the end of each dialysis session. Peripheral blood and catheter blood samples were collected once before the intervention and monthly thereafter, for up to six months, and blood culture performed for detection of various bacterial strains.
Results. The findings showed no significant difference in the infection rate (positive peripheral blood or catheter cultures) between the Taurolock and vancomycin groups ($P > .05$). Additionally, there was no significant difference in the duration of catheter implantation in individuals with positive and negative cultures ($P > .05$). Furthermore, no significant correlation was found between comorbidities and catheter-related infection in patients of the two groups ($P > .05$).
Conclusion. There was no significant difference between the two groups in the rate of catheter-related infection. Therefore, vancomycin lock solutions can be good alternatives to Taurolock solution for preventing catheter-related infections.

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INTRODUCTION

One of the most important components of care for patients with end-stage kidney disease (ESKD) is managing and controlling vascular access. Currently, a significant number of hemodialysis patients receive dialysis through cuffed tunneled catheters. In fact, central venous catheters are used in more than half of all hospitalized patients, and over five million are implanted globally each year.[1,2] However, central venous catheters

can have adverse effects, including infectious complications leading to hospitalization, mortality, and increased medical costs. Infection is one of the main causes of hospitalization and the second most common cause of death in hemodialysis patients.[3,4] Catheter-related bloodstream infection (CRBSI) is a major cause of morbidity and mortality in these patients.[5] The incidence of CRBSI is reported 0.9 to 2 episodes per patient-year in patients using catheters as vascular access. [6,7] Central venous catheter infections are responsible for 15 to 30% of all deaths of hemodialysis patients and 2% of all hospitalizations.[8] Risk factors for catheter-related infections include long-term catheter use, recent history of CRBSI, recent any surgery, diabetes mellitus, and iron overload .[9,10] Central venous catheters may also have thrombotic or mechanical complications, and anticoagulant solutions are used to maintain the patency of catheter lumen when it is not in use. Despite several studies[11,12,13] in this field, no definitive measure has been proposed for preventing catheter-related infections.[11] In addition, there is currently no specific antibiotic or antibiotic dose proven to be effective in the antibiotic lock method and heparin.[11] However, antibiotic coverage of uncuffed catheters has been shown to be effective in cancer patients with acute kidney injury.[12] The use of an antibiotic lock technique limits intraluminal catheter colonization with different micro-organisms and consequently the development of CRBSI. Taurolock is one of the antibacterial lock solutions that has claimed to prevent infection and bacterial biofilms formation and improve the catheters patency rate. Taurolock contains taurolidine and 4% citrate, which is provided for the prevention of CRBSI. Taurolock solutions were significantly associated with a lower incidence of CRBSI when compared to heparin lock solutions.[13] The manufacturers also propose that its use can reduce infection rates by up to 90% with no adverse effects.[14,15] Taurolidine has shown to have a broad bactericidal activity against a wide variety of Gram-positive and Gram-negative organisms as well as fungi. It is not an antibiotic, and no antimicrobial resistance has been observed against it in laboratory conditions.[16]

Vancomycin is a glycopeptide antibiotic derived from Amycolathepsis Orientalis bacteria and is one of the non beta-lactam antibiotics.[17] The majority of CRBSI cases should be treated with empirical therapy for Gram-positive cocci, and treatment options should include glycopeptide antibiotics because many coagulase-negative staphyloccocal infections are resistant to beta-lactams.[18] Glycopeptide antibiotics are widely used for experimental treatment in patients with catheter-related infections.[19] Aminoglycoside combined treatment with penicillin or vancomycin is recommended only in cases where the patient is in a critical condition.[20]

This study was conducted to evaluate the efficacy of treatment with vancomycin antibacterial lock compared with Taurolock solution in preventing CRBSI in hemodialysis patients. This study also investigated the effects of different risk factors on catheter-related infection.

MATERIALS AND METHODS

Study Setting And Participants

This triple blind randomized clinical trial was conducted between June 2020 and July 2021 on hemodialysis patients with cuffed central venous catheters in four dialysis centers in Tehran. The inclusion criteria for the study were: 1) patients undergoing chronic hemodialysis through central venous cuffed catheters, 2) providing written consent to participate in the study, and 3) patients over 18 years old. The exclusion criteria were: 1) pregnancy, 2) history of addiction, 3) history of active and systemic infections before catheter insertion, 4) removal of catheter following A-V fistula insertion or kidney transplantation, 5) history of any surgery during the last year, and 6) history of drug allergies to antibiotics. The sample size in this study was estimated to be 100 people, by using Cochran's formula, which is used in cross-sectional descriptive studies. Fourteen patients did not continue the study due to the spread of the COVID-19, leading to examining, only 86 people at the end of the study.

