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Efficacy of Half Dose and One Third Dose of Injection Taurolock® for Tunneled Double Lumen Catheter Lock Solution

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ABSTRACT

Objective: To compare the efficacy of TaurolockHEP500®, as half and one third of standard dose on prevention of catheter related blood stream infection (CRBSI) and catheter dysfunction in patients undergoing hemodialysis via tunneled double lumen catheter.

Study Design: Quasi-experimental study.

Place and Duration of Study: Department of Nephrology, Armed Forces Institute of Urology, Rawalpindi, Pakistan, and Pak Emirates Military Hospital Rawalpindi, Pakistan from Sep, 2023 to Apr, 2024.

Methodology: The study recruited 314 patients, were divided into two groups; Group-A (n=157) and Group-B (n=157). Injection TaurolockHEP500® was administered into the tunneled double lumen catheter as half doses for Group-A and one third doses for Group-B. The rest of the space in catheter's lumen was filled with heparin. All the patients were then followed for 3 months. Blood samples for culture and sensitivity, were taken from both ports of their tunneled catheters and from a peripheral vein simultaneously to confirm CRBSI during fever spike in hemodialysis. Moreover, blood flow rates were monitored during each session to detect catheter dysfunction.

Results: Catheter function and blood culture didn't show a significant difference among two study groups (Group-A and Group-B) with p-values 0.702 and 0.556 respectively.

Conclusion: The catheter lock solution TaurolockHEP500® even in one third dose, after each session of hemodialysis, can significantly reduce the rate of bacteremia and catheter dysfunction.

Keywords: Catheter Related Infection, Hemodialysis, Taurolidine.

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INTRODUCTION

Chronic kidney disease (CKD) affects approximately 16% adults worldwide.[1] About 152 million individuals of Pakistan are suffering from ESRD.[2] Kidney transplant is preferred renal replacement therapy but availability of donor, and financial constraints limit its accessibility.[3] Consequently, most of the patients are left with option of hemodialysis.[1]

Hemodialysis demands an effective vascular access to ensure proper blood flow during dialysis. Arteriovenous fistula (AVF) is preferred for vascular access, but requires 6 weeks for maturation.[4] In contrast to AVF, tunneled catheters, used for long term hemodialysis, don't necessitate maturation to initiate hemodialysis.[5] However, they are susceptible to catheter related blood stream infection (CRBSI) due to bacterial colonization as well as thrombosis.[6] CRBSI is defined as an infection occurring in patients with an indwelling dialysis catheter, exhibiting fever (>38°C) or chills during dialysis without any other obvious cause of infection, with positive blood cultures of the samples obtained from both hubs of catheter and peripheral vein on simultaneously.[7]

These infections are second leading cause of demise in hemodialysis patients.[7] Whereas catheter-associated thrombosis is primary cause of catheter dysfunction in 30 to 40% of the cases.[6] Catheter dysfunction is defined as the inability of catheter to do a single dialysis session without recurrent pressure alarm or its failure to attain average blood flow rate of at least 250 mL/min.[8]

Catheter lock solutions containing antimicrobial agents and heparin are instilled into tunneled catheter lumens after each session of hemodialysis and withdrawn prior to next session, without systemic administration to prevent CRBSI and thrombosis.[9]

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TaurolockHEP500®, comprising taurolidine, 4% citrate and heparin 500IU/mL, a lock solution, known for two-fold reduction in CRBSI as it has shown a broad bactericidal and anti-fungal activity without developing antimicrobial resistance.[10] Such lock solution are expensive so a modality is needed to prevent bacteremia and catheter dysfunction at lower expenses.

METHODOLOGY

This Quasi-experimental study was conducted at Armed Forces Institute of Urology Rawalpindi and Pak Emirates Military Hospital Rawalpindi from September, 2023 to April, 2024. Research was started after the official approval of Institutional Review Board (IRB) Armed Forces Institute of Urology Rawalpindi (Uro-Adm-Trg-1/IRB/2023/006). The sample size of 314, 157 for each group was calculated using Epitools, keeping confidence interval of 0.95, power of 0.8 and population proportions of catheter related bacteremia 0.3 and 0.161 in control and case groups respectively.[11]

Inclusion Criteria: This study included patients who were undergoing hemodialysis via a tunneled double lumen catheter with blood flow rate (BFR) of > 250 mL/min at the start of the study and without previous history of CRBSI.[8]

Exclusion Criteria: Patients with catheter dysfunction defined by a (BFR) of < 250 mL/min, allergic to used drugs, with previous history of catheter dysfunction and CRBSI, IV drug abusers, changing dialysis from catheter to AVF or immunocompromised were excluded from the study.[8,11]

Patients fulfilling the selection criteria were recruited and informed consent was taken. They were then divided into two groups i.e., Group-A and Group-B, by using online computer software for randomization as shown in Figure-1.

Figure-: Patient Flow Diagram (n=314)

Baseline serum C-reactive protein (CRP) levels of all the patients were determined at the start of the study. After every session of hemodialysis, injection TaurolockHEP500® was administered into the tunneled double lumen catheter as half doses for Group-A11 and one third doses for Group-B. The rest of the space in the catheter's lumen was filled with heparin. All the patients were then followed for 3 months. Patients of both the groups were observed to detect fever spikes during each session of dialysis, those depicted fever and chills, their blood samples were collected to measure serum CRP levels and blood samples for cultures and sensitivity, were taken from both ports of their catheters and a peripheral vein simultaneously to confirm CRBSI. Moreover, blood flow rates were monitored during each session to detect catheter dysfunction.

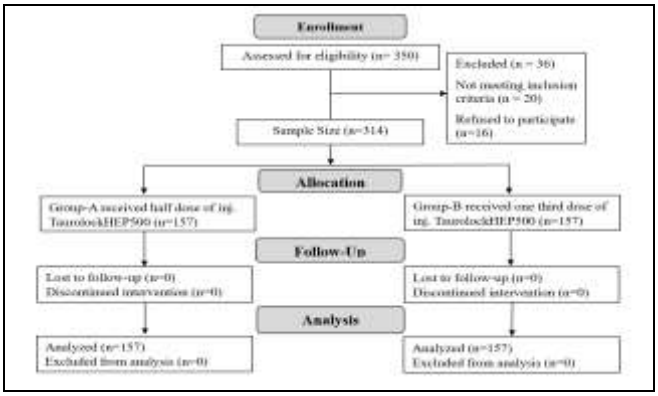

Figure-: Patient Flow Diagram (n=314)

The Statistical Package for Social Sciences Version 25 (IBM SPSS) was used for statistical analysis. The frequency (percentages) and Mean±SD was calculated for qualitative and quantitative variables. The normality of data was checked using Shapiro-Wilk test and skewed variables were represented using median inter-quartile range. The chi-square test was used to see statistical significance. *p*-value <0.05 was taken as significant.

RESULTS

There were 258(82.17%) males and 56(17.83%) females with cumulative age of 49.96±10.85 years. There were 251(79.94%) with diabetes mellitus, 203(64.65%) with hypertension, 7(2.23%) had catheter dysfunction and 12(3.82%) had CRBSI. The serum CRP levels were 10.0 (8.0–11.52) mg/L. The populations and group statistics are explained in Table-I.

None of the comparison groups including catheter dysfunction and blood culture showed statistical significance (p=0.702, p=0.556) as shown in Table-II.

Infection i.e blood culture was significantly correlated with catheter dysfunction (p=0.001) thus showing infection is associated with catheter blockage/ dysfunction (Table-III)

DISCUSSION

The tunneled double-lumen catheters have long been in use for hemodialysis. Due to their frequent handling and somewhat semi-permanent insertion

into the body, they tend to acquire infection. To prevent infections, tunneled double lumen catheter lock solutions are used, amongst them the TauroLockHEP500® is a taurolidine containing solution. In our resource constrained country, we tried to see the effect of a half dose TauroLockHEP500® solution (Group-A) and a one third dose of TauroLockHEP500® solution (Group-B). In a sample size of 314 individuals, equally divided (n=157) among the groups, the catheter dysfunction was seen in 3 individuals of Group-A while in 4 individuals in Group-B. Similarly, blood cultures were more positive (n=7) in Group-B as compared to Group-A (n=5). Though the frequency of catheter dysfunction and blood culture positivity was lower in Group-A than in Group-B, there was non-significant statistical difference between the two groups.

Table-I: Baseline Characteristics (n=314)

Variable	Total Sample Population (n=314)	Taurolock Treatment Group	
		Group-A (n=157)	Group-B (n=157)
Age (years)	49.96±10.854	50.01±11.22	49.90±10.51
Gender			
Male	258(82.17%)	126(80.25%)	132(84.07%)
Female	56(17.83%)	31(19.75%)	25(15.93%)
Comorbid			
Hypertension	203(64.65%)	102(64.97%)	101(64.33%)
Diabetes Mellitus	251(79.94%)	126(79.62%)	125(79.62%)
Symptoms			
Fever (°C)	12(3.82%)	5(3.18%)	7(4.46%)
Rigor and Chills	12(3.82%)	5(3.18%)	7(4.46%)
Catheter Dysfunction	7(2.23%)	3(1.91%)	4(2.55%)
Blood Cultures	12(3.82%)	5(3.18%)	7(4.46%)
Serum CRP Levels (mg/L)	10.0 (8.0 – 11.52)	10.0 (8.60– 12.0)	9.30 (7.0– 11.35)
Duration of Catheter Placement (months)	4.68±1.940	4.71±1.96	4.64±1.92

In our extensive literature search, we were able to find only one international study but no local study was found on the subject topic. Golmohamadi *et a*l., studied a sample size of 152 patients divided in control and case groups. They found a significant difference between the two groups at different but fixed durations. The half dose of TauroLockHEP500® was also able to decrease the infection rate significantly (p<0.05).[11] In our study, though we did not compare the half dose of TauroLockHEP500® against the full dose but the half dose of TauroLockHEP500® against the one third dose of TauroLockHEP500®. In this study we did not find a significant difference between the two dosing regimens. This can be due to differences in tunneled catheters used and duration of observations (smaller in our study). Fontseré *et al*., and Zwiech *et al*., found the TauroLockHEP500® effective in decreasing catheter related blood infections.[12,13] In this study too, we found that TauroLockHEP500® decreased not only the infection but also the infection rate.

Table-II: Association Amongst Different Study Variables (n=314)

Parameters	Patient Groups		*p*-value
	Group-A (n=157)	Group-B (n=157)	
Catheter Function (n=314)			
Functional	154(98.09%)	153(97.45%)	0.702
Dysfunction	3(1.91%)	4(2.55%)	
Blood Culture (n=314)			
Positive	5(3.18%)	7(4.46%)	0.556
Negative	152(96.82%)	150(95.54%)	

XTable-III: Association Between Infection and Catheter Dysfunction (n=314)

Parameters	Catheter Dysfunction		*p*-value
	Functional (n=307)	Dysfunction (n=7)	
Blood Culture (n=314)			
Negative	297(96.74%)	5(71.43%)	0.001
Positive	10(3.26%)	2(28.57%)	

In a systematic review and cost effectiveness analysis carried by Kavosi Z *et al*., it was found that taurolidine citrate was a better option in curbing CRBSI.[14] In this study though we didn't compare TauroLockHEP500® against other agents but we also found it to be effective in catering catheter infections. In another systematic review and meta-analysis conducted in the Netherlands, the researchers' found taurolidine lock solutions to be effective but at the same time they also recommended further research and analysis to establish the firm association and relationship between the two.[15] Liu *et al*. in their research established that the antimicrobial containing solutions like Taurolock were more effective in curtailing catheter related infections.[16] These findings are similar to the findings of this study, where a lesser number of infections were found in TauroLockHEP500® solution.

In a double blind trial conducted in Belgium, the prophylactic use of taurolidine urokinase lock solution (Taurolock-U), despite they did not find a statistical difference between the two groups but taurolidine

containing lock solution was associated with a lesser number of infections and catheter malfunctions.[17] In a study comparing Taurolidine Urokinase with taurolidine Heparin, found that taurolidine Urokinase was a better alternative in preventing all cause catheter dysfunction and catheter related blood site infections.[8] Murray *et al.*, also in their research concluded that Taurolidine solution are better in decreasing the frequency of infection in hemodialysis catheters.[18] Likewise in another study combination of Taurolock with heparin was an effective modality of curing catheter related infections than the heparin alone.[19]

LIMITATIONS OF STUDY

There are certain limitations in our study. First of all, it has small sample size. Secondly, the duration of study is also short, so the results / relationship might be different in large and long duration studies. Moreover, it was double center study, a multi-center study might give better insight into the issue. Therefore, we suggest a large multicenter interventional clinical trial for longer duration might be done to see the relationship between the TauroLockHEP500®, catheter malfunction and infection rate.

CONCLUSION

Administration of TauroLockHEP500® at one third of standard dose is as effective as its half dose in reduction of both bacteremia and catheter dysfunction in hemodialysis patients. This approach provides a cost-effective alternative to full and half doses of this costly lock solution and support its broader application in clinical practice.

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Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

GM & NK: Data acquisition, data analysis, critical review, approval of the final version to be published.

SS & FI: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

RN & MI: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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