

Prevention of Catheter Related Blood Stream Infection Using Heparin Plus Gentamicin Catheter Lock Solution in Comparison to Heparin Alone. A Randomized controlled study.

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ABSTRACT

INTRODUCTION: Optimal survival and the quality of life of patients with end stage renal disease (ESRD) on long term hemodialysis (HD) is largely dependent upon the adequacy of dialysis through an appropriately placed and properly functioning permanent vascular access with minimal mechanical complications and infection rates. The objective of the study was to: compare the frequency of catheter related blood stream infection (CRBSI) episodes with heparin alone vs heparin in combination with gentamicin in patients of ESRD on HD.

STUDY DESIGN:

Randomized controlled trial over a 6 months period.

METHODOLOGY:

A total of 110 patients fulfilling the selection criteria were enrolled in the study from nephrology ward of Allied Hospital, Faisalabad and randomly divided in two groups. In Group A, at the end of each HD session, each port of the catheter was filled with 5000 U/mL of unfractionated heparin solution according to the volume of the ports. In Group B dialysis catheter lumens were locked with gentamicin in addition to heparin at 5000 U/mL. The final concentration of gentamicin in the antibiotic lock solution was 5 mg/mL. Patients were followed up for next hemodialysis session. Blood cultures were obtained when CRBSI was clinically suspected and sent to the laboratory of the hospital. Reports were assessed and CRBSI episodes were noted.

RESULTS:

Out of 110 cases (55 in each group), mean age was calculated as 48.75 ± 13.57 and 49.95 ± 15.73 years in Group-A and B respectively. Males representation was higher in both groups, 52.73%(n=29) in Group-A and 60%(n=33) in Group-B. CRBSI was significantly higher in Heparin alone group: 29.09%(n=16) in Group-A and 9.09%(n=5), $p=0.007$.

CONCLUSION:

We conclude that combination of heparin and gentamicin as compared to heparin alone is better in prevention of CRBSI in patients being dialyzed through temporary venous catheter.

KEYWORDS:

End stage renal disease, hemodialysis, catheter related blood stream infection (CRBSI), heparin, gentamicin.

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INTRODUCTION

Chronic Kidney Disease (CKD) is a worldwide public health problem. It is recognized as a common condition that is associated with an increased risk of cardiovascular disease and end stage renal disease (ESRD). Chronic kidney disease affects all races, but, in the United States, a significantly higher incidence of ESRD exists in blacks than in whites; the incidence rate for blacks is nearly 4 times that for whites.^{1,2}

Patients with CKD generally progress to ESRD. The rate of progression depends on the underlying diagnosis, on the successful implementation of secondary preventive measures, and on the individual patient.³

Central venous catheters (CVCs) are used for vascular access in hemodialysis patients who have no alternative access or are waiting placement/ maturation of a permanent access. The major complications of CVCs are catheter-related bloodstream infection (CRBSI) and clotting in the catheter lumen.⁴ Infections related to CVCs are an important cause of morbidity and mortality for hospitalised patients as well as outpatients.⁵ Hemodialysis performed 6 times per week significantly increased the risk of vascular access complications compared with a conventional 3-day per week regimen in one study.³ A study reported the CRBSI episodes in 5/74 (6.76%) cases with gentamicin plus heparin and in 18/75 (24%) cases with heparin alone. The difference between both groups was highly significant (p-value=0.002).⁶

CRBSI remains a major cause for the catheter loss and has been associated with significant morbidity and mortality among haemodialysis patients. Paucity of data exists regarding incidence of CRBSI from Pakistan. In a recent study CRBSI incidence was noted to be 17 % with temporary vascular catheters.⁷

Heparin is an anticoagulant and is usually used as catheter lock solution in CKD patients on HD and suppose to have some antimicrobial effect.⁸ Still the incidence of CRBSI is very high with heparin alone.^{6,7} Gentamicin is a good prophylactic antibiotic that can be used to reduce CRBSI episodes.⁶ We therefore

conducted the this study to prove that gentamicin can prevent CRBSI compared to Heparin alone.

