International Journal Of Health Medicine and Current Research
E - ISSN : 2528 - 3189
P - ISSN : 2528 - 4398

International Journal of Health Medicine and Current Research
Vol. 3, Issue 01, pp.785-791, March, 2018

DOI:
10.22301/IJHMCR.2528-3189.785

Article can be accessed online on:
http://www.ijhmcr.com

ORIGINAL ARTICLE

INTERNATIONAL JOURNAL OF HEALTH MEDICINE AND CURRENT RESEARCH

EFFECT OF CEFTAZIDIME AND CLOXACILLIN AS AN ANTIBIOTIC PERMANENT HEMODIALYSIS CATHETER BLOCKER SOLUTION IN PREVENTION OF CATHETER RELATED BLOOD STREAM INFECTIONS

Mohammad Saad Forghani [1], Mohsen Rajabnia [2], Bahram Nikkhoo [3], Jamal Modarres Gorji [1*]

[1] Department of Internal Medicine, Kurdistan University of Medical Sciences, Sanandaj, Iran.
[2] Student Research Committee, Kurdistan University of Medical Sciences, Sanandaj, Iran.
[3] Cellular and Molecular Research Center, Kurdistan University of Medical Sciences, Sanandaj, Iran.

ARTICLE INFO

Article History:
Received 16th January, 2017
Received in revised form
16th February, 2018
Accepted 28th February, 2018
Published online 20th March, 2018

Key words:
Hemodialysis, Catheter Infection, Antibiotic, CRBSI.

Correspondence to Author:
Jamal Modarres Gorji
Kurdistan University of Medical Sciences, Abider Street, Sanandaj, Iran.
Postal code: 66186-34683
Tel: +989336583929,
Fax: +00 98 87 33237760

E-mail:
kweasm@yahoo.com

ABSTRACT

Background and Objective: Patients with end stage renal function (ESRD) require vascular access for hemodialysis and infection is the most common delayed complication of central venous catheters. The aim of this study was to evaluate the effect of using two antibiotics, ceftazidime and coloxacillin, as a permanent hemodialysis catheter blocker solution in the prevention of catheter-related blood infections.

Materials and Methods: This clinical trial was performed on 64 patients undergoing hemodialysis in Tohid Hospital in Sanandaj, 2016-2017. Patients were divided into two groups of intervention and controls (placebo). The duration of follow up was 6 months in this study. All patients were evaluated during dialysis and in each session for further evaluations of unwanted drug reactions, skin complications such as rash, itching and other side effects. For data analysis, STATA software version 12, independent t-test and chi-square test were used.

Results: The results of this study showed that the mean duration of hemodialysis in the intervention group was 19.76 ± 4.28 and the control group was 27.5 ± 4.96 months. Most of the microorganisms have been grown in the blood culture of the subjects in both *Staph Aureus* groups.

Citation: Mohammad Saad Forghani [1], Mohsen Rajabnia [2], Bahram Nikkhoo [3], Jamal Modarres Gorji [1*], 2018 "Effect Of Ceftazidime And Cloxacillin As An Antibiotic Permanent Hemodialysis Catheter Blocker Solution In Prevention Of Catheter Related Blood Stream Infections", *International Journal of Health Medicine and Current Research*, 3, (01), 785-791.

There was a significant relationship between the mean duration of hemodialysis catheter in the intervention group and the control group. (p = 0.004).

The number of hemodialysis catheter-related infections (CRBSI) in the intervention group, which ceftazidime and chloroxacillin antibiotics were addedto the heparin solution, was lower than that of the control group using the routine heparin lock method alone (2.95%). In contrast, 4 cases (13.33%), but according to P.Value(P=0.064), this difference was not significant.

Conclusion: *Staph Aureus* is the most common organism involved in central venous catheter infection in hemodialysis patients. The above findings can be used to evaluate the diagnosis and initiate experimental therapy in these patients.

INTRODUCTION

With progression of the chronic kidney disease (CKD) to stage 4 (GFR <30 ML / MIN / 1.73 m2), in addition to multidisciplinary care, appropriate method for renal replacement therapy (RRT) should be considered (1). RRT involves kidney transplantation, hemodialysis and peritoneal dialysis. Hemodialysis is performed via Arteriovenous fistula (AVF), Venous catheter, Arteriovenous graft. The intravenous catheters are two types of Tunneled and Untunneled (2). Catheter related blood stream infection (CRBSI) is one of the most serious complications of tunneled catheters. Catheter related bacteremia occurs in 2-5.5 cases per 1000 patients in a day (3, 4). Although the incidence of CRBSI varies in different studies, the incidence of CRBSI in tunneled cuffed catheter is 0.5-5.5 per 1000 catheters per day (5, 6).

