Comparing the Efficacy of Gentamicin-heparin Solution to Heparin Alone as Catheter Related Blood Stream Infection in Patients Undergoing Hemodialysis.

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ABSTRACT

Catheter Related Blood Stream Infection (CRBSI) using non tunnelled catheters may be as high as 3.8/1000 catheter days and 11.9% according to local literature from Pakistan. Antibiotics with anticoagulants (e.g. Heparin) can be used to fill up the lumen of the catheter post dialysis in an attempt to prevent CRBSI. We performed a prospective randomized study to evaluate gentamicin catheter lock to prevent CRBSI.

Methods:
Hemodialysis patients initiating dialysis from the temporary jugular catheter between ages 18-80 were included. 100 each group of patients were randomized to A and B groups. patients randomized in two groups using a random numbers allocation table.
GROUP A: After insertion the catheters of patients locked with a combination of Gentamicin (GENTICIN 5 mg/mL) 2 mL and Heparin 5000 Units (1 mL) according to the catheter volume (1.4 cc in venous port and 1.2 cc in arterial port). The catheters locked with the combination solution after each dialysis session.
GROUP B: The catheters locked with Heparin 5000 units (1 mL) diluted in two mL normal saline. Catheters locked with heparin after all dialysis sessions until the end of study period.
RESULTS
Mean age was 50.06+12.09 in Grop A and 54.24+12.66 years in Group B, and 27(54%)were males. Comparison of efficacy of Gentamicin - Heparin solution to heparin alone as catheter lock for prevention of CRBSI shows that 6%(n=3) in Group-A and 28%(n=14) in Group-B developed CRBSI (p= 0.003)
CONCLUSION
The efficacy of gentamicin- heparin solution in preventing CRBSI is better than heparin alone when used as catheter lock solution in patients undergoing hemodialysis via temporary internal jugular catheter. A higher efficacy with gentamicin proves its usage as an effective and economical lock solution for prevention of CRBSI.
Key words: Catheter lock solution, Catheter related blood stream infection, temporary access catheter.
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PJKD 2019;(4):67-73

INTRODUCTION

Hemodialysis through temporary vascular access is a lifesaving intervention undertaken in patients with Acute or Chronic Kidney Disease (CKD) without permanent vascular access on presentation for dialysis. In developing countries temporary vascular access is commonly established using a non-cuffed, non-tunnelled double lumen haemodialysis catheter in any of the internal jugular, subclavian or femoral sites. The rate of Catheter Related Blood Stream Infection (CRBSI) using non tunnelled catheters may be as high as 3.8/1000 catheter days1 and 11.9%2 according to local literature.

Antibiotics with anticoagulants (e.g. Heparin) can be used to fill up the lumen of the catheter post dialysis in an attempt to prevent CRBSI. This technique is termed catheter locking[3]. Many antibiotics have been used as antibiotic lock solutions (ALS) to prevent CRBSI. A recent meta-analysis takes into account seven studies and supports that ALS may decrease the incidence of CRBSI thus preventing morbidity and mortality [4].

Another meta-analysis commenting upon 29 studies enumerates ALS that have been used (vancomycin, gentamicin, cefazolin, ceftazidime and cefotaxime) suggests that the use of ALS is a useful measure in the reduction of CRBSIs[5]. The efficacy of CRBSI was 24(96%) in the gentamicin group and 19(76%) in the heparin group ($P = 0.003$)[6,7] .

In our country where the usual temporary vascular access is a non-tunnelled haemodialysis catheter and strategies of infection prevention may not be up to international standards there is a rationale to test ALS. As such local studies on this topic are not available. It would seem that gentamicin being the least expensive may be an ideal choice to be used as ALS to prevent CRBSI in our population where catheter replacement and systemic antibiotics may prove to be very expensive in case CRBSI occurs.

METHODS:

Our study was designed as a randomized controlled study. Total of 100 patients presenting to the Nephrology Unit, Fatima Memorial Hospital and requiring hemodialysis via temporary internal Jugular catheter, from July 2013 to December 2013 were randomized.

INCLUSION CRITERIA: Patients of either gender aging between 18-80 years with history of acute and chronic kidney disease requiring dialysis for minimum of 4 weeks.

EXCLUSION CRITERIA: Patients already having a temporary vascular access or replacement over guide wire or femoral catheters were excluded. Any patient already on systemic antibiotics or too ill to survive by 6 weeks were also excluded.

DATA COLLECTION PROCEDURE: A total of 100 patients admitted in nephrology unit fulfilling the inclusion criteria enrolled in the study after obtaining approval from the Institutional Review Board. Informed consent obtained both for participation in the study as well as insertion of haemodialysis catheter. The patients randomized in two groups using a random numbers allocation table.

GROUP A: After insertion the catheters of patients locked with a combination of Gentamicin (GENTICIN 5 mg/mL) 2 mL and Heparin 5000 Units (1 mL) according to the catheter volume (1.4 cc in venous port and 1.2 cc in arterial port). The catheters locked with the combination solution after each dialysis session.

GROUP B: The catheters locked with Heparin 5000 units (1 mL) diluted in two mL normal saline. Catheters locked with heparin after all dialysis sessions until the end of study period.

Patients monitored and followed up vigilantly through the dialysis room and out-patient clinic. At each follow up patient asked about the symptoms suggestive of CRBSI and adherence to the study protocol.

DATA ANALYSIS:

Total of 100 cases were enrolled (50 each in both groups) using 5% level of significance, 90% power of test, with an expected percentage of prevention of CRBSI in Gentamicin as 96% and heparin group as 76%.[7]

The data collected was entered in SPSS version 19. For qualitative variable like gender and CRBSI , frequencies and percentages were determined respectively. The groups were compared using independent chi square test for significant differences between rates of CRBSI. A p value of 0.05 or less was considered significant.