MATERIALS AND METHODS

STUDY DESIGN:

It was a prospective Randomized controlled trial over a six month period. The study was conducted at Nephrology Ward, Department of Nephrology, Allied Hospital, Faisalabad, Pakistan.

Catheters related blood stream infection (CRBSI) episode:

It was measured as CRBSI occurring in blood stream of patient (confirmed through laboratory investigations i.e. isolation of the same organism in blood cultures drawn from the peripheral blood and catheter, and with no other cause for the infection) during the period between catheter insertion and the first positive blood culture obtained from that catheter after administration of catheter lock solution in previous hemodialysis.

SAMPLE SIZE:

Sample size of 110 cases; 55 in each group is calculated with 80% power of test, 5% level of significance and taking expected percentage of CRI episodes i.e. 6.76% with combination of gentamicin with heparin and 24% with heparin alone in patients of chronic kidney disease on hemodialysis.⁶ We used non-Probability, Purposive sampling for data collection.

Inclusion Criteria: Patients of any age and gender with diagnosis of ESRD (as per operational definition) on hemodialysis having central venous catheters inserted for hemodialysis.

Exclusion Criteria: Deranged LFTs (ALT>40IU, AST>40IU), medical record of current malignant diseases, pregnancy, severe anemia (Hb<10 g/dl) due to dialysis.

Patients with chronic hypertension (BP \geq 140/90mmHg on medical record), or with medical record of cardiac problems.

Abnormal coagulation profile or active bleeding episodes requiring management.

DATA COLLECTION PROCEDURE:

After approval from hospital ethical committee, 110 patients fulfilling the selection criteria was enrolled in the study from nephrology ward of Allied Hospital, Faisalabad. Informed consent was taken. Demographic information (name, age, gender and contact) was recorded. Patients were randomly divided in two groups by using computer generated random number table. Patients in group A was given Heparin alone while patients in B group was given Heparin in addition with Gentamicin. In A group, at the end of each haemodialysis session, each port of the catheter was filled with 5000 U/mL of unfractionated heparin solution according to the volume of the ports. In B group, dialysis catheter lumens were locked with gentamicin in addition to heparin at 5000 U/mL. The final concentration of gentamicin in the antibiotic lock solution was 5 mg/mL. Upon completion of each dialysis session, all the gentamicin-heparin locks were instilled into both lumens of the dialysis catheter, and withdrawn immediately prior to the next dialysis session. Patients were followed up for next hemodialysis session. Blood cultures were obtained when catheter-related bacteraemia was clinically suspected and sent to the laboratory of the hospital. Reports were

assessed and CRI episodes were noted (as per operational definition). All the data was collected using the proforma by myself (attached).

DATA ANALYSIS:

SPSS (version 16.0, Chicago Illinois, USA) was used for data analysis. Quantitative variables like age, serum creatinine and GFR was presented by calculating mean and standard deviation. Qualitative variables like gender and catheter related infection episodes were presented in form of frequency and percentage. Both groups were compared for catheter related infection episodes by using chi-square test taking p-value \leq 0.05 as significant.

RESULTS

A total of 110 cases (55 in each group) fulfilling the inclusion/exclusion criteria were enrolled to compare the frequency of catheter related infection (CRI) episodes with heparin alone with heparin in combination with gentamicin in patients of End stage renal disease on hemodialysis. Age and gender distribution is shown in table 1 and 2.

Comparison of CRBSI in both groups revealed significantly lesser episodes of CRBSI : 29.09%(n=16) in Group-A vs 9.09%(n=5) in Group-B (p= 0.007), Table No. 3.

TABLE 1: Age distribution among 110 hemodialysis patients dialyzed with temporary vascular access catheter and randomized to Group A: Heparin vs Group B: Heparin plus gentamicin catheter lock solution.