Catheter Infections are the second cause of mortality after cardiovascular disease in patients undergoing hemodialysis. Most of these infections are related to hemodialysis vascular access, which leads to increased mortality and morbidity in these patients (2, 7, 8). CRBSI is developing after the release of the bacteria or endotoxin from the Biofilm created at the internal surface of the catheter. Biofilm is a structur contains bacteria and bacteria-matrix, which are stably attached to the inner wall of the catheter and it occurs only 80 days after hemodialysis catheter insertion (9, 10). In 111383 Patients under hemodialysis from January 1998 to December 2000 at 6 Hemodialysis Centers of Oregon and Idaho of USA, hemodialysis infection were prospectively investigated which the tunneled catheter infection rate was 13.6% (P <0.0001), while with temporary catheter was 32.6% (P <0.0001) and by was AVF 2.2% (P = 0.002) (11).

Fever and chills are the most sensitive CRBSI clinical symptoms and in some cases sepsis sign and symptoms can occur including hemodynamic impairment, hypotension, and disturbance of consciousness that can be mild to severe. The presence of sepsis symptoms after initiation of dialysis suggests the bacterial endotoxin entry from catheter to systemic circulation (12, 13).

Based on the definition of CDC in the United States, CRBSI is divided into three definite, probable and possible categories (14). Staphylococcal species are one of the most commonly causes of bacteria in CRBSI. CRBSI is associated with mortality, high morbidity and high costs. Mortality of CRBSI due to Staphylococcus aureus is high and is about 20% in hemodialysis patients (15). Also gram-positive and gram-negative bacteria are involved in this disorder, leading to endocarditis, osteomyelitis, epidural abscess and septic arthritis, and death if left untreated (16, 17).Treatment of catheter-associated bacteremia with systemic antibiotics will often not be effective without catheter removal, and only 22-37% of cases respond to systemic antibiotics (18).

The risk of CRBSI varies considerably according to the catheter insertion site and the duration of the catheter insertion. In the study of Matthew J et al., CRBSI, for catheters in the femoral vein were 3.1% in the first week and 10.7% in the second week, and for Jugular vein catheters, 1.7% in the first week and 4.6% in the second week. Relative risk of bacteremia was 3.1 in patients with femoral catheter versus internal Jugular (95% CI, 1.1 to 8.5) (19).

Several ways are recommended to reduce the risk of CRBSI, including hands hygiene by nurses, using aseptic techniques, teaching aseptic methods and controlling infection in hemodialysis staff, teaching patients (on hand hygiene, catheter care, sign and Symptoms of infection), reduced use of a catheter with timely AVF insertion, or graft, using chlorhexidine as an antiseptic solution, antimicrobial ointment and hub disinfection of hemodialysis catheter (20).

In addition to the standard methods used in hemodialysis centers, the use of antibiotic solutions as a catheter blocker has been considered to reduce the risk of CRBSI. Due to the pathogens responsible for this complication (including gram positive and gram negative bacteria), the used antibiotic composition should cover a variety of pathogens. Antibiotics should cover common pathogens, although most CRBSI cases are secondary to gram-positive bacteria, however, the risk of CRBSI with gram-negative bacteria is also significant (21).

According to our observations, the mortality rate and the number of patients who are admitted to the different wards of the hospital because of catheter infections or need to removal of the catheter, is high. These complications are associated with high therapeutic costs (despite the mentioned standard preventive methods). Therefore, it seems logical to use other methods such as antibiotic solutions to prevent CRBSI. Further studies on the effectiveness of this method can lead to the provision of useful antibiotic protocols in reducing CRBSI. This study was designed to evaluate the efficacy of a solution containing two antibiotics, ceftazidime and coloxicillin, as a catheter blocker solution in the prevention of CRBSI in patients with chronic dialysis via Tunneled Catheter, due to the appropriate coverage of the pathogens.