RESULTS

Patient characteristics are shown in **table 1.** Comparison of efficacy of Gentamicin - Heparin solution to heparin alone as catheter lock for prevention of CRBSI shows that 6%(n=3) in Group-A and 28%(n=14) in Group-B developed CRBSI (p= 0.003), **table 2.**

Stratification according to age showed a significant difference among patients >50 years of age compared to younger age patients (p=0.01) who were in in group A, **Table 3**. Patients having more dialysis sessions had a chance to develop CRBSI while in group A (p=0.01) **Table 4.**

TABLE No. 1: Baseline characteristics

	Group-A (n=50)	Group-B (n=50)
Age(Years)	50.06±12.09	54.24±12.66
Male	27(54%)	29(58%)
Female	23(46%)	21(42%)

DISCUSSION

Catheter-related bloodstream infection remains a major cause for the catheter loss, and has been associated with significant morbidity and mortality among haemodialysis patients[1]. Many investigators have selected gentamicin as an antibiotic for preventive purposes, but available data of gentamicin lock solutions are relatively limited, and cannot be easily compared because of the different concentrations of gentamicin and citrate used in various studies [5].

This study was planned with the view that in our country where the usual temporary vascular access is a non-tunnelled haemodialysis catheter and strategies of infection prevention may not be up to international standards there is a rationale to test ALS. As such local studies on this topic are not available.

TABLE No. 2: Comparison of efficacy of gentamicin - heparin solution to heparin alone as catheter lock for prevention of catheter related blood stream infection (CRBSI)

CRBSI	Group-A (n=50)		Group-B (n=50)	
	No. of patients	%	No. of patients	%
Yes*	3	6	14	28
No	47	94	36	72
Total	**50**	**100**	**50**	**100**

*Between Group A and B P value=0.003

In our study, 100 cases (50 in each group) of both gender Undergoing hemodialysis for first time and having acute or chronic kidney disease with usual indications for haemodialysis through temporary vascular access (non-tunnelled haemodialysis catheter) were included. Comparison of efficacy of Gentamicin - Heparin solution to heparin alone as catheter lock for prevention of catheter related blood stream infection shows that 6%(n=3) in Group-A and 28%(n=14) in Group-B developed CRBSI while remaining 94%(n=47) in Group-A and 72%(n=36) had no findings of the morbidity.

TABLE No. 3: Stratification for catheter related blood stream infection (CRBSI) with regards to age of the patients.

Group Age 15-49 years	Yes	No	P value
A	2	22	0.22
B	5	16	
Group Age 50-80	**Yes**	**No**	**P Value**
A	1	25	0.01
B	9	20	

A meta-analysis commenting upon 29 studies enumerates the antibiotic lock solutions that have been used (vancomycin, gentamicin, cefazolin, ceftazidime and cefotaxime) suggests that the use of ALS is a useful measure in the reduction of CRBSIs[5]. The efficacy of CRBSI was 96% in the gentacin plus heparin group and 19(76%) in the heparin group (P = 0.003)[6,7]. These findings are in agreement with our study.

Another recent meta-analysis takes into account seven studies and supports that ALS may decrease the incidence of CRBSI thus preventing morbidity and mortality[4]. KM Chow and others8 investigated the effect of antibiotic lock solutions for preventing catheter-related bacteraemia in patients receiving haemodialysis and recorded that there were 18 and five catheter-related bacteraemia episodes before and after recourse to gentamicin antibiotic locks, respectively. Staphylococcus aureus contributed to over half (65%) of the total bacteraemia episodes. Use of gentamicin antibiotic locks significantly reduced CRBSI episodes per 1000

TABLE No. 4: Stratification for catheter related blood stream infection (CRBSI) with regards to number of haemodialysis sessions.

Group 1-6 sessions	CRBSI		P value
	Yes	No	
A	1	14	0.18
B	5	13	
Group 7-12 sessions	CRBSI		P value
A	2	23	0.01
B	9	33	

catheter days from 4.6 to 1.5 (P=0.002). Kaplan-Meier survival analysis using the log rank test showed significantly better bloodstream infection–free survival associated with using gentamicin antibiotic locks (P=0.032). A similar survival advantage was associated with gentamicin antibiotic locks when the analysis was restricted to non-tunnelled catheters. They concluded that the use of gentamicin lock solutions effectively reduced CRBSI in haemodialysis patients, including those with non-tunnelled catheters. The above study corresponds to the results revealed in our study.

Kim SH[9] evaluated the efficacy of catheter-restricted filling using an antibiotic lock solution in preventing CRBSI and concluded that the results suggest that ALT may be a beneficial means of reducing the CRBSI rate in hemodialysis patients with non-cuffed catheter.

In an in vitro hemodialysis catheter study by Vercaigne et al[10] it was found that a combination antibiotic–heparin lock had a higher sterilization effect on methicillin-resistant S. epidermidis than a single antibiotic–heparin lock. They also found that a gentamicin–heparin lock solution and a cefazolin–gentamicin–heparin lock solution showed similar bactericidal effects.

Conclusion:
In conclusion, we concur with the results of previous studies that the efficacy of gentamicin-heparin solution in preventing CRBSI is better than heparin alone when used as catheter lock solution in patients undergoing hemodialysis via temporary internal jugular catheter. A higher efficacy with gentamicin proves its usage as an effective and economical lock solution for prevention of CRBSI.

Disclosure:
None disclosed by authors.

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