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Infections in patients submitted to hemodialysis: a systematic review

Infecções em pacientes submetidos a procedimento hemodialítico: revisão sistemática

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ABSTRACT

Objective: Infection is one of the main complications of dialysis procedures to correct renal injury, with a significant impact on morbidity mortality in chronic and critically acute dialysis patients. The objective of this work was to review literature on infection in patients submitted to hemodyalisis.

Methods: A survey of publications from 1990 to March 2008 was carried out in the database COCHRANE, PubMed/MEDLINE, Latin-American and Caribbean literature on Health Sciences and Nursing database. In Health Science (DECS) and Medical Subject Headings Section (MeSH) from |PubMed/MEDLINE the following descriptors were used: infection; cross infection; bacteremia; renal dialysis; renal failure;acute renal failure; hemofiltation; hemodiafiltration; renal replacement therapy.

Results: Thirty three articles were selected. Most publications were American, from 2001 to 2005 and mainly about vascular access-related infection. Studies diverged on the definition of infection and nomenclature, hindering comparisons. Fiver articles covered different infection topographies, 16 studied vascular access-related infections in the different types of vascular accesses, nine specifically focused on temporary central catheters for hemodialysis and only three studied infections in intensive care unit patients. Temporary central catheters for hemodialysis were identified as the principal risk factor.

Conclusion: There is a need for studies about infection incidence in critically ill, submitted to dialysis with temporary catheters, due to acute renal injury to define a causal relationship and risk factors to orient adequate prevention and control measures.

Keywords: Infection; Cross infection; Bacteremia; Renal dialysis; Renal insufficiency, acute; Renal insufficiency, chronic

INTRODUCTION

Patients with renal impairment are at high risk of developing infection due to low immunity, severe clinical condition and need of vascular accesses for renal replacement therapy (RRT).[1]

Dialysis methods that use extracorporeal circulation have been employed in care of critically ill patients in the intensive care unit (ICU) as is the case of acute renal injury (ARI), in general of multifactorial etiology (sepsis, ischemia by hemodynamic instability nephrotoxic cause) or chronic renal injury (CRI) due to terminal disease or chronic worsened by ischemia or

nephrotoxicity.[1]

In patients with CRI submitted to hemodialysis in specialized centers, vascular access related infections are significant as they may cause disseminated bacteremia or loss of access, in addition to bloodstream infections (BSI), presenting higher mortality and associated costs.[2] Vascular access-related infections (VARI) include local catheter insertion site infections (LCISI)) as well as BSI.

Accesses used for hemodialysis include the arteriovenous fistula (AVF), arterioveneous grafts and cuff or tunneled central venous catheters.[3,4] In hospitalized critically ill patients temporary catheters are preferred due to immediate access.

In ICU patients, the kidney fails with more frequency requiring RRT in about 5% to 42% of critically ill patients.[5-7] In addition to the high rate of renal dysfunction, associated mortality rates remain high from 40 to 90%.[6] Added to renal injury, in the ICU infection is one of the most frequent complications, comprising more than 20% of all cross infections.[8,9]

Considering the impact of renal injury and infection in critically ill patients, this study proposed a review of literature on the frequency of infections in patients with renal injury submitted to hemodialysis.

METHODS

A review of references on the incidence of infections in adult patients submitted to hemodialysis from January 1990 to March 2008 was carried out. Searches were initially conducted from the electronic evidence based practice – COCHRANE, with follow-up in PubMed/MEDLINE, Latin-American and Caribbean literature on Health Sciences. Nursing database (BDENF). Other sources were the links for references of studies selected from the databases of the Universidade de São Paulo (DEDALUS) and of the Universidade Estadual de Campinas.

In the search, the descriptor of the Bireme Health Science DeCS) and the *Medical Subject Headings Section* (MeSH) of PubMed/MEDLINE: Infection; cross infection; bacteremia; renal dialysis; kidney failure, chronic kidney failure, acute; hemofiltration; hemodiafiltration; renal insufficiency, acute; renal insufficiency, chronic; renal replacement therapy. For not indexed descriptors the terms used were bloodstream infection and hemodialysis.

Studies were first assessed by the title and abstract including those that addressed incidence of infection in patients with CRI as well as with ARI, hospitalized and/or submitted to procedure in specialized centers. Exclusive studies on viral infections, costs, specific treatments, technologies of infection prevention (i.e. antibiotics, impregnated catheters) nasal bearers of pathogens, risk factors, outbreaks and infection in specific populations (for instance, dialysis diabetic patients) were excluded. Studies on incidence of infection that also address some exclusion criteria were considered. Studies in which eligibility was questionable were assessed by two reviewers and discrepancies were resolved by consensus.

For analyses, articles were divided into four categories:

- Different infection topographies in patients with CRI; 5 articles
- VARI stratified by different types of vascular access in patients with CRI: 16 articles
- VARI in patients with CRI with renal injury, in the ICU: 3 articles.

Selected articles were analyzed according to year of publication, site, and sample, type of study, incidence and type of infections.

RESULTS

Seventy-nine articles were found and of these 33 regarding the subject were selected (41.8%), 31 in the PubMed/MEDLINE,[4,10-39] one in LILACs[40] and one abstract published in the proceedings of an international congress.[41] Twenty seven full articles and six abstracts were analyzed. Of the analyzed abstracts[14,24,25,29,33,41] only one had all the information needed to analyze the factors compiled in this study.

The largest number of publications was concