

CENTRAL VENOUS CATHETER-RELATED BLOODSTREAM INFECTION IN HEMODIALYSIS: AN INTEGRATIVE REVIEW

INFECÇÃO DA CORRENTE SANGUÍNEA RELACIONADA A CATETER VENOSO CENTRAL PARA HEMODIÁLISE: REVISÃO INTEGRATIVA

INFECCIÓN DE LA CORRIENTE SANGUÍNEA RELACIONADA CONCATÉTER VENOSO CENTRAL PARA HEMODIÁLISIS: REVISIÓN INTEGRATIVA

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Objective: identify the scientific evidence present in publications related to central venous catheter-related infection in hemodialysis. **Method:** integrative literature review. The search was conducted in the databases of the Latin American and Caribbean Center on Health Sciences Information (LILACS) and the United States National Library of Medicine (PubMed), in December 2015. **Results:** the 13 studies analyzed demonstrated high rates of catheter-related infection, with the *Staphylococcus aureus* being the most commonly found microorganism. Some of the risk factors mentioned for infection, regarding the patients, were hypertension, diabetes mellitus, and hypoalbuminemia. The length of use of the catheter was among the risk factors for infection. **Conclusion:** the results present possible alternatives that can help prevent and reduce catheter-related infections.

Descriptors: Evidence-Based Nursing; Review; Catheter-Related Infections.

Objetivo: identificar evidências científicas presentes nas publicações relacionadas à infecção em cateter venoso central para hemodiálise. Método: revisão integrativa de literatura. A busca foi realizada nas bases de dados Literatura Latino-Americana e do Caribe em Ciências da Saúde (LILACS) e Biblioteca Nacional de Medicina dos Estados Unidos (PubMed), no mês de dezembro de 2015. Resultados: os 13 estudos analisados demonstraram altos índices de infecção relacionados a cateter, sendo o Staphylococcus aureus o micro-organismo mais observado. Alguns fatores de risco para infecção citados, relacionados ao paciente, foram hipertensão, diabetes mellitus e hipoalbuminemia. O tempo de uso do cateter esteve entre os fatores de risco para infecção. Conclusão: os resultados apresentam possíveis alternativas que podem auxiliar na prevenção e redução das infecções relacionadas ao cateter.

Descritores: Enfermagem Baseada em Evidências; Revisão; Infecções Relacionadas a Cateter.

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*Objetivo: identificar evidencias científicas encontradas en publicaciones relacionadas a la infección en catéter venoso central para hemodiálisis. Método: revisión integrativa de literatura. La búsqueda fue realizada en las bases de datos Literatura Latinoamericana y del Caribe en Ciencias de la Salud (LILACS) y Biblioteca Nacional de Medicina de los Estados Unidos (PubMed), en diciembre de 2015. Resultados: los 13 estudios analizados expresaron altos índices de infección relacionados con el catéter, constituyendo el *Staphylococcus aureus* el microorganismo más observado. Algunos de los factores de riesgo de infección mencionados, relacionados con el paciente, fueron: hipertensión, diabetes mellitus e hipoalbuminemia. El tiempo de uso del catéter constó entre los factores de riesgo de infección. Conclusión: los resultados presentan posibles alternativas que pueden colaborar en la prevención y reducción de infecciones relacionadas con el catéter.*

Descriptores: Enfermería Basada en la Evidencia; Revisión; Infecciones Relacionadas con Catéteres.

Introduction

Hemodialysis is the most commonly used renal replacement therapy (RRT) in patients with chronic or acute kidney failure. In this procedure, vascular access is needed to provide adequate flow for the passage of blood through the dialyzer⁽¹⁾. Arteriovenous fistula (AVF) is the most indicated vascular access, as it presents a lower risk of complications⁽²⁾. However, when it is not possible, or in emergency situations, a central venous catheter (CVC) is indicated.

Central venous catheters, which are widely used for hemodialysis, have several advantages, such as easy access, possibility of immediate use after insertion, and the fact that they are painless during hemodialysis⁽³⁾. Among their disadvantages, there are the poor positioning of the catheter, thrombosis, and bloodstream infection; the latter, considered the most frequent complication, may lead to death in critical cases.

