



## COMPARING EFFICACY OF DIFFERENT LOCK SOLUTIONS IN PREVENTING CATHETER RELATED BLOOD STREAM INFECTION IN HEMODIALYSIS PATIENTS

<sup>1</sup>Dr. Prasun Roy, <sup>\*2</sup>Dr. Sanjay Dasgupta, <sup>3</sup>Dr.Smita Subhash Divyaveer, <sup>4</sup>Dr.Avinandan Banerjee, <sup>5</sup>Dr. Tanima Das Bhattacharya and <sup>6</sup>Dr. Prof Rajendra Pandey

<sup>1</sup>Department of Nephrology- Burdwan Medical College- Burdwan, 713104

<sup>2</sup>Associate Professor- Department of Nephrology- NRS Medical College, Kolkata, 700014

<sup>3</sup>Assistant Professor- Department of Nephrology- PGIMER, Chandigarh, 160012

<sup>4</sup>Department of Nephrology- CMRI, Kolkata, 700027

<sup>5</sup>Assistant Professor- Department of Nephrology – NRS Medical College, Kolkata, 700014

<sup>6</sup>Professor and HOD- Department of Nephrology- IPGIMER, Kolkata, 700020

### ARTICLE INFO

#### Article History:

Received 6<sup>th</sup> March, 2020

Received in revised form 15<sup>th</sup>

April, 2020

Accepted 12<sup>th</sup> May, 2020

Published online 28<sup>th</sup> June, 2020

#### Key words:

Catheter related infection, Hemodialysis, Heparin, Gentamicin

### ABSTRACT

**Background:** Hemodialysis (HD) is most common form of renal replacement therapy available for patients with end stage renal disease in India. The most common vascular access used in patients initiating HD in India is non-cuffed catheter. However, it has significant infective complications.

**Objective:** To compare effect of two different catheter lock solution i.e. Heparin (H) versus heparin plus gentamicin (HG) lock on catheter lifespan and incidence of dialysis catheter related blood stream infections (CRBSI).

**Materials and methods:** This is a single centre prospective randomized controlled study conducted at tertiary care hospital from February 2017 to August 2018. All patients with end stage renal disease initiating dialysis via non- tunnelled and non-cuffed catheter were screened for enrolment. 47 eligible patients were randomized into two groups. Control group (H) received standard lock with Heparin. HG group received lock with heparin plus Gentamicin. Catheter lifespan and catheter related blood stream infection (CRBSI) rate in the two groups was compared. In those who developed CRBSI, catheter was removed if fever persisted for 2 days despite empirical antibiotic therapy or blood flow during dialysis was persistently less than 200ml/min. Blood culture and catheter tip culture, if catheter was removed was done for suspected CRBSI. Culture and sensitivity pattern was noted.

**Results:** 109 patients were screened. 47 participants satisfied the eligibility criteria and were included in the study. Average catheter duration was  $40.62 \pm 7.89$  days. Overall the cumulative incidences of CRBSI at the end of the study period were 5.76 events per 1000 catheter-days. 11 (23.4%) patients developed catheter related infection during the study. Incidence of CRBSI in control (H) group was 7.97 events per 1000 catheter-days versus 3.88 events per 1000 catheter-days in HG group. Catheter lifespan in H and HG group was  $38.17 \pm 7.15$  days and  $42.96 \pm 7.99$  days respectively ( $p=0.036$ ). 4 out of 24 patients in HG group developed growth of organisms in contrast to 7 out of 23 in H lock group.

**Conclusions:** Use of Gentamicin plus heparin lock solution in non-tunnelled non-cuffed HD catheter as compared to standard Heparin lock alone decreases the rate of catheter related blood stream infection and a modest but statistically significant increase in catheter lifespan.

Copyright©2020 Dr. Prasun Roy et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

### INTRODUCTION

The prevalence of end-stage renal disease (ESRD) is increasing with an enormous financial burden on society.[1] Although exact incidence of using cuffed vs non cuffed catheter is not available in our country, but experience shows that non-cuffed catheter is used in a significant number of

patients especially in resource limited settings. Infection is second leading cause of death in hemodialysis patients, next to cardiovascular disease. Unfortunately, there has not been any major advancement in the past two decades that has been successful in reducing either infection-related morbidity or mortality in this patient population.