METHODS

This study was a double-blind randomized clinical trial (RCT), which was performed on all patients with chronic kidney disease who needed hemodialysis via tunnelled catheter referred to the hemodialysis ward of Tohid Hospital of Sanandaj in 2016-2017. Exclusion criteria of this study was alteration of vascular access to AVF, kidney transplantation in the 6-months period of the study, transferring of the patient to a location other than the metioned center that have no possibility of monitoring, a patient who does not wish to continue to collaborate in the study, use of Tarolac solution as antibiotic lock and patients who have received antibiotics for any reasons other than CRBSI. Sampling was done so that all patients who had inclusion criteria (64 patients) undergoing chronic hemodialysis via tunnelled hemodialysis catheter referred to hemodialysis ward of Tohid Hospital after explaining the study methods and obtaining written consent and approval by the ethics committee of Kurdistan University of Medical Sciences and they were randomly divided into two groups of intervention and control groups (34 and 30 patients respectively). The duration of follow up was 6 months in this study. All patients were evaluated during dialysis and in each session for unwanted drug reactions and skin complications such as rash, itching and other side effects. Based on the volume written on the catheter, needed amount of solution prepared by ceftazidime 10 mg / ml (Elixir Pharmaceutical Co. Boroujerd, Iran) added to a solution of cloxacillin 100 mg / ml (Dana Pharmaceutical Co.Tabriz) and heparin (Daroopakhsh Pharmaceuticals Co.Tehran, Iran) entered the lumen of patient's catheter after each dialysis procedure and then we blocked the catheter. Based on the mentioned definition, we divided CRBSI outcomes into three groups of definite CRBSI, Probable CRBSI, and Possible CRBSI. To analyze the data of the study, STATA software version 12 was used. At first, Chi-square and independent t-test were used for comparison between the two groups in terms of confounding variables. The significance level in all tests was considered to be 5%.

RESULTS

In this study, 34 cases were in the intervention group and 30 in the control group. 39 (60.9%) of them were male and 25 (39.1%) were female. Descriptive results of this study (Table 1) showed that the mean age of the intervention group was 17.49 ± 62.67 y/o and of the control group was 59.9 ± 13.9 y/o, the mean BMI of the intervention group was 22.47 ± 0.77 and of the control group was 24.26 ± 0.86 and also the mean of albumin level of the intervention group was 0.141 ± 4.397 and of the control group was 0.122 ± 4.446. The mean duration of referral time in the intervention group was 0.417 ± 9.147 and in the control group was 0.438 ± 10.233 months, the mean duration of hemodialysis in the intervention group was 19.76 ± 4.28 and in the control group was 4.96 ± 27.5 months and the mean duration of hemodialysis catheter insertion in the intervention group was 0.7 ± 10.5 and in the control group was 1.21 ± 14.56 months. In this study, most of patients in both groups have kidney failure due to hypertension or diabetes (Table 2).

Table 1. The Mean Of Studied Variables In The Studied Groups.

Variable	Group	Frequency	Mean	Standard Deviation	P Value
Age	Intervention	34	62.674	17.49	0.4337
	Control	30	59.5	13.96	
BMI	Intervention	34	22.47	0.77	0.1387
	Control	30	24.2	0.86	

Serum albumin	Intervention	34	4.397	0.141	0.7945
	Control	30	4.446	0.122	
period of Participation in the study	Intervention	34	9.147	0.418	0.782
	Control	30	10.233	0.438	
Period of hemodialysis	Intervention	34	19.76	4.28	0.24
	Control	30	27.5	4.96	
Period catheter insertion	Intervention	34	10.5	0.7	0.004
	Control	30	14.56	1.21	

Table 2. Frequency Of Causes Lead To Kidney Failure In The Studied Groups.

Group	Causes Lead to Kidney Failure					P Value
	Diabetes	Hypertension	Glomerulonephritis	Nephrolithiasis	Other causes	
Intervention	10 (29.41%)	14 (41.18%)	0 (0%)	0 (0%)	10 (29.41%)	0.029
control	12 (40%)	9 (30%)	2 (6.67%)	4 (13.33%)	3 (10%)	
Total	22 (34.38%)	39 (35.94%)	2 (3.13%)	4 (6.25%)	13 (20.31%)	

The results of this study showed that in both groups, jugular catheter was used for hemodialysis. In this study, 58 cases (90.63%) had no catheter-related infection, 4 cases (7.81%) were infected and only 1 (1.56%) had a possible infection. In this study, only 1 case (1.56%) of skin infection was observed in the catheter site. Most of the microorganisms grown in the blood cultures of the subjects in both groups were 3 cases of *Staphylococcus Aureus* (4.68%) that only one case was in the intervention group and one case was *Staphylococcus Epidermidis*(1.56%) and also one case was E. coli (1.56%) which both last cases were in the control group.