Bloodstream infections (BSI), associated with vascular devices, are among the major healthcare-related infections, and account for 60% of nosocomial infections. They are associated with a high mortality rate, longer hospital stay and high costs for health care⁽⁴⁾.

Among the risk factors for the development of infections, the most prominent are the length of time the catheter is present, its place of insertion, and catheter manipulation by health professionals⁽⁵⁾. The main microorganism involved in these infections is *Staphylococcus aureus*^(6,7).

In a systematic literature review published in 2010, with ten studies involving 786 patients,

some interventions proved to be effective in preventing hemodialysis catheter-related infections. One example is the use of topical mupirocin to reduce the risk of catheter-related bacteremia (RR 0.17, 95% CI 0.07 to 0.43), which had a significant effect on infections caused by *Staphylococcus aureus*. However, the use of transparent polyurethane dressing, compared to dry gauze dressing, did not show evidence of prevention of local infection⁽⁸⁾.

Central venous catheter care, including that of hemodialysis, should be routinely adopted by the healthcare team, with the use of precautions necessary for catheter handling, as recommended by the Centers for Disease Control and Prevention (CDC). Among the recommendations, there is the adoption of a package of preventive measures for insertion and handling of central venous catheters, which is effective in reducing vascular catheter-related bloodstream infections⁽⁹⁾.

Nurses involved in direct patient care have the responsibility to know all the evidence related to the prevention of infections. Their actions should be based on up-to-date knowledge, aiming at providing safe and quality care.

The use of central venous catheters in hemodialysis is a common practice and presents several advantages for patients, either urgently or not. Thus, it is important to investigate factors related to the presence of infection, because this is the most common complication, leading to more serious consequences.

The objective of this review is to identify scientific evidence present in publications related

to central venous catheter-related infection in hemodialysis.

Method

This is an integrative literature review, a method used to synthesize and expand a given theme with the support of review of a wide variety of studies⁽¹⁰⁾. It is one of the methods to study evidence-based practice, and is organized in six stages: creation of the guiding question; literature search or sampling; data collection; critical analysis of studies included; discussion of data and presentation of the integrative review⁽¹¹⁾.

Based on the research question “Which scientific evidence is found in the publications regarding central venous catheter-related infection in hemodialysis?”, the articles were searched in the Latin American and Caribbean System on Health Sciences Information (LILACS) and the National Library of Medicine of the United States (PubMed) databases, in December 2015.

The search was guided by the PICO strategy, with the descriptors organized as follows: P - adult OR young adult; I - catheters OR catheterization OR central venous catheterization; C - not applicable; O - infection OR catheter-related infections. The descriptors were crossed, according to the Boolean logic, following the sequence “P” and “I” and “O” and then “I” and “O”. The second search was performed only to obtain more publications.

A total of 230 articles were found in the LILACS database, of which three were included. The others were excluded because they addressed other types of catheterization, that is, they did not correspond to the object of the study. In the PubMed database 1,572 articles were found, of which 83 were selected at first. Repeated articles that addressed other types of catheterization, and did not correspond to the object of study were excluded. The abstracts of the initially

selected articles were read for final selection of the sample.

The inclusion criteria applied were: articles published in the five years prior to this study (2010-2015); in Portuguese, English or Spanish; available in full online; exclusively related to central venous catheter for hemodialysis. Studies related to other types of catheter (arterial, pulmonary, peripheral, peritoneal), other vascular accesses for AVF hemodialysis, studies addressing other types of complications, rather than infection, and case studies, reports and editorials were excluded.

After applying the inclusion and exclusion criteria, the 13 articles that composed the final sample were selected. These were read in full and organized according to an instrument, containing: research theme, general objective, study design, level of evidence, sample/subjects, intervention, control, results, and conclusions. The articles were classified into levels of evidence⁽¹²⁾ as follows: level I – at least one systematic review of multiple well-designed randomized controlled trials; level II – at least one well-designed, randomized, controlled clinical trial; level III – well-designed clinical trial, without randomization, of studies of only one group of before-and-after type, cohort study, of time series, or case-control studies; level IV – non-experimental studies by more than one research center or group; level V – opinions from respected authorities, based on clinical evidence, descriptive studies or expert committee reports.

