

Original article

Applying endoluminal catheter colonization surveillance cultures in renal dialysis unit- an effort to reduce catheter related blood stream infection rate

Shereen H. Ahmed ^{*1}, Ahmed W. Mahdy ², Hany Bauiomy ³, Afaf F. Khamis ⁴

1- Medical Microbiology and Immunology Department, Faculty of Medicine, Benha University, Benha, Egypt.

2- Internal medicine Department, Faculty of Medicine, Benha University, Benha, Egypt.

3- Anesthesia & Intensive Care Department, Faculty of Medicine, Benha University, Benha, Egypt.

4- Clinical and chemical pathology Department, Faculty of Medicine, Benha University, Benha.

ARTICLE INFO

Article history:

Received 3 August 2020

Received in revised form 6 September 2020

Accepted 9 September 2020

Keywords:

Surveillance cultures
Central venous catheter
Antibiotic lock therapy
Hemodialysis

ABSTRACT

Introduction: Catheter related blood stream infection (CRBSI) is a common complication with the use of central venous catheters (CVC) in hemodialysis patients. The study was designed to evaluate the effect of implementation of surveillance cultures (SCs) on the rate of CRBSIs. **Method:** This prospective cohort study was done over a period of 6 months on hemodialysis patients with internal jugular vein catheters. Catheter related blood stream infection rates (BSI) were measured and compared in the 2 included groups, the study group (15 patients) and the control group (15 patients). In both groups, conventional infection prevention and control measures were applied. Patients in the study group were checked for intraluminal microbial colonization every 2 weeks by SCs. According to SCs results, patients were classified into 4 groups, then according to the group they were managed with antibiotic lock therapy (ALT) with or without systemic antibiotics. **Results:** Of the collected 140 SCs from the study group, 108 (77%) were negative and 32 (23%) were positive. Eighteen cases in groups 2 & 3 received ALT and 6 patients in group 4 received ALT and systemic antibiotic. SCs succeed to eliminate intraluminal microbial colonization in all positive cases except for 1 case in group 2 and 3 cases in group 4. The CRBSI rate was 2.14 per 1,000 catheter days in the study group compared to 5.57 per 1,000 catheter days in the control group ($P=0.037$). **Conclusion:** This study shows that the implementation of periodic SCs is associated with a significant reduction in the CRBSI rates in hemodialysis patients.

Introduction

End-stage renal disease (ESRD) is a major health problem in Egypt. In 2017, there were 7.1 million (95% UI 6.6 to 7.7) cases of chronic kidney disease that resulted in 13115 (95% UI 11314 to 14968) deaths [1]. There are efforts to establish national guidelines for hemodialysis in Egypt and assess the compliance with these guidelines including infection control practices with the limited resources [2-4].

Dialysis carries the risk of high mortality and morbidity. The annual mortality rate in one center study done in 2007 in Egypt was 8% [4] and it was 10% in Saudi hemodialysis patients in 2016 [5]. Patients on hemodialysis have a 26-fold higher risk of bloodstream infection compared to general population [6]. In United States, infection is the second leading cause of hospitalization and death in patients with ESRD [7]. The mean rates of blood

DOI: 10.21608/MID.2020.39751.1052

* Corresponding author: Shereen Helmy Ahmed

E-mail address: shmicro@hotmail.com

stream infections (BSI) in hemodialysis patients ranges from 0.5 to 27.1 per 100 patient/month, 77% of these BSI are access-associated in patients with central lines [8] .

Among the different types of hemodialysis access, central venous catheter (CVC) is the commonest source of bacteremia. About 77% of BSI in hemodialysis patients are access-associated in patients with central lines [8]. It is estimated that 37000 of BSI occurred among hemodialysis patients in united states in 2008 are related to central lines [9] . Although it is better to avoid the use of CVC to prevent CVC-related infections [10], The tunneled CVCs are used as long-term vascular access when the arteriovenous fistula (AVF) possibilities were exhausted or as a temporary vascular access in acute kidney injury, delayed AVF maturation, till transplantation and before peritoneal dialysis [11] .

The ability of bacteria and fungi to survive and proliferate within the biofilm that initially formed from the host proteins promotes intravascular catheter colonization with protection from host immune defenses and antimicrobial agents [12]. The data obtained from several studies indicate that the intraluminal microbial colonization of hemodialysis catheters often precedes BSI [13–17].

Different approaches and trials have been done to minimize luminal colonization and BSI [16,18–21]. One of the suggested methods to check the luminal colonization is endoluminal surveillance cultures (SCs), but few studies were done to evaluate this method [15,22,23] . The aim of this study was to evaluate the effect of implementation of SCs on the rate of CRBSIs.

Materials and methods

Setting and study design

This prospective cohort study was conducted on patients undergoing regular catheter hemodialysis in the Dialysis Unit at Benha University Hospital, Egypt during the period from February 2018 to July 2018. The study was approved by the ethics committee of the institution and all enrolled patients gave informed consents.

Patients already having internal jugular vein inserted tunneled cuffed central venous catheter (TCC) and patients who got jugular vein TCC inserted during the study period were included. Patients left the study when they were transferred to another center, when their TCC were permanently removed due to any cause or upon death. All needed data were collected prospectively for all patients.

The patients were divided into 2 groups, the study group and the control group. Surveillance cultures were applied only in the study group. Both groups were observed for CRBSIs during the study period. Infection control measures for TCC insertion and maintenance were applied in both groups according to the internal written policy [24]. Catheters were inspected for exit site and tunnel infection and managed in both groups according to the internal guidelines [24,25].

Surveillance cultures

The colonization of the inner surface lumen of the CVC was assessed every 2 weeks by SCs described by **Rodríguez et al.** [26]. Five to ten ml of blood: heparin (3:2) mixture were collected from the arterial catheter lumen before connecting the patient to the hemodialysis machine. The withdrawn sample was inoculated into aerobic blood culture bottle then incubated for 5 days in an automated blood culture system (BacT/Alert, bioMèrieux, Durham, NC). We didn't draw from a line that had an antibiotic agent administered through it during previous hour. Time-to positivity (TTP); defined as the span of time from the start of culture incubation to the detection of microbial growth by an automated system [27] was recorded for SCs signaled positive which then subcultured for isolation and identification of microorganisms.

Based on SCs results, patients were grouped into 4 groups and managed as proposed by **Brañas et al.** [23] :

group 1: SCs were negative, then no special management was required.

group 2: SCs were positive for CoNS, streptococcus viridians group, Corynebacterium spp. Micrococcus spp. or bacillus spp. with TTP >14 hours. Antibiotic lock therapy was implemented after ensuring that it was colonization rather than contamination by repeating the SC before the next hemodialysis session. ALT (according to the colonizing bacteria) with heparin, was given after each hemodialysis sessions in the next 2 weeks after reporting the positive culture result.

group 3: positive for organisms as in group 2 with TTP ≤ 14 hours. Then, catheter colonization was considered, and ALT was implemented as described in group 2.

group 4: SCs were positive for any other microorganism (e.g. *Staphylococcus aureus*, *Enterococcus* species., Gram-negative bacilli, *Candida* spp., ...). This was highly suspected for

CRBSI, so blood cultures from a peripheral vein and the CVC were withdrawn for confirmation, ALT was implemented, and patients were clinically assessed for systemic antibiotic therapy and managed according to the applied guidelines [28].

Diagnosing CRBSIs

Patients in both groups were observed clinically during the study period for CRBSIs. Any suspected case was diagnosed by a differential time to positivity where diagnosis was done when identical organism (i.e. same species and antibiogram) was recovered from the hub blood culture and from the percutaneous peripheral blood culture and the hub blood culture signaled positive result at least 2 hours earlier than the peripheral blood cultures [25].

Microbial identification

Microbial identification and susceptibility testing were done using Automated Sensititre System (TREK Diagnostic system, Inc., Cleveland, Ohio).

Statistical analysis

Groups were compared using Fisher exact test for categorical variables and Mann-Whitney U test for continuous variables. Data analysis was performed using Medcalc software version 19.4.0. Categorical data were presented as number and percentages while quantitative data were expressed as mean \pm standard deviation. The rate of CRBSI was calculated as incidence and was reported per 1,000 catheter days in both groups then the relative risk was calculated. The accepted level of significance in this work was stated at P -values < 0.05 .

Results

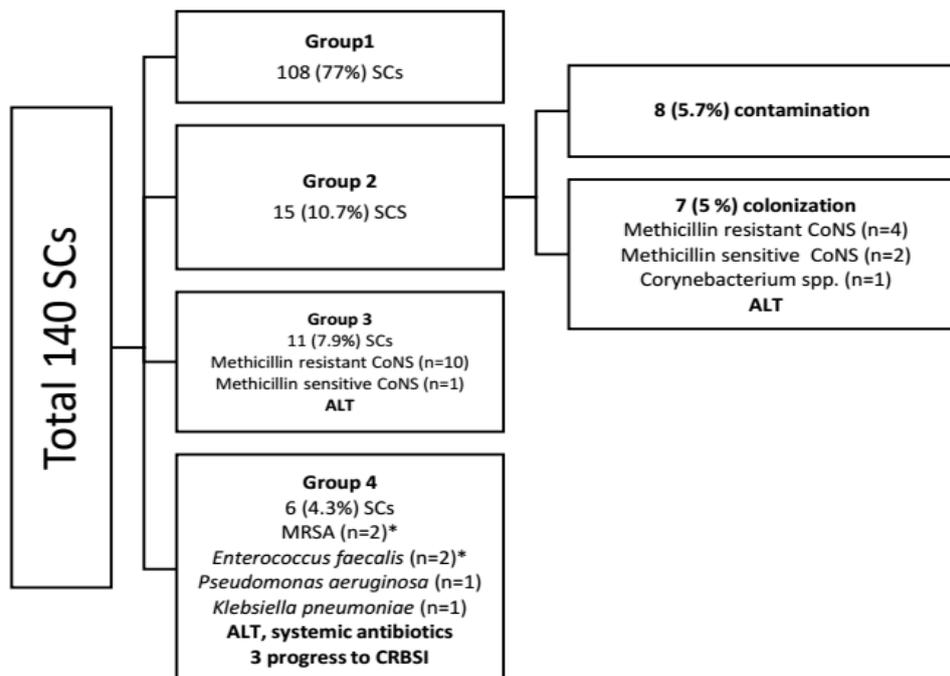
A total of 30 patients were included in the study of which 23 were with pre-existing CVC and 7 were get their CVC inserted during the study period. They required a total of 41 TCCs, 11 were removed during the study period, all because of infection. Seven patients left the study before its allotted time ended: 1 patient in the study group was transferred to other center, 1 patient in the control group the catheter no further required, and 5 patients died (2 in the study group, 3 in the control group). Details of patients' number and characteristics in both study and control groups are shown in **table (1)**.

During the study period, a total of 140 SCs were collected from the study group patients with a mean number per patient of 9.3 ± 2 . Of these, 108 (77%) were negative (group1), 15 (10.7%) SCs were in group 2, 11(7.9%) were in group 3 and 6 (4.3%) were in group 4. All group 2 SCs were repeated on the next dialysis session to confirm colonization, 8

(5.7%) yield no growth so the previous results were considered as contamination while 7 (5%) were truly colonized as the same results were obtained. Out of the total 24 SCs that revealed luminal colonization, eighteen (12.8%) cases in groups 2 & 3 received ALT and six (4.3%) patients in group 4 received ALT and systemic antibiotic according to the isolated microorganism and followed up for development of CRBSI. Results of SCs and the isolated microorganisms and the outcomes in the study group are summarized in **figure (1)**.

Both study groups were observed for CRBSI. Six CRBSIs were reported in the study group, and 17 CRBSIs in the control group. Three out of the 6 CRBSI reported in the study group followed the positive SCs despite ALT and systemic antibiotic administration and the causative organisms were the same as those recovered from the SCs (2 *Enterococcus faecalis*, 1 *Staphylococcus aureus*). The overall rate of CRBSIs per 1,000 CL days was 2.14 in the study group compared to 5.56 in the control group. This result showed 61.5% reduction in CRBSIs rate in the study group in comparison with the control group (**Table 2**).

In the both groups, *Staphylococcus aureus* was the most predominant isolated organism in CRBSI cases. In the study group, none of CRBSI was caused by Gram negative rods. Three of the cases in that group caused by endoluminal colonization as they were preceded by positive SCs with the same organism while the last SCs done for the other 3 cases before developing CRBSI were negative. The CRBSI causing microorganisms are shown in **table (3)**.

Figure 1. Results of endoluminal surveillance culture in the study group patients.

*One MRSA and 2 *Enterococcus faecalis* colonized cases progress to CRBSI, SC, surveillance culture; ALT, antimicrobial lock therapy; CoNS, coagulase-negative Staphylococcus; MRSA, methicillin resistant *Staphylococcus aureus*; CRBSI, catheter-related blood stream infection

Table 1. Comparison of patients' characteristics in both included groups.

Variable	Study group (n = 15)	Control group (n=15)	P value
Age (years)*	64.6 ± 9.18	58 ± 11	0.11
Male sex n (%)	(8) 53.3%	(9) 60%	1.00
Follow-up (days)*	151.7 ± 32.2	162.8 ± 35.4	0.27
Time from TCC insertion to beginning the study (days)*	33.9 ± 31	40.4 ± 25.8	0.43
Patients with pre-existing CVC	11	12	-
Patient catheter inserted during the study period	4	3	-
Catheter site insertion, n (%)			
Internal jugular vein	30	30	-
Number of catheters used during the study	19	22	-
Catheters removed/catheters used	4/19 (21%)	7/22 (31.8%)	0.51

*Data are expressed as means ± SD

Table 2. CRBSI rate in the study group and control group.

	Study group	Control group	RR (CI =95%)	P value
No. of CRBSI	6	17	2.59 (1.02-6.6)	0.037
No. of CL days	2796	3049		
CRBSI rate per 1,000 CL days	2.14	5.57		

RR, relative risk; CL, central line; CI, confidence interval

Table 3. Isolated microorganisms form CRBSI cases in the two groups.

Microorganism	Control group n (%)	Study group n (%)
<i>Staphylococcus aureus</i>	8 (47)	3 (33.3)
<i>Coagulase Negative Staphylococcus spp.</i>	4 (23.5)	1(33.3)
<i>Enterococcus faecalis</i>	1 (5.9)	2(33.3)
<i>Klebsiella pneumoniae</i>	2 (11.8)	0 (0)
<i>Escherichia coli</i>	1 (5.9)	0 (0)
<i>Enterobacter cloacae</i>	1(5.9)	0 (0)
Total	17	6

Discussion

Long-term tunneled cuffed catheters are frequently used a vascular access in patients on hemodialysis. A very common complication among these patients is CRBSI, with subsequent morbidities and increased risk of mortality. Removal of the CVC is a part of treatment of CRBSI in most patient populations. However, there are several difficulties that make such decision of catheter removal in patients undergoing hemodialysis not an easy one. Such difficulties include higher rates of venous thrombosis and stenosis in these patients that can lead to lack of future hemodialysis access sites and the presence of a feasible access site is very important for these patients who undergo dialysis for long period [29].

With application of SC, the CRBSIs rate is markedly reduced (61.5 % less than the control group) in the study group due to periodic surveillance for endoluminal colonization and prompt early eradication with ALT with or without systemic antibiotic according to the culture result. Surveillance culture in our study protected 18 patients (group 2&3) with *CoNS* colonized catheters and 3 patients (group 4) colonized with *Staph. aureus* and 2 Gram negative rods from possible CRBSI. Unfortunately, CRBSI couldn't be prevented in the other 3 patients in group 4. The other 3 CRBSI incidents reported in the study group were caused by 2 *Staph. aureus* and 1 *CoNS* despite the negative result of the preceding SC. These cases resulted from infection at the catheter exit site.

Endoluminal catheter colonization have been studied through other different methods [15,30]. We used surveillance culture described by **Rodríguez-Aranda et al.** [26]. It concludes that culture of blood-heparin mixture from arterial or venous lumens had similar values for sensitivity

(84.2 and 90.0%, respectively) and specificity (96.3 and 96.3%, respectively). This method was used by **Brañas et al.** [31] to evaluate it in prevention of CRBSIs in hemodialysis patients. In that study the results also were permissive as the rate of CRBSIs decreased to 0.27 per 1,000 catheter days compared with previous rate of 1.65 per 1,000 catheter days.

Endoluminal colonization as a risk factor for CRBSIs was a target of many studies. Most of these studies revealed the predominance of *CoNS* colonization of catheters. In **Dittmer et al.** study, 35% developed bacteremia with the same organisms already colonized their catheters and concluded that the colonization of catheter is mostly present 16 weeks after insertion [32]. **Fux et al.** observed colonization of the catheter inner lumen in 17.2% of the catheters that was dominated by multidrug-resistant *CoNS* [13]. In a study done by **Koch et al.**, 62.5% of catheters were positively colonized with predominance of *Staphylococcus epidermidis* (68%) and 75% of catheters present for more than 30 days were colonized [30]. In addition to infection prevention and control guidelines for and maintenance of dialysis catheters several attempts have been tried to further decrease the catheter related infections. These attempts ranged from topical antibiotic application [33–35] to antibiotics locked in the catheter lumen between dialysis sessions insertion [14,16,18–21,36]. These studies blindly apply the prophylactic antibiotic, and this carries the major risk of development of antibiotic resistance in addition to the financial burden. Surveillance cultures with subsequent management according to the result has an advantage of targeted choice of antibiotic according to the isolated microorganism and antibiotic susceptibility results.

Limitations of this study are small number of patients included in the study and enrollment of patients with previously inserted catheters.

Investigation for other catheter related infections (exit site infection and tunnel infection) was required to clearly identify the source of CRBSIs, whether intra or extraluminal.

Conclusion

Endoluminal SCs is a convenient approach for early detection of luminal surface colonization and rapid initiation of preventive measures to eliminate such colonization before progression into blood stream infection. This is evidenced by reduction in CRBSI rate among hemodialysis patients with CVC with the application of endoluminal SCs. Further studies on larger number of patients to investigate the efficacy and cost-effectiveness of endoluminal SCs as a CRBSI preventive measure are recommended.

Conflict of interest statement: None declared.

Funding sources: None.

Acknowledgements

Authors appreciate the efforts of nurses and staff of Benha University Hospitals for their efforts and support to conduct this study.

References

- 1-Bikbov B, Purcell CA, Levey AS, Smith M, Abdoli A, Abebe M, et al. Global, regional, and national burden of chronic kidney disease, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. *The Lancet* 2020; 395(10225): 709-733.
- 2-Ahmed AM, Allam MF, Habil ES, Metwally AM, Ibrahiem NA, Radwan M, et al. Development of practice guidelines for hemodialysis in Egypt. *Indian journal of nephrology* 2010; 20(4): 193-202.
- 3-Ahmed AM, Allam MF, Habil ES, Metwally AM, Ibrahiem NA, Radwan M, et al. Compliance with haemodialysis practice guidelines in Egypt. *Eastern Mediterranean health journal = La revue de sante de la Mediterranee orientale = al-Majallah al-sihhiyah li-sharq al-mutawassit* 2013;19(1):4-9.
- 4-Ibrahim S. Quality of care assessment and adherence to the international guidelines considering dialysis, water treatment, and protection against transmission of infections in university hospital-based dialysis units in Cairo, Egypt. *Hemodialysis International* 2010; 14(1): 61-67.
- 5-Saudi Center for Organ Transplantation. Annual Report 2016 Hemodialysis in the Kingdom of Saudi Arabia. Published online 2016. Available at: <http://www.scot.gov.sa/webb/Reports/12?lang=n>
- 6-Skov Dalgaard L, Nørgaard M, Jespersen B, et al. Risk and Prognosis of Bloodstream Infections among Patients on Chronic Hemodialysis: A Population-Based Cohort Study. *PloS one*. 2015;10(4):e0124547-e0124547. doi:10.1371/journal.pone.0124547
- 7-Saran R, Robinson B, Abbott KC, Agodoa LY, Bhave N, Bragg-Gresham J, et al. US Renal Data System 2017 Annual Data Report: Epidemiology of Kidney Disease in the United States. *American journal of kidney diseases : the official journal of the National Kidney Foundation* 2018; 71(3 Suppl 1): A7.
- 8-Klevens R, Edwards J, Andrus M, Peterson K, Dudeck M, Horan T. Special Report: Dialysis Surveillance Report: National Healthcare Safety Network (NHSN)—Data Summary for 2006. *Seminars in Dialysis* 2008; 21(1): 24-28.
- 9-Downham G, Jones E, Peterson P, Mourad MY, Lindberg C, Patel PR, et al. Reducing bloodstream infections in an outpatient hemodialysis center - New Jersey, 2008-2011. *Morbidity and Mortality Weekly Report* 2012; 61(10): 169-173.
- 10-Böhlke M, Uliano G, Barcellos FC. Hemodialysis Catheter-related Infection: Prophylaxis, Diagnosis and Treatment. *The Journal of Vascular Access* 2015; 16(5): 347-355.
- 11-Weijmer MC, Vervloet MG, ter Wee PM. Compared to tunnelled cuffed haemodialysis catheters, temporary untunnelled catheters are