The analytical results of this study showed that there was no significant relationship (P> 0.05) between mean age, BMI, albumin level, duration of referral, hemodialysis duration, hemodialysis catheter type, catheter-related infection and microorganisms grown in blood cultures in the intervention group and the control group. However, there was a significant relationship between the cause of kidney failure in the studied groups (P = 0.029). Also, there was a significant relationship between the mean duration of hemodialysis catheter insertion in the intervention group and the control group (p = 0.004).

The number of hemodialysis catheter-related infections (CRBSI) in the intervention group, which ceftazidime and colaxacillin antibiotics were added to to the heparin solution, was lower than that of the control group which the routine heparin lock method was used (one (2.95%) versus 4 cases (13.33%)), but according to the P.Value (P=0.064), this difference was not significant (Table 3).

Table 3. Frequency Of Types Of Catheter Related Infections In The Studied Groups.

Group	Types of catheter related infections			P Value
	Absence	Probable	Possible	
Intervention	33 (97.05%)	1 (2.95%)	0 (0%)	0.064
control	26 (86.66%)	3 (10.00%)	1 (1.33%)	
Total	59 (92.18%)	4 (6.25%)	1 (1.56%)	

DISCUSSION

One of the replacement therapies in the end-stage renal disease is hemodialysis. Infections are the second cause of mortality after cardiovascular diseases in patients undergoing hemodialysis. Many of these infections are related to vascular access to hemodialysis, which increases mortality and morbidity in these patients (8). Our aim in this study was to evaluate the effect of using two antibiotics, ceftazidime and coloxacillin, as a permanent hemodialysis catheter blocker solution in the

prevention of catheter-related blood stream infections. In this study 34 (53.13%) patients were in the intervention group and 30 (46.87%) were in the control group. In this study, 39 (60.94%) were male and 25 (39.06%) were female so male sex was more in both groups. The results showed that the mean age of the intervention group was 17.49 ± 62.647 y/o and the control group was 13.96 ± 59.5 y/o and the intervention group had a higher mean age and there was no statistically significant relationship (p=0.4337). In the study of Sani et al. From 65 patients, 34 (52.3%) were female and 31 (47.7%) were male. The smallest of them were 26 years old and the largest of them were 81 years old. Their average age was 54.9 years. The results of this study showed that the incidence of catheter infection in women was slightly higher than that of men. However, there was no association between the age of the patients and the catheter related infection (22). In our study, the mean BMI of the intervention group was 22.47 ± 0.77 and the control group was 24.2 ± 0.86, the control group had a higher BMI and had no statistically significant relationship (p = 0.1387). In this study, the mean albumin level of the intervention group was 0.141 ± 4.397 and the control group was 0.122 ± 4.446, so the control group had a higher mean albumin level but this relationship statistically was not significant (p = 0.7945). The mean duration of referral time in the intervention group was 0.417 ± 9.147 and in the control group was 0.438 ± 10.233 months. The results show that the mean duration of referral was less in the intervention group, but there was no statistically significant relationship. (p = 0.0782). In this study, also the cause of renal insufficiency has been studied. The most frequent cause of referral was diabetes and hypertension (36-34%). There was statistically significant relationship between the cause of the kidney failure in the two studied groups (p = 0.029).