Traditionally, management of catheter related blood stream infection (CRBSI) included catheter removal and replacement, but treatment with antibiotics alone, without catheter

\*Corresponding author: Dr. Sanjay Dasgupta

Associate Professor, Department of Nephrology, NRS Medical College, Kolkata 700014

replacement, can be successful [2]. Though arterio-venous fistula (AVF) is the best form of vascular access, most patients still initiate dialysis via non-tunnelled noncuffed HD catheter (NT NC Cath). Late referral to nephrologists in advanced stages of renal failure, non-availability of facilities for tunnelled catheter insertion and reluctance of patients to accept need of renal replacement in future are the main reasons for the use of NT NC Cath for dialysis initiation. CRBSI is a relatively common complication of NT NC Cath and can delay AVF placement till resolution. Increased longevity of NT NC Cath without CRBSI will allow time for a definitive access i.e. AVF creation and maturation.

Heparin lock post dialysis is routinely practised in most HD centres for prevention of thrombosis which can also act as nidus for infection. The objective of this study is to compare catheter survival and the incidence of catheter related blood stream infection using heparin (H) lock alone versus heparin plus gentamicin (HG) lock in hemodialysis patients with NT NC Cath.

## MATERIALS AND METHODS

The study is a single centre prospective open label randomized parallel group interventional study conducted in the Department of Nephrology, IPGME& R and SSKM Hospital, Kolkata, India from February 2017 to December 2018. All patients with end stage renal disease admitted in the Department of Nephrology, those attending OPD services and those referred to this department from other hospitals requiring dialysis initiation via NT NC cath were screened as per the following inclusion and exclusion criteria.

### Inclusion Criteria

1. Patients receiving hemodialysis with new jugular NT NC cath.
2. Patients willing to continue the prescribed schedule of dialysis.

### Exclusion Criteria

1. Patients <18 yr age
2. Pregnant or lactating female
3. Known allergy or contraindication to heparin or gentamicin
4. Currently being treated for CRBSI
5. Received antibiotic treatment within 14 days prior to enrolment
6. Patients already having central line catheter

Institutional ethics committee approval was obtained. All eligible participants were enrolled after taking written informed consent and randomized into two groups using computer generated random group allocation. The control group (H) received heparin and HG received heparin plus gentamicin as described below.

**Control group (H):** 2 ml of 5000 unit/ml Injection heparin is added to 2ml Normal Saline to make a final concentration 2500 units/ ml. Volume instilled in each lumen was as per the catheter specification.

**HG group:** Preparation of lock solution: 0.5 ml of Injection Gentamicin (concentration 40 mg/ml ) diluted with 9.5 ml of Normal Saline (concentration = 2 mg/ml) was prepared. 2ml of this solution was added to 2 ml of Injection heparin 5000 U/ml to make a total volume of 4 ml. Final concentration of 1mg/ml

Gentamicin with 2500 IU/ml Heparin was used as lock solution.

Volume instilled in each lumen was as per the catheter specification.

Patients were followed up every 2 weeks till an event of CRBSI necessitating removal of catheter or removal of catheter for any reason.

Catheter care protocols conformed to standard guidelines for haemodialysis vascular access.[3] This included catheter insertion using strict asepsis and application of povidone-iodine ointment at the catheter exit site; the right internal jugular vein was used whenever possible. During dialysis, haemodialysis catheters were handled only by trained dialysis staff. Catheters were not used for routine blood sampling or drug administration. To minimise the risk of contamination during haemodialysis, the vascular catheter hubs were removed in a strictly sterile manner, with immediate connection to reduce exposure to air. The exit site was cleaned, and after each dialysis session a povidone-iodine impregnated dressing was applied. No concomitant nasal mupirocin was used during that period.

Definition of CRBSI as per Kidney Disease Outcomes Quality Initiative (KDOQI) 2012: if any of the following were present, patient was classified to have CRBSI.

**Definite:** Same organism from a semi quantitative culture of the catheter tip (>15 Colony Forming Unit/catheter segment) and from blood culture in a symptomatic patient with no other apparent source of infection.

**Probable:** Defervescence of symptoms after antibiotic therapy with or without removal of the catheter, in the setting in which blood culture confirms infection, but catheter tip does not (or catheter tip does, but blood does not) in a symptomatic patient with no other apparent source of infection.