- associated with more complications already within 2 weeks of use. *Nephrology Dialysis Transplantation* 2004;19(3): 670-677.
- 12-**Mermel LA**. What is the evidence for intraluminal colonization of hemodialysis catheters? *Kidney International* 2014;86(1):28-33.
- 13-**Fux CA, Uehlinger D, Bodmer T, Droz S, Zellweger C, Mühlemann K**. Dynamics of hemodialysis catheter colonization by coagulase-negative staphylococci. *Infection control and hospital epidemiology* 2005; 26(6): 567-574.
- 14-**LaPlante KL, Mermel LA**. In vitro activity of daptomycin and vancomycin lock solutions on staphylococcal biofilms in a central venous catheter model. *Nephrology, dialysis, transplantation: official publication of the European Dialysis and Transplant Association - European Renal Association* 2007;22(8):2239-2246.
- 15-**Del Pozo JL, Aguinaga A, Garcia-Fernandez N, Hernaez S, Serrera A, Alonso M, et al**. Intra-catheter leukocyte culture to monitor hemodialysis catheter colonization. A prospective study to prevent catheter-related bloodstream infections. *The International journal of artificial organs* 2008;31(9):820-826.
- 16-**Boyce JM**. Prevention of central line-associated bloodstream infections in hemodialysis patients. *Infection control and hospital epidemiology* 2012; 33(9): 936-944.
- 17-**Wagner J, Schilcher G, Zollner-Schwetz I, Hoenigl M, Valentin T, Ribitsch W, et al**. Microbiological screening for earlier detection of central venous catheter-related bloodstream infections. *European journal of clinical investigation* 2013;43(9):964-969.
- 18-**Kim SH, Song KI, Chang JW, Kim SB, Sung SA, Jo SK, et al**. Prevention of uncuffed hemodialysis catheter-related bacteremia using an antibiotic lock technique: a prospective, randomized clinical trial. *Kidney international* 2006;69(1):161-164.
- 19-**Saxena AK, Panhotra BR, Sundaram DS, Al-Hafiz A, Naguib M, Venkateshappa CK, et al**. Tunneled catheters' outcome optimization among diabetics on dialysis through antibiotic-lock placement. *Kidney international* 2006;70(9):1629-1635.
- 20-**Al-Hwiesh AK, Abdul-Rahman IS**. Successful prevention of tunneled, central catheter infection by antibiotic lock therapy using vancomycin and gentamycin. *Saudi journal of kidney diseases and transplantation: an official publication of the Saudi Center for Organ Transplantation, Saudi Arabia* 2007;18(2):239-247.
- 21-**Maki DG, Ash SR, Winger RK, Lavin P**. A novel antimicrobial and antithrombotic lock solution for hemodialysis catheters: a multi-center, controlled, randomized trial. *Critical care medicine* 2011;39(4):613-620.
- 22-**Guiot HF, Helmig-Schurter A v, van 't Noordende JM**. The relevance of cultures of catheter-drawn blood and heparin-lock fluid to diagnose infection in hematologic patients. *Annals of hematology* 1992;64(1):28-34.
- 23-**Brañas P, Morales E, Ríos F, Sanz F, Gutiérrez E, Quintanilla N, et al**. Usefulness of endoluminal catheter colonization surveillance cultures to reduce catheter-related bloodstream infections in hemodialysis. *American journal of infection control* 2014;42(11):1182-1187.
- 24-**O'Grady NP, Alexander M, Dellinger EP, Gerberding JL, Heard SO, Maki DG, et al**. Guidelines for the prevention of intravascular catheter-related infections. *American Journal of Infection Control* 2011; 39(4 SUPPL.).