Intervention

The written informed consent was obtained from all the patients before enrolling in the study. Ethical code number of this study was IR.SBMU.MSP.REC.1399.753 and also was registered by IRCT 20210921052544N1 code number. The patients were enrolled in the study and assigned specific codes for randomization. The hemodialysis patients with cuffed central venous catheter were divided into

two groups according to a triple-blind type of study. In the first group, pre-made and commercially available Taurolock solution was used at the end of each dialysis session. In the second group, an antibacterial lock solution was used, consisting of a combination of vancomycin and heparin. The antibacterial lock solution was prepared by combining 500 mg vancomycin with 10 mL distilled water or normal saline to obtain a concentration of 50 mg/mL. Then, 1 mL (50 mg) of the prepared solution was diluted with 9 mL of 0.9% sodium chloride to obtain a final concentration of 5 mg/mL vancomycin and a total volume of 10 mL. Finally, 1.5 mL (containing 7.5 mg vancomycin) of the prepared solution was injected into each permcath line, and the remaining volume of the line was filled with 5000 units of heparin. The solution, prepared in this way, can be stored under sterile conditions in the refrigerator for up to 72 hours.[21] Samples were collected from patients' catheters before the intervention, at the end of each month for up to 6 months, and samples were cultured to detect possible bacterial strains.

The followings were considered before sampling:

a. Blood culture was prepared before administering antibiotics.[22]
b. The catheter lines were clamped and the surrounding area disinfected with alcohol.
c. A 10 mL syringe was connected and 10 mL of blood was drawn from each catheter line and the catheter was clamped. After discarding this volume of blood another 10 mL syringe was connected, the catheter line was opened, and 10 mL blood samples were taken and placed in special blood culture bottles. Two aerobic and anaerobic bottles were used and the samples were stored in the refrigerator before being delivered to the laboratory.

Catheter-related infection is defined as the occurrence of local and/or systemic symptoms of infection (fever, chills, hemodynamic instability, altered mental status, catheter dysfunction, hypothermia, nausea/vomiting, and generalized malaise) with a positive culture from the catheter or peripheral blood samples, and recorded for each episode. At the end of research, patients' information from the last 6 months was recorded, including all local and systemic infection episodes, as well as the number of positive cultures. Information regarding diabetes mellitus, arterial blood pressure, ischemic heart disease, body mass index (BMI), anemia, hypoalbuminemia, location of catheter, and the frequency of catheter use per week were considered as risk factors for infection in hemodialysis patient.

Data Collection and Measurement

The data collection tool in this project was a researcher-designed questionnaire. The questionnaire recorded demographic information of the patients (age, sex) and other information such as the rate of infection caused by the catheter, underlying diseases, time and place of catheter insertion and a measurement of hemodialysis adequacy (Kt/V).

Statistical Analysis

The results were analyzed by SPSS version 18 software, using descriptive and analytical tests. Mean and standard deviation were used for quantitative variables in the descriptive part, while number and percentages were used for qualitative variables. In the analytical part, the information obtained from clinical infection and central vein catheter culture were compared by using t-Test, Chi-Square, and ANOVA tests, at the significance level of $P < .05$ in all tests. Finally, the rate of infection caused by the catheter and the episodes of infection were determined and compared between the two groups. The effect of other intervening factors including catheter stay, catheter location, and conditions predisposing patients to infection, on the occurrence of infection was also investigated.

RESULTS

Initially, 143 patients were included in the study but 57 patients were excluded due to the following reasons: changing the dialysis center (12 patients), end of dialysis due to significant improvement in renal function (10 patients), changing the dialysis method or receiving a kidney transplant (8 patients), changing catheter for reasons other than infection (10 patients), and non-referrals (2 patients), and dying before the end of the study (15 patients). Finally, a total of 86 hemodialysis patients participated in the study. Forty-two people (48.8%) received Taurolock solution and 44 (51.2%) received vancomycin. Patients' characteristics are shown in Table 1.