**Possible:** Defervescence of symptoms after antibiotic treatment or after removal of catheter in the absence of laboratory confirmation of blood stream infection in a symptomatic patient with no other apparent source of infection.

In case of probable CRBSI, catheter was removed if fever persisted for 2 days in spite of empirical antibiotic therapy and/or blood flow during dialysis is persistently less than 200ml/min.

In case of catheter removal catheter tip end were taken aseptically, and then thoroughly washed with phosphate buffer saline (pH 7.2) to remove non-adherent cells. The devices were dipped into the tubes containing 5 ml Brain heart infusion (BHI) broths (Hi-Media, India), and then squeezed a little with the help of sterile forceps, and incubated at 37°C for 24 hours. One loopful of broth from each tube was subcultured on blood agar (Hi-Media, India) plates. Isolated colonies were provisionally identified based on growth characteristics, morphology, motility, and biochemical test results.[5]

Catheter salvage was attempted when clinically reasonable (*i.e.*, in all cases in which the clinical presentation was not severe [no hypotension or other features of severe sepsis] and an adequate initial response to antibiotic treatment was seen within 48 hours [afebrile and symptoms resolved]). Empirical treatment consisted of vancomycin and ceftazidime. When

indicated (by features of severe sepsis or the persistence of fever after 48 hours of antibiotic therapy), catheter removal was carried out within 24 hours of the decision.

**Statistical analyses**

Statistical analysis was performed using the Statistical Package for the Social Sciences (Windows version 20.0; SPSS Inc, Chicago [IL], US). All data were expressed as mean ± standard deviation, unless otherwise specified. Data were compared by Chi squared test, Fisher’s exact test, Student *t* test, or one-way analysis of variance, as appropriate. A p value of less than 0.05 was considered significant. All probabilities were two-tailed. Antimicrobial susceptibility tests for all bacterial isolates were performed by Kirby-Bauer disk diffusion method.

**Primary outcome**

1. Mean duration of catheter survival in the control and gentamicin group.
2. Incidence of catheter related blood stream infection in the control and gentamicin group.

**RESULTS**

Total 109 patients were assessed for eligibility. 56 patients were excluded of which 49 patients had not met inclusion criteria and 7 patients declined to participate. Rest 53 patients were randomized according to a computer generated random number table in two groups. 27 patients were allocated to heparin plus gentamicin lock group and 26 patients were allocated to heparin only lock group. 3 patients were lost to follow up in each group as shown in figure 1. Twenty four patients of heparin plus gentamicin lock group and 23 patients of heparin only lock group were analysed according to per protocol analysis. Baseline parameters have been shown in table 1.

Incidence of catheter related blood stream infection was 3.88/1000 catheter days in HG group and 7.97/1000 catheter days in H lock group as shown in table 2 and figure 2. However, this difference was statistically not significant. The catheter life span was 42.96 ± 7.99 days and 38.17 ± 7.15 days in HG and H groups respectively (figure 3). This difference was statistically significant.

In our study 11 patients showed growth of organism, out of 47 patients analysed as shown in figure 4. 5/11 patients showed growth of methicillin resistant Staphylococcus aureus (MRSA), 4/11 patients E. coli, 1/11 each showed growth of S. epidermidis, and Pseudomonas aeruginosa respectively. 4 out of 24 (16.66%) patients in HG lock group developed growth of organisms in contrast to 7 out of 23 (30.43%) patients in heparin only lock group. In HG group 3 patients showed gram negative organism growth- all E.coli and 1 gram positive organism- MRSA. In heparin only group, 5 patient showed gram positive organism growth- 4 MRSA, 1 S. epidermidis; and 2 gram negative organisms- 1 E.coli and 1 P. aeruginosa.

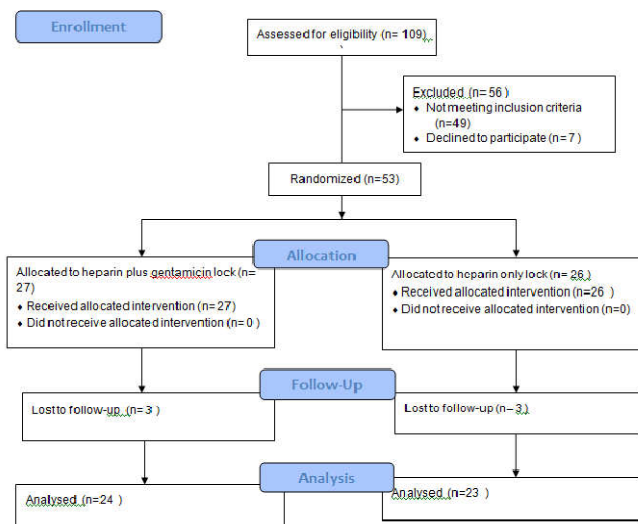
**Table 1** Comparison of baseline characteristics in heparin and heparin with gentamicin groups