In the study of Sani et al., in the case of underlying disease type, 87.7% had heart disease and 55.4% diabetes, 41.3% had hypertension and 6.2% had immunodeficiency (22). Results of our study and other studies highlight the importance of prevention in these patients. In this study, the association of risk factors such as diabetes mellitus and high blood pressure and immune deficiency with catheter-associated infection was consistent with most of the researches (12). The mean duration of hemodialysis in the intervention group was 19.76 ± 4.28 and the control group was 4.96 ± 27.5 months. There was no significant relationship between the two groups (p = 0.24). But the mean in the intervention group was much lower than the control group. The mean duration of hemodialysis catheter insertion in the intervention group was 10.5 ± 0.7 months and the control group was 14.16 ± 1.21 months so this was less in the intervention group and there was a significant relationship between the two groups (p = 0.004). Descriptive results of this study showed that in both groups, Jugular catheter was used for hemodialysis. But in the control group, only one case of femoral catheter was used for hemodialysis. In this study, 7.81% were probable to be infected and only 1.56% were possible to be infected. There was no significant relationship between hemodialysis catheter related infection in the two groups (p = 0.469). In the study of Sani et al., among the 65 studied patients, there were 41 patients (63.1%) who had a history of catheter infections in the past that determine the importance of preventing recurrent infection in these patients. The results of this study showed that among the factors affecting the prevalence of catheter related infection, the previous history of infection, is one of the risk factors for increasing the infection with the catheter, which was similar to most of the studies (22). In our study, in 98.44% of patients no skin infection was detected in the catheter site and only in 1.56% was observed. In the study of Sani et al. in terms of the clinical signs of catheter insertion infection among the patients, the highest clinical symptom contributing to the diagnosis, was the sensitivity of the catheter site to the touching with 80% (52 people) which this point is very importante in examining of patients with a possible catheter infection (22). The descriptive results of this study showed that the most microorganisms grown in the blood culture of the subjects were *Staphylococcus Aureus* in both groups. In the intervention group, there was a case of *Staphylococcus Aureus* and in the control group two cases of *Staphylococcus Aureus*, one case of *Staphylococcus Epidermidis* and one E. coli case, but this relationship was not statistically significant (p = 0.130). In the study of Sani et al., The type of organism obtained from positive culture results in the studied patients, the highest percentage was *Staphylococcus Aureus* (67.7%), followed by *Klebsiella Pneumoniae* (13.6%) and the lowest was *Staphylococcus Epidermidis* (9.3%), which this findings can be considered in the experimental treatment in patients with the possibility of central venous catheter infection (22). In the study of Christopher w et al. in the lock antibiotic group, a catheter infection with staphylococcus (0.3 / 1000 catheter days) and a six patients in he heparin lock group (4/1000 catheter days (P = 0.02)) was reported (23).

In this study, the number of infections related to hemodialysis catheter (CRBSI) in the intervention group, which ceftazidime and chloroxacillin antibiotics was added to heparin solution, was lower than that of the

control group using the routine heparin lock method (one case (2.95%) versus 4 cases (13.33%)), but with respect to P.Value 0.064, this difference was not significant.

The results of the study of Moghadas et al. showed that the number of cases of CRBSI in the intervention group was only two cases (0.58 per 1000 catheter-days) and in the control group, 11 cases (4.4 per 1000 catheter-days), which there was a significante difference between the two groups (P=0.002) (24).

CONCLUSION

Staphylococcus aureus is the most common organism involved in central venous catheter infection in hemodialysis patients and the duration of hemodialysis catheter insertion is one of the important factors in the development of infection. As a result, mentioned findings can be used to evaluate the diagnosis and initiate experimental therapy in these patients. Also, in this study, there was no statistically significant relationship between the use of the two antibiotics (ceftazidime and coloxacilin as a permanent blocker for hemodialysis catheter) and the development of blood-associated infections related to the hemodialysis catheter, although the number of hemodialysis catheter related blood stream infections in the control group was higher. For further results we recommend that more studies on the effects of various antibiotics on the prevention of catheter related blood infections with larger population and at a different time interval to be done.