Results

Thirteen articles published between 2010 and 2014 were included. Regarding the method of choice, there was a predominance of prospective cohort studies. Chart 1 shows the characteristics of each study regarding their year of publication, objective, method and level of evidence.

Chart 1 – Characteristics of studies regarding year of publication, objective, method, and level of evidence

Study/year	Objective	Method (Level of evidence)
1/2010 ⁽¹³⁾	To evaluate the incidence of risk factors of BSI in patients with CVC for hemodialysis and to identify the microorganisms isolated in the bloodstream	Follow up. (Not applicable).
2/2011 ⁽¹⁴⁾	To determine if the dialysis catheter can be recovered by systemic antibiotic therapy and antibiotic lock.	Cohort study. (Level III).
3/2011 ⁽¹⁵⁾	To investigate the efficacy of the organoselenic antimicrobial agent - selenocyanatodiacetic acid (SCAA) - in preventing the development of <i>Staphylococcus aureus</i> biofilms, both in vivo and in vitro, when applied as a coating on the external and internal surfaces of hemodialysis catheters.	Not specified. (Not applicable).
4/2011 ⁽¹⁶⁾	To assess the incidence of catheter-related bloodstream infection in critically ill patients treated with continuous hemo(dia)filtration.	Prospective observational study. (Level III).
5/2011 ⁽¹⁷⁾	To compare a solution of minocycline and EDTA with unfractionated heparin for the prevention of catheter-related bacteremia in patients undergoing hemodialysis.	Multicentric, randomized, controlled study. (Level II).
6/2011 ⁽¹⁸⁾	To determine whether routine microbiological surveillance prevents catheter-related BSI.	Cohort study. (Level III)
7/2013 ⁽¹⁹⁾	To investigate the occurrence of BSI in patients with end-stage renal disease using CVC for hemodialysis.	Prospective cohort study. (Level III).
8/2014 ⁽²⁰⁾	To evaluate the impact of a lock solution (prophylactic antibiotic) on the incidence of catheter-related BSI.	Cohort, prospective study. (Level III).
9/2014 ⁽²¹⁾	Review of recent techniques that reduce the complications of temporary dialysis catheters and are relevant to the practice and training of nephrologists.	Review. (Not applicable).
10/2014 ⁽²²⁾	To compare the incidence of catheter-related BSI in elderly and non-elderly patients.	Retrospective study. (Level III).
11/2014 ⁽²³⁾	To compare the risks of infection of the dialysis catheters according to the choice of the lock solution used in patients of an intensive care unit (ICU) during the interdialytic period.	Quasi-experimental study. (Not applicable).
12/2014 ⁽²⁴⁾	To assess the efficacy of surveillance for the screening and treatment of chronic kidney disease (CKD) patients on hemodialysis, colonized by <i>Staphylococcus aureus</i> , and to determine the most effective intervention to eradicate the transmission of the bacterium among these patients.	Systematic review. (Level I).
13/2014 ⁽²⁵⁾	To determine the proportions of systemic antibiotic cure, antibiotic lock solution, and replacement of catheter with guidewire.	Systematic review and meta-analysis. (Level I).

Source: Created by the authors.

All studies included reported results regarding hemodialysis catheter-related bloodstream infection. The results presented data on incidence and risk factors, as well as comparative studies

of antimicrobial lock solutions and heparin. The main results and the conclusions of the articles are described on Chart 2.

Chart 2 – Synthesis of results and study conclusions

(to be continued)