Variables	Gentamicin + Heparin Lock (n=24)	Heparin Only Lock (n=23)	P value
Age (yrs)	42.21 ± 20.9	45.65 ± 22.25	0.59
Sex (male)	13 (54.17%)	12 (52.17%)	0.89
Living place (urban)	13 (54.17%)	10 (43.48%)	0.46
Number of previous access	1.5 ± 0.98	1.78 ± 0.9	0.31
HD session per wk	2.54 ± 0.51	2.48 ± 0.51	0.67

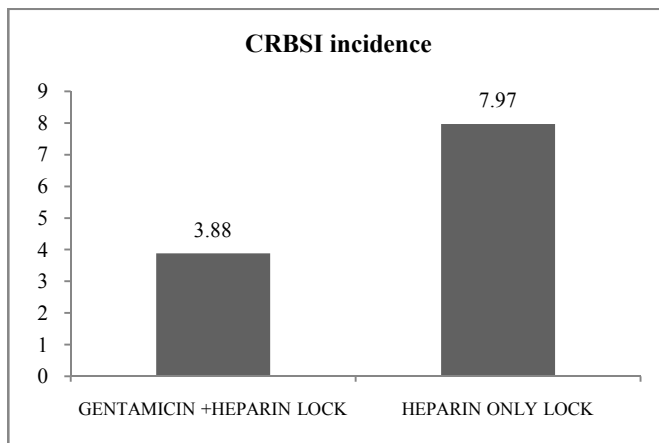
HD vintage (months)	12.17 ± 5.98	12.74 ± 5.67	0.74
Hemoglobin (gm/dl)	8.87 ± 1.1	8.65 ± 0.95	0.46
Albumin (mg/dl)	3.31 ± 0.54	2.92 ± 0.57	0.20

**Table 2** Outcomes in control (heparin) and Gentamicin group

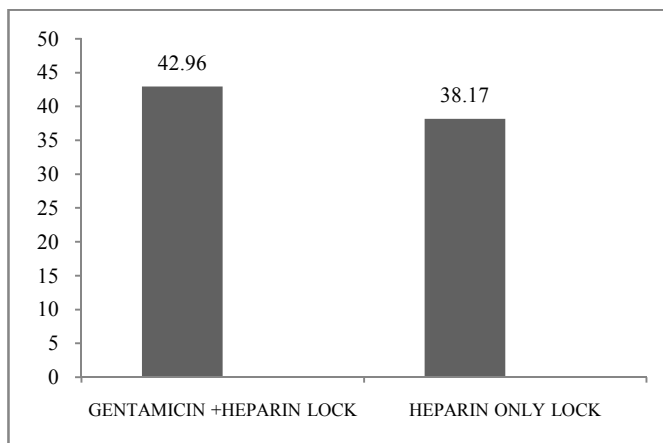
Variables	Gentamicin + Heparin Lock (n=24)	Heparin Only Lock (n=23)	P Value
Catheter lifespan (days)	42.96 ± 7.99	38.17 ± 7.15	0.036
CRBSI incidence	3.88 / 1000 catheter-days	7.97 /1000 catheter-days	0.24



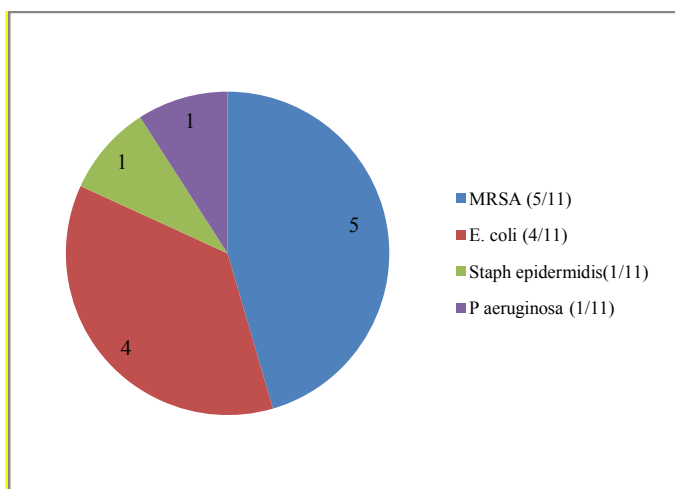
**Figure 1** Flowchart of study participants