- 25-**Mermel LA, Allon M, Bouza E, Craven DE, Flynn P, O'Grady NP, et al.** Clinical practice guidelines for the diagnosis and management of intravascular catheter-related infection: 2009 Update by the Infectious Diseases Society of America. *Clinical infectious diseases: an official publication of the Infectious Diseases Society of America* 2009;49(1):1-45.
- 26-**Rodríguez-Aranda A, Alcazar JM, Sanz F, García-Martín F, Otero JR, Aguado JM, et al.** Endoluminal colonization as a risk factor for coagulase-negative staphylococcal catheter-related bloodstream infections in haemodialysis patients. *Nephrology Dialysis Transplantation* 2011;26(3):948-955.
- 27-**Martín-Gutiérrez G, Martín-Pérez C, Gutiérrez-Pizarraya A, Lepe JA, Cisneros JM, Aznar J.** Time to positivity of blood cultures in patients with bloodstream infections: A useful prognostic tool. *Enfermedades infecciosas y microbiología clínica* 2017;35(10):638-644.
- 28-**Justo JA, Bookstaver PB.** Antibiotic lock therapy: review of technique and logistical challenges. *Infection and drug resistance* 2014;7:343-363.
- 29-**Aslam S, Vaida F, Ritter M, Mehta RL** Systematic review and meta-analysis on management of hemodialysis catheter-related bacteremia. *Journal of the American Society of Nephrology : JASN* 2014;25(12):2927-2941.
- 30-**Koch M, Coyne D, Hoppe-Bauer J, Vesely TM.** Bacterial colonization of chronic hemodialysis catheters: Evaluation with endoluminal brushes and heparin aspirate. *The journal of vascular access* 2002;3(1):38-42.
- 31-**Brañas P, Morales E, Ríos F, Sanz F, Gutiérrez E, Quintanilla N, et al.** Usefulness of endoluminal catheter colonization surveillance cultures to reduce catheter-related bloodstream infections in hemodialysis. *American Journal of Infection Control* 2014;42(11):1182-1187.
- 32-**Dittmer ID, Sharp D, McNulty CA, Williams AJ, Banks RA.** A prospective study of central venous hemodialysis catheter colonization and peripheral bacteremia. *Clinical nephrology* 1999;51(1):34-39.
- 33-**Lok CE, Stanley KE, Hux JE, Richardson R, Tobe SW, Conly J.** Hemodialysis infection prevention with polysporin ointment. *Journal of the American Society of Nephrology : JASN* 2003;14(1):169-179.
- 34-**Johnson DW, van Eps C, Mudge DW, Wiggins KJ, Armstrong K, Hawley CM, et al.** Randomized, controlled trial of topical exit-site application of honey (Medihoney) versus mupirocin for the prevention of catheter-associated infections in hemodialysis patients. *Journal of the American Society of Nephrology : JASN* 2005;16(5):1456-1462.
- 35-**McCann M, Moore ZE.** Interventions for preventing infectious complications in haemodialysis patients with central venous catheters. *The Cochrane database of systematic reviews* 2010;(1):CD006894.
- 36-**Zhang J, Wang B, Li R, Ge L, Chen K-H, Tian J.** Does antimicrobial lock solution reduce catheter-related infections in hemodialysis patients with central venous catheters? A Bayesian network meta-analysis. *International urology and nephrology* 2017;49(4):701-716.