Study/ year	Main results	Conclusion
1/2010 ⁽¹³⁾	2,061 suspected cases of catheter-related infection were identified. Of these, 1,436 (70%) had positive blood culture. After obtaining blood cultures from the catheter lumen and the dialysis line, a broad-spectrum antibiotic (vancomycin and ceftazidime) was started, together with antibiotic lock therapy. Catheter replacement was required in 33% of <i>S. aureus</i> infections, and in only 12.5% of cases with <i>S. epidermidis</i> .	<i>S. epidermidis</i> infection can be treated with systemic and lock antibiotics, but in cases of <i>S. aureus</i> infection, catheter removal is recommended.
2/2010 ⁽¹⁴⁾	Of the 156 patients included in the study, 94 developed BSI. Patients who had CVC implanted in the jugular vein had a 56% higher chance (RR: 1.56; 95% confidence interval: 1.50-5.65) of developing BSI than those who had a catheter implanted in a subclavian vein. Patients with BSI had a 50% higher risk of death.	The incidence of BSI in this study is high (61%). The risk factors for the development of BSI were: implantation of the catheter in the internal jugular vein, catheter time and length of hospital stay ($p = 0.04$ and $p < 0.001$).
3/2011 ⁽¹⁵⁾	Biofilm formation was visualized on the internal and external surfaces of the catheter segments not coated by the antimicrobial SCAA. In contrast, it was not detected on the surface of the catheters coated with SCAA.	The SCAA coating was non-toxic, durable, and inhibited the development of <i>S. aureus</i> biofilms, in vitro and in vivo. The use of SCAA has the potential to prevent <i>S. aureus</i> catheter-related infections.
4/2011 ⁽¹⁶⁾	Eight (4.6%) of the 173 patients had positive blood cultures. Six patients had catheter-related BSI and all were caused by coagulase-negative staphylococci. The cumulative incidence of catheter-related BSI in this study was 3.8 per 1,000 days of catheter. The time of use of the central venous catheter ($p = 0.02$) and preexisting chronic skin disease ($p = 0.042$) were the only risk factors for catheter-related BSI found in this analysis.	The incidence of BSI in critical patients in the intensive care units was 3.8 per 1,000 days of catheter.
5/2011 ⁽¹⁷⁾	During the 90-day period, a total of 8,748 catheter-days was analyzed (4,371 catheters per day in the minocycline-EDTA group, and 4,376 catheters per day in the heparin group). The incidence of catheter-related bacteremia was significantly lower in the M-EDTA group ($P = 0.003$). There were 19 in the heparin catheter group, and 5 in the M-EDTA group. The survival of the bacteremia-free catheter was significantly higher in the M-EDTA group (91.3%) than in the heparin group (69.3%).	M-EDTA solution reduces catheter-related bacteremia in patients on hemodialysis during a period of 90 days.
6/2011 ⁽¹⁸⁾	Fifty-one patients who used 64 catheters were included. Twenty-one episodes of catheter-related BSI were reported in 14 patients. A total of 1,521 samples was obtained through the catheter lumen. All 21 episodes of BSI were preceded by catheter colonization. The microorganism found in the catheter was the same that caused the infection.	The results indicated that surveillance cultures, based on readily available samples, can be used to predict the risk of developing infection.

Chart 2 – Synthesis of results and study conclusions

(to be continued)