**Figure 2** Catheter related blood stream infection (CRBSI) [in events per 1000 days]



**Figure 3** Average catheter lifespan (in days) in heparin and gentamicin plus heparin groups



**Figure 4** Types of organisms in patients with CRBSI

## DISCUSSION

Studies from India have reported that [6] in about 75% of cases requiring hemodialysis initiation, the first vascular access was non-tunneled non-cuffed catheter, followed by AV fistula and permcath. It was also found that, in majority of resource limited setting; the common practice is to continue hemodialysis with that same access rather changing the access to cuffed catheter before maturation of AV fistula.

There are many studies available comparing efficacy of various lock solutions in tunneled cuffed catheter; however there was a very limited number of study available for lock solutions in NT NC dialysis catheter. As per our knowledge, no such study is available in Indian scenario. So, this study was contemplated.

The baseline parameters like age, sex, living place, number of previous access, mean number of dialysis per week, hemodialysis vintage, haemoglobin level- all are comparable in H and HG groups.

In a retrospective study, Chow *et al* showed [7] that use of gentamicin antibiotic locks significantly reduced catheter related bacteraemia episodes from 4.6 /1000 catheter days to 1.5/1000 catheter days. This change was statistically significant. In their study, however, catheter lifespan was not changed significantly. This difference may be attributed to the fact that over the time frame of their retrospective study, not only the practice of using antibiotic solution has changed; other practices influencing CRBSI may also have changed. Moreover, antibiotic concentration used in their study was 5mg/ml with heparin 5000 U/ml, whereas we have used a concentration of 1mg/ml with 2500 U/ml heparin in our study. However, the major similarity of this study with ours was that it was also performed in a setting where majority patients had uncuffed catheter (~95% of their patients).

In a study published in 2000 by Matthew J *et al.*, [8] the risk of bacteremia in uncuffed non-tunneled catheter showed a catheter related blood stream infection incidence of 3.8/1000 catheter days. In other studies, [9], the rate of CRBSI was 3.9/1000 catheter days and 9.7/1000 catheter days respectively. These incidences are quite similar to our study.

The frequency of catheter-related bacteremia in several large case series has ranged between 2.5 and 5.5 episodes per 1000 catheter-days, which corresponds to an incidence of 0.9 to 2 episodes of bacteremia per catheter-year [10]

In another prospective study involving 108 tunneled catheter-dependent hemodialysis patients, the cumulative likelihood of catheter-related bacteremia was 35 percent within three months and 48 percent within six months of catheter insertion [11]

However, the incidence of infection and risk of infection over time vary significantly according to site of insertion. Difference between number of femoral venous access and internal jugular venous access may attribute this difference of incidence of CRBSI.

In an uncontrolled observational study in Newzealand, Abbas *et al* [12] showed use of gentamicin plus heparin lock was associated with reductions in rates of CRBSI and hospitalization for CRBSI by 52% and 69% for patients with tunneled catheters locked continuously since their insertion compared with those with tunneled catheters that were not, respectively.

In a multicentric study in northern California, Moran *et al* showed Gentamicin 320 µg/mL in 4% sodium citrate used as a routine catheter lock in CVCs in patients on maintenance hemodialysis therapy markedly decreases the incidence of catheter-related bloodstream infection and is as effective as heparin 1,000 U/mL in preventing catheter clotting. [13] This study was parallel-group, randomized, multicenter clinical trial, with patients blinded to study intervention. However this study was also performed in tunnelled cuffed catheter.

In their study Chow *et al* showed predominance of gram positive organism (Staphylococcus aureus and coagulase negative staphylococci with only 1 gram negative organism in gentamicin lock group only (E. coli)[7]

In fact, while comparing the organism growth from aforementioned studies, a common pattern is predominance of gram positive organism with Staphylococcus aureus and epidermidis being the commonest with variable percentage of gram negative organism.