As seen in Table 1, there was no significant

Table 1. Patients Characteristics in 2 Groups of the Patients

Variable	Number (%)		*P*
	Taurolock	Vancomycin	
Gender			
Male	21 (50)	23 (52.3)	> .05
Female	21 (50)	21 (47.7)	
Age (mean ± SD), y	58.66 ± 15.82	63.36 ± 13.2	> .05
BMI			
< 20	5 (11.9)	4 (9.1)	
20 to 28.5	21 (50)	29 (65.9)	> .05
≥ 28.5	16 (38.1)	11 (25)	
Hemodialysis Duration, y			
< 1	8 (19)	4 (9.1)	
1 to 2	18 (42.9)	15 (34.1)	> .05
> 2	16 (38.1)	25 (56.8)	
Mean Kt/V			
0.8 to 1	12 (28.6)	12 (27.3)	
1 to 1.2	21 (50)	21 (47.7)	> .05
> 1.2	9 (21.4)	11 (25)	
Catheter Carriage Duration, mo			
< 6	3 (7.1)	1 (2.3)	
6 to 12	14 (33.3)	10 (22.7)	> .05
12 to 24	12 (28.6)	24 (54.5)	
> 24	13 (31)	9 (20.5)	
Catheter Position in Central Vein			
Femoral	4 (9.5)	1 (2.3)	
Right Jugular	35 (83.3)	38 (86.4)	> .05
Left Jugular	3 (7.1)	5 (11.4)	

difference in age ($P > .05$), gender ($P > .05$), BMI ($P > .05$), ESKD duration ($P > .05$), and hemodialysis adequacy (Kt/V) ($P > .05$) between the two groups. Additionally, there was no significant difference in the duration of catheter usage ($P > .05$) and the location of catheter ($P > .05$) between the two groups.

Furthermore, various infection risk factors, including diabetes mellitus, hypertension, ischemic heart disease (IHD), heart failure (HF), smoking and, hemoglobin and albumin levels after 6 months, were compared between the two groups. It was found that none of these risk factors were significantly different in the two groups (in all cases, $P > .05$) (Table 2).

The blood culture of 13 patients (15.1%) [5 patients (11.9%) in the Taurolock group and 8 patients (18.1%) in the vancomycin group] were positive (Table 3). The most common microorganisms were staphylococcus aureus and staphylococcus epidermidis in about 60% of both groups. Thus, the results showed that there was no significant difference between the incidence of infection (positive culture) and type of microorganism in the two treatment groups ($P = .05$).

Moreover, there was no significant correlation between different risk factors such as age, gender, underlying diseases, duration of catheter implantation, and its location with blood culture results in the two groups ($P > .05$).

DISCUSSION

In many patients undergoing chronic hemodialysis, central venous catheters are used as the main vascular access. CRBSI are the most serious complication of venous catheters and are associated with morbidity and mortality in these patients.[23,24] Several pathogenic microorganisms, which colonize inside permcaths, can easily form bacterial biofilms, eventually spreading to the bloodstream. Intraluminal antibiotic injection is used as a preventive method for biofilm formation and bacterial colonization in the catheters.[21,23] Since Gram-positive cocci are the main pathogens that form bacterial biofilms, vancomycin can be an appropriate choice to prevent infections caused

Table 2. Description and Comparison of Risk Factors in 2 Groups of Patients

Variable	Taurolock	Vancomycin	*P*
	Number (%)	Number (%)	
Diabetes			
Yes	20 (47.6)	22 (50)	> .05
No	22 (52.4)	22 (50)	
HTN			
Yes	31 (73.8)	37 (84.1)	> .05
No	11 (26.2)	7 (15.9)	
IHD			
Yes	12 (28.6)	14 (31.8)	> .05
No	30 (71.4)	40 (68.2)	
HF			
Yes	10 (23.8)	16 (36.4)	> .05
No	32 (76.2)	28 (63.6)	
Smoking			
Yes	8 (19)	9 (20.5)	> .05
No	34 (81)	35 (79.5)	
Hb after 6 months			
< 11	15 (35.7)	14 (31.8)	> .05
≥ 11	27 (64.3)	30 (68.2)	
Serum Alb After 6 months			
< 3.5	9 (21.4)	6 (13.6)	
≥ 3.5	33 (78.6)	38 (86.4)	> .05
≥ 28.5	16 (38.1)	11 (25)	

Abbreviations: HTN, hypertension; IHD, ischemic heart disease; HF, heart failure; Hb, hemoglobin; Alb, albumin.