Study/ year	Main results	Conclusion
7/2013 ⁽¹⁹⁾	Of the 59 patients with end-stage renal disease using CVC for hemodialysis, 30 (50.8%) developed bacteremia, 7 (11.6%) had bacteremia and fungemia, and 22 (37.3%) had no confirmation of BSI. The overall infection rate was 62.8% (95% CI, 50.4-75.1%). Of the 124 blood cultures, 65 (52.4%) were positive. Gram-positive cocci (n = 18, 27.7%) were the most observed microorganisms, and <i>S. aureus</i> was responsible for most infections.	A high prevalence of Gram-negative bacteria was observed among patients receiving hemodialysis by means of a CVC. It is important to identify which pathogens cause BSI among patients in hemodialysis units, to guide initial therapy.
8/2014 ⁽²⁰⁾	There was a total of 174 catheter-related BSI over the study period: 142 catheter-related infections in the heparin period and 32 infections in the antibiotic-lock period. The rate of catheter-related BSI in the antibiotic lock period (0.45/1000 catheter days) was 73% lower than in the heparin period (1.68/1000 catheter days, p = 0.001).	The results of this study show that the use of antibiotic lock was associated with a substantial reduction in catheter-related BSI.
9/2014 ⁽²¹⁾	Multiple interventions can reduce the rate of catheter-related infection, for example: the use of bundles is relevant data to be integrated in practice and in the education of nephrologists, to reduce infection; use of lock solutions; antimicrobial catheters and dressings of transparent film or sterile gauze, which should be replaced every 48 h.	To minimize risks, it is necessary to allow training of nephrologists still inexperienced, to properly select the location of catheter insertion and to use citrate lock instead of heparin.
10/2014 ⁽²²⁾	There were 190 episodes of hemodialysis catheter-related BSI in non-elderly patients (infection rate of 1.97 events per 1,000 catheter days) and 18 episodes in elderly patients (infection rate of 0.55 events per 1,000 catheters per day). The risk of catheter-related BSI decreased by 10% for each five-year increase in the patient's age (HR, 0.89, 95% CI, 0.85-0.93, p = 0.001).	Elderly patients aged 75 years or more on hemodialysis with a catheter have a much lower risk of catheter-related BSI than younger patients.
11/2014 ⁽²³⁾	A total of 596 critically ill patients received saline or heparin lock solution (standard) or citrate lock. Among the 464 patients who received standard solution, the incidence of catheter colonization was 27.6% (95% CI, 27.7 to 52.2). Among the 132 patients who received citrate, the incidence of catheter colonization was 14.4% (95% CI, 13.0-30.9).	The use of citrate as a lock solution reduces the risk of colonization of the catheter tip and, therefore, may improve safety of hemodialysis in the ICU. The same solution was also associated with lower catheter dysfunction.
12/2014 ⁽²⁴⁾	A total of 2,374 patients were included in the analysis. The probability of <i>S. aureus</i> infection at the hemodialysis catheter site was 87% lower in the mupirocin group than in the control group (odds ratio [OR], 0.13, 95% confidence interval [CI], 0.05-0.34, p <0.001). Mupirocin applied to the catheter exit site in <i>S. aureus</i> patients was the most effective treatment and reduced the probability of skin infection at the exit site of the catheter by 87% compared to no treatment or placebo (OR, 0.13; 95% CI, 0.05-0.34, p = 0.000).	Mupirocin ointment effectively reduces the risk of infection at the site of CVC for hemodialysis, as well as the risk of catheter-related bacteremia. No other intervention has been shown to be effective in the long term.

Chart 2 – Synthesis of results and study conclusions

(conclusion)

Study/ year	Main results	Conclusion
13/2014 ⁽²⁵⁾	Twenty-three articles were selected. In total, 1,596 hemodialysis patients were divided into groups at the treatment baseline with systemic antibiotic (n = 697), antibiotic lock solution (n = 546), or guidewire (n = 353). Antibiotic lock solution and catheter replacement with guidewire had similar cure rates, higher than systemic antibiotics alone (OR, 2.08, 95% CI, 1.25 to 3.45, p = 0.01 for solution of antibiotic lock, OR, 2.88, 95% CI, 1.82 to 4.55, p = 0.001 for change for guidewire versus systemic antibiotics). Healing ratios were higher for coagulase-negative staphylococci followed by Gram-negative bacilli and <i>Staphylococcus aureus</i> . Among <i>S. aureus</i> infections, guidewire switching led to a greater proportion of cure than systemic antibiotics or antibiotic lock solution (OR, 3.33, 95% CI, 1.17 to 9.46, p = 0.02, OR, 4.72, 95% CI, 1.79-12.46, p = 0.002, respectively).	Hemodialysis catheter-related bacteremia should be treated with guidewire switching, or antibiotic lock solution. Future studies should prospectively address which strategy is best, isolated and for specific pathogens.

Source: Created by the authors.

Discussion

The studies analyzed demonstrated high catheter-related infection rates. In a study with 173 patients using CVC, the cumulative incidence of infection was 3.8/1000 catheters per day⁽¹⁶⁾. In another study with a population of 51 patients who used 64 catheters, 21 developed BSI⁽¹⁸⁾. The third study found a global infection rate of 62.8% (95% CI, 50.4-75, 1%) in a population of 54 CVC hemodialysis patients⁽¹⁹⁾.

Some risk factors for infection related to the patient were cited by the studies, such as hypertension, diabetes mellitus and hypoalbuminemia. When the microorganisms responsible for infection were observed in the catheter, the presence of Gram-positive cocci was noted, with *Staphylococcus aureus* being responsible for most of the episodes^(14,19,22). In one study, *S. aureus* infections accounted for 33% of catheter replacements, whereas *S. epidermidis* infection accounted for 12.5%. In the latter case, systemic antibiotic and lock therapy is efficient, requiring no catheter replacement⁽¹⁴⁾.