REFERENCES

1. Wouters OJ, O'donoghue DJ, Ritchie J, Kanavos PG, Narva AS. Early chronic kidney disease: diagnosis, management and models of care. Nature Reviews Nephrology. 2015;11(8):491.
2. Pisoni RL, Young EW, Dykstra DM, Greenwood RN, Hecking E, Gillespie B, et al. Vascular access use in Europe and the United States: results from the DOPPS. Kidney international. 2002;61(1):305-16.
3. Mermel L. Infectious Disease Society of America; American College of Critical Care Medicine; Society for Healthcare Epidemiology of America. Guidelines for the management of intravascular catheter-related infections. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. 2001;32:1249-72.
4. Swartz RD, Messana JM, Boyer CJ, Lunde NM, Weitzel WF, Hartman TL. Successful use of cuffed central venous hemodialysis catheters inserted percutaneously. Journal of the American Society of Nephrology. 1994;4(9):1719-25.
5. Oliver MJ, Callery SM, Thorpe KE, Schwab SJ, Churchill DN. Risk of bacteremia from temporary hemodialysis catheters by site of insertion and duration of use: a prospective study. Kidney international. 2000;58(6):2543-5.
6. Tokars JI, Light P, Anderson J, Miller ER, Parrish J, Armistead N, et al. A prospective study of vascular access infections at seven outpatient hemodialysis centers. American journal of kidney diseases. 2001;37(6):1232-40.
7. Rayner HC, Pisoni RL, editors. Opinion: The Increasing Use of Hemodialysis Catheters: Evidence from the DOPPS on Its Significance and Ways to Reverse It. Seminars in dialysis; 2010: Wiley Online Library.
8. Bethesda, MD: National Institutes of Health. National Institute of Diabetes and Digestive and Kidney Diseases. US Renal Data System, USRDS 1998 Annual Data Report. Available at:http://wwwusrdsorg/adr_1998htm. 1998.
9. Pourchez T, Morinière P, Fournier A, Pietri J. Use of Permcath (Quinton) catheter in uraemic patients in whom the creation of conventional vascular access for haemodialysis is difficult. Nephron. 1989;53(4):297-302.
10. Passerini L, Lam K, Costerton JW, King EG. Biofilms on indwelling vascular catheters. Critical care medicine. 1992;20(5):665-73.
11. USRDS: United States Renal Data System.Causes of death. . American journal of kidney diseases : the official journal of the National Kidney Foundation. 1997;30(2 Suppl 1):S107-17.
12. Stevenson KB, Hannah EL, Lowder CA, Adcox MJ, Davidson RL, Mallea MC, et al. Epidemiology of hemodialysis vascular access infections from longitudinal infection surveillance data: predicting the impact of NKF-DOQI clinical practice guidelines for vascular access. American journal of kidney diseases. 2002;39(3):549-55.
13. Saad TF. Central Venous Dialysis Catheters: Catheter-Associated Infection. Seminars in dialysis. 2001;14(6):446-51.
14. Poole CV, Carlton D, Bimbo L, Allon M. Treatment of catheter-related bacteraemia with

an antibiotic lock protocol: effect of bacterial pathogen. Nephrology Dialysis Transplantation. 2004;19(5):1237-44.
15. Saad TF. Bacteremia associated with tunneled, cuffed hemodialysis catheters. American journal of kidney diseases. 1999;34(6):1114-24.
16. Raad I, Costerton W, Sabharwal U, Sadlowski M, Anaissie E, Bodey GP. Ultrastructural analysis of indwelling vascular catheters: a quantitative relationship between luminal colonization and duration of placement. Journal of Infectious Diseases. 1993;168(2):400-7.
17. Marr KA, Sexton DJ, Conlon PJ, Corey GR, Schwab SJ, Kirkland KB. Catheter-related bacteremia and outcome of attempted catheter salvage in patients undergoing hemodialysis. Annals of internal medicine. 1997;127(4):275-80.
18. Tanriover B, Carlton D, Saddekni S, Hamrick K, Oser R, Westfall AO, et al. Bacteremia associated with tunneled dialysis catheters: comparison of two treatment strategies. Kidney international. 2000;57(5):2151-5.
19. Costerton JW, Stewart PS, Greenberg EP. Bacterial biofilms: a common cause of persistent infections. Science. 1999;284(5418):1318-22.
20. Control CfD, Prevention. CDC approach to BSI prevention in dialysis facilities. Atlanta: Author Retrieved from http://wwwcdcgov/dialysis/prevention-tools/core-interventionshtml. 2013.
21. Leekha S, Terrell CL, Edson RS, editors. General principles of antimicrobial therapy. Mayo Clinic Proceedings; 2011: Elsevier.
22. Tavanaee Sani A, Eslami Nowkandeh AR, Ghorbany H. Central Venous Catheter Related Infection among Patients on Hemodialysis. medical journal of mashhad university of medical sciences. 2012;55(2):110-5.
23. McIntyre CW, Hulme LJ, Taal M, Fluck RJ. Locking of tunneled hemodialysis catheters with gentamicin and heparin. Kidney international. 2004;66(2):801-5.
24. Moghaddas A, Abbasi M-R, Gharekhani A, Dashti-Khavidaki S, Razeghi E, Jafari A, et al. Prevention of hemodialysis catheter-related blood stream infections using a cotrimoxazole-lock technique. Future microbiology. 2015;10(2):169-78.

****