Age (in years)	Group-A (n=55)		Group-B (n=55)	
	No. of patients	%	No. of patients	%
15-40	21	38.18	18	32.73
41-80	34	61.82	37	67.27
Total	55	100	55	100
Mean \pm sd	48.75 \pm 13.57		49.95 \pm 15.73	

Discussion:

Optimal survival and the quality of life of patients with ESRD on long term HD has improved in the west owing to adequacy of dialysis through an appropriately placed and properly functioning permanent vascular access with minimal mechanical complications and infection rates.⁹

CRBSI remains a major cause for the catheter loss and has been associated with significant morbidity and mortality among HD patients. The risk of bacteremia with tunnel cuffed catheters averages 2.3 per 1000 catheter days, which translates into an approximate 20 to 25 percent risk over the average duration of use.¹⁰ The

Table 2: gender distribution among 110 hemodialysis patients dialyzed with temporary vascular access catheter and randomized to Group A: Heparin vs Group B: Heparin plus gentamicin catheter lock solution.

Gender	Group-A (n=55)		Group-B (n=55)	
	No. of patients	%	No. of patients	%
Male	29	52.73	33	60
Female	26	47.27	22	40
Total	55	100	55	100

bacteremia rate ranges from 0.1 to 5.5 per 1000 catheter days in prospective studies of tunneled catheters associated with a 22 to 38 percent rate of metastatic infectious complications or death.¹⁰ For non-tunneled catheters, the development of exit-site infection or bacteremia requires prompt removal of the catheter and appropriate intravenous antibiotic therapy.¹¹

TABLE 3: Comparison of Catheter related blood stream infection episodes among 110 hemodialysis patients dialyzed with temporary vascular access catheter and randomized to Group A: Heparin vs Group B: Heparin plus gentamicin catheter lock solution.

CRBSI	Group-A (n=55)		Group-B (n=55)	
	n	%	n	%
Yes	16	29.09	5	9.09*
No	39	70.91	50	90.91
Total	55	100	55	90.91

*P value=0.007

Our findings are in agreement with a study reporting the CRBSI episodes in 5/74 (6.76%) cases with gentamicin plus heparin compared to 18/75 (24%) cases with heparin alone and that was statistically significant (p-value=0.002).⁶

Concerns however, have been raised about stability of the commonly used antibiotics with heparin, possibly resulting in a concentration insufficient to be active as an antimicrobial, and potentially reducing long-term catheter function and patency rates (due to precipitation). Gentamicin has been studied combined with sodium citrate (with its own intrinsic antibacterial action) as an alternative

catheter restricted anticoagulant in an attempt to negate this issue.¹² Its use has been shown to reduce line sepsis rates in a prospective controlled study of new line insertions and increasing clearance rates when combined with systemic antibiotics in the treatment of CRI.¹³ Gentamicin (at a dose of 5 mg/mL), however, does appear sufficiently stable when combined with heparin to maintain a concentration sufficient to decrease the incidence of infection in central venous catheters, with an in vitro reduction in intraluminal concentration of only 8%.¹⁴

Christopher W et al studied the use of gentamicin locking of catheters (in combination with standard heparin rather than previously reported citrate) to reduce CRBSI rates.¹⁵ They recorded only one infective episode in the Gentamicin group (0.3/1000 catheter days) compared to 10 episodes in six patients in the heparin alone group (4/1000 catheter days, P = 0.02) and concluded that the practice of locking newly inserted tunneled central venous catheters with gentamicin and heparin is an effective strategy to reduce line sepsis rates, and is associated with beneficial effects on erythropoietin requirements.

Our study therefore complements these previous international studies for the role of Gentamicin in prevention of CRBSI. However, further local studies are required to authenticate the findings of our study.

CONCLUSION

Combination of heparin and gentamicin as compare to heparin alone is associated with significant lower rate of CRBSI in patients of ESRD initiating HD with a temporary catheter. We recommend that it should be the routine practice in such patients, however further local studies are needed.

Conflict of interest:

None declared

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