Topical mupirocin was effective in the treatment of *S. aureus* infections at the catheter insertion site, and the probability of acquiring infections was 87% lower when compared to

other interventions (OR 0.13; 95% [CI], 0.05-0.34, p <0.001). Mupirocin applied at the catheter exit site in *S. aureus* patients was the most effective treatment and reduced the probability of skin infection⁽²⁴⁾.

As for the insertion site of the catheter, the internal jugular was preferred compared to the subclavian and femoral veins^(19,22). According to international recommendations, the subclavian vein is not recommended for catheter insertion for hemodialysis due to the risk of stenosis. The femoral site is not recommended either, because it is related to higher rates of infection. However, one of the studies indicates that patients who used an internal jugular catheter were 56% more likely to develop infection when compared to those who had a catheter implanted in the subclavian⁽¹³⁾.

Patients admitted to ICU are more likely to develop infections. In these settings, catheter-related infection is widely observed. A study developed in ICU patients with CVC hemodialysis found an infection incidence of 3.8/1000 catheter-days. The risk factors related to infection were the time of use of the CVC (p = 0.02), and preexisting chronic skin disease (p = 0.042)⁽¹⁶⁾.

The lock solution is also relevant in preventing catheter-related infections. Currently, heparin is still the most widely used solution, but studies show that the use of antimicrobial-related lock solutions has greater benefits, and a reduction in catheter-related bacteremia episodes^(17,20). In a study that analyzed the impact of the antibiotic lock solution on the incidence of infection compared with heparin, the infection rate related to the catheter was 0.45/1000 catheter-days, when antibiotic lock was used, and 1.68/1,000 catheter-day, when heparin was used⁽²⁰⁾. The minocycline and EDTA solution, compared to unfractionated heparin, was also analyzed, and found a positive result in relation to the decrease in bacteremia⁽¹⁷⁾. Citrate was associated with a reduction in the risk of colonization of the catheter tip, and also with lower rates of catheter dysfunction⁽²³⁾.

When the antibiotic lock solution was compared to other interventions, it was observed that it was effective, as well as the replacement of the catheter with guidewire, which was more effective than the use of an isolated systemic antibiotic (OR, 2.08; 95% CI, 1.25 to 3.45, $p = 0.01$ for antibiotic lock solution; OR, 2.88, 95% CI, 1.82 to 4.55, $p = 0.001$ for guidewire exchange versus systemic antibiotics)⁽²⁵⁾.

Among other strategies to reduce catheter-related infections there is the use of bundles, a package of measures that, when practiced together, are effective in reducing infection rates⁽²¹⁾. These measures are already recommended by the CDC, which shows the extreme importance of using a maximum barrier precaution (cap, mask, sterile apron, sterile gloves and large sterile fields) associated with other recommendations to reduce the chances of colonization of the device at the time of insertion.

A single study cited the catheter lining with antimicrobial to prevent *S. aureus* biofilm formation on the external and internal surface of the catheter⁽¹⁵⁾. The results were positive, showing that the coating prevents biofilm formation, consequently leading to a reduction in infection rates.

Routine microbiological surveillance has proven to be effective, and this strategy can be used to predict possible catheter-related infections, although other studies are needed to evaluate this strategy cost-effectiveness⁽¹⁸⁾.

Conclusion

Central venous catheter-related infections in hemodialysis are present and pose major health risks. Nurses, responsible for the direct and comprehensive care of patients, should find ways to reduce this burden, aiming at the safety of ill individuals. For this purpose, continuous update of the nurses' knowledge is imperative.

The studies found in the present review point to several strategies for the prevention and treatment of catheter-related infections in patients undergoing hemodialysis. Considering the risks to these patients, it is extremely important to know the factors that lead to the development of infection, as well as to know the evidence that can guide decision making, in order to provide quality care.

Collaborations:

1. Conception, design, data analysis and interpretation: Mitzy Tannia Reichembach Danski, Leticia Pontes and Alessandra Amaral Schwanke;
2. Article writing and relevant critical review of the intellectual content: Mitzy Tannia Reichembach Danski, Leticia Pontes, Alessandra Amaral Schwanke and Jolline Lind;
3. Final approval of the version to be published: Mitzy Tannia Reichembach Danski, Leticia Pontes, Alessandra Amaral Schwanke and Jolline Lind.

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