Table 3. Blood Culture Results According to Different Parameters in 2 Groups

Variables	Culture Result			
	Taurolock		Vancomycin	
	Positive	Negative	Positive	Negative
Gender				
Male	3	18	3	20
Female	2	19	5	16
Diabetes				
Yes	1	19	5	17
No	4	18	3	19
IHD				
Yes	1	11	3	11
No	4	26	5	25
Smoking				
Yes	1	7	2	7
No	4	30	6	29
HF				
Yes	0	10	3	13
No	5	27	5	23
Catheter Position				
Right Jugular	4	31	8	30
Left Jugular	1	2	0	5
Femoral	0	2	0	1
Catheter Carriage Time, mo				
< 6	0	3	0	1
6 to 12	2	12	2	8
12 to 24	2	10	3	21
> 24	1	12	3	6

Abbreviations: IHD, ischemic heart disease; HF, heart failure.

by these biofilms.[23,25] Therefore, antibacterial lock with vancomycin and Taurolock solution were compared in the prevention of catheter-related infections in our study.

The results of our study show that the rate of catheter-related infections in the Taurolock group (12%) and the vancomycin group (18%) is not significantly different ($P > .05$).

Similar to our study, other researchers have also reported the use of the antibacterial lock technique with vancomycin in adults and children in eradicating CRBSI. In a study conducted by Liang *et al.*, the rate of catheter-related bloodstream infection in very low birth weight preterm infants in the vancomycin antibacterial lock group (4.4%) was significantly lower than the control group (21.7%).[26] In a six-year retrospective study, Alonso *et al.* collected data on patients with permcaths and CRBSI. They reported a success rate of about 42% with systemic antibiotics and vancomycin within 3 months and 71% until the end of the treatment.[27] Beigi *et al.* also showed that the administration of vancomycin-Lock therapy through catheter is more effective than its intravenous injection and leads to an increase in the durability of the catheter.[28] Al Hwiesh *et al.* reported that the rate of infection, bacteremia, and sepsis in hemodialysis patients was significantly lower in the group with the antibacterial lock solution (containing gentamicin and vancomycin) in comparison with the Taurolock solution within 12 months.[23] Their study emphasizes that a combination of two different antibiotics, containing gentamicin and vancomycin, is more effective in preventing permcath infections. The findings of our study were inconsistent with their results.

In the study by Bueloni *et al.* on 127 hemodialysis patients, the efficacy of antibacterial lock with a combination of cefazolin, gentamicin, and heparin) and Taurolock (Taurolock, citrate, and heparin) was the same in both groups, this fining is consistent with the results of our study. Although different antibiotics were used in this study.[29]

Filiopoulos *et al.* compared a group of patients

receiving Taurolock solution and heparin in a non-tunneled catheter with a group getting gentamicin and heparin alone, and reported no significant difference in the rate of catheter-related infections over a course of three months.[30]

In a meta analysis published by Labriola *et al.*,[31] it was reported that antibacterial lock with antibiotic reduced the rate of catheter-related infections. The variation between the outcomes of this study and those of another that utilized gentamicin lock suggests that gentamicin might be more potent than alternative solutions. This disparity in the results regarding catheter-related bloodstream infections (CRBSI) could be attributed to the utilization of gentamicin in one study and its absence in the other. Further investigation is warranted to better understand the reasons behind these differences and to refine our approach to prevent CRBSI effectively. There is a growing concern regarding the emergence of antibiotic resistance and development of the adverse effects from the prolonged use of antibiotics in antibacterial locks of permcaths. The emergence of multidrug-resistant (MDR) organisms has been shown to be an important cause of healthcare-associated infections and is accompanied with significant morbidity and mortality, especially in hemodialysis patients.[32] However, since Taurolidine used in Taurolock is an antiseptic, no bacterial resistance has been reported with its use.[33] It should be noted that our study was conducted on 86 patients and the small sample size could be considered as a limitation of this study.

CONCLUSION

The results of the present study showed that catheter-related infections decreased in patients who received antibacterial lock treatment during the 6-month period. However, there was no significant difference between patients who received vancomycin compared with those who received Taurolock ($P > .05$). Our findings suggest that the administration of antibacterial lock with vancomycin in central vein catheters can be an effective strategy in reducing catheter-associated infections in hemodialysis patients. Therefore, it seems that antibacterial lock with vancomycin could be a suitable substitute for the expensive Taurolock solution. However, it is worth mentioning that the use of antibiotics may lead to the emergence of multi-drug-resistant microorganism (MDR) infections, whereas taurolidine is a disinfectant solution, which does not induce drug resistance.

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Conflict of Interest Disclosures

The authors declare that they have no competing interests.

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