Unpublished data from our own institute showed that in in-patients gram negative organism growth is majority in blood cultures especially in critically ill patients. So, local pattern of growth of organism or antibiotic use practice may be the cause of this difference with our result. The key to the success of antibiotic lock solutions appears to be their ability to attain intraluminal concentrations 100-fold in excess of the minimal inhibitory concentration.

## CONCLUSION

Our study showed that heparin plus gentamicin antibiotic lock improves the infection-free lifespan of dialysis catheters, decreases the rate of catheter related blood stream infection in patients with NT NC cath.

**Conflict of Interest:** None to declare.

## Bibliography

1. Hsu CY, Vittinghoff E, Lin F, Shlipak MG. The incidence of end-stage renal disease is increasing faster than the prevalence of chronic renal insufficiency. *Ann Intern Med.* 2004;141:95–101. ]
2. Capdevila JA, Segarra A, Planes AM, Ramirez-Arellano M, Pahissa A, Piera L, Martinez-Vazquez JM: Successful treatment of haemodialysis catheter-related sepsis without catheter removal. *Nephrol Dial Transplant* 8: 231–234, 1993]
3. Clinical Practice Guideline Vascular Access For Haemodialysis Uk Renal Association 6th Edition Final Version - Mick Kumwenda, SandipMitra, Claire Reid, Posted at [www.renal.org/guidelines](http://www.renal.org/guidelines)
4. Vascular AW. Clinical practice guidelines for vascular access. *American journal of kidney diseases: the official journal of the National Kidney Foundation.* 2006 Jul;48:S248.
5. Collee JG, Miles RS, Watt B. Tests for the identification of bacteria. In: Collee JG, Marmion BP, Fraser AG, Simmons A, Editors. *Practical Medical Microbiology.* 14th ed. Churchill Livingstone, Imprint of Elsevier India; 2006. p. 131-78.
6. Bansal D, Kher V, Gupta KL, Banerjee D, Jha V.: Haemodialysis vascular access: current practices amongst Indian nephrologists: *J Vasc Access.* 2018 Mar;19(2):172-176
7. KM Chow, YL Poon, MP Lam, KL Poon, CC Szeto, Philip KT Li Antibiotic lock solutions for the prevention of catheter-related bacteraemia in haemodialysis patients- - *Hong Kong Med J* Vol 16 No 4 # August 2010
8. Matthew j. Oliver, sandra m. Callery, kevin e. Thorpe, steven j. Schwab, and david n. Churchill: Risk of bacteremia from temporary hemodialysis catheters by site of insertion and duration of use: A prospective study: *Kidney International*, Vol. 58 (2000), pp. 2543–2545
9. Almirall J, Gonzalez J, Rello J, *et al.* Infection of hemodialysis catheters: incidence and mechanisms. *Am J Nephrol* 1989; 9:454 / KairaitisLK, Gottlieb T: Outcome and complications of temporary haemodialysis catheters. *Nephrol Dial Transplant* 14:1710–1714, 1999
10. Allon M, Depner TA, Radeva M, *et al.* Impact of dialysis dose and membrane on infection-related hospitalization and death: results of the HEMO Study. *J Am Soc Nephrol* 2003; 14:1863
11. Lee T, Barker J, Allon M. Tunneled catheters in hemodialysis patients: reasons and subsequent outcomes. *Am J Kidney Dis* 2005; 46:501
12. Abbas SA, Haloob IA, Taylor SL, Curry EM, King BB, Van der Merwe WM, Marshall MR *Am J Kidney Dis.* 2009 Mar;53(3):492-502. Effect of antimicrobial locks for tunneled hemodialysis catheters on bloodstream infection and bacterial resistance: a quality improvement report
13. Moran J, Sun S, Khababa I, Pedan A, Doss S, Schiller B- *Am J Kidney Dis.* 2012 Jan; 59(1):102-7. - A randomized trial comparing gentamicin/citrate and heparin locks for central venous catheters in maintenance hemodialysis patients

### How to cite this article:

Dr. Prasun Roy *et al* (2020) 'Comparing Efficacy of Different Lock Solutions in Preventing Catheter Related Blood Stream Infection In Hemodialysis Patients', *International Journal of Current Advanced Research*, 09(06), pp. 22497-22501. DOI: <http://dx.doi.org/10.24327/ijcar.2020.22501.4440>

\*\*\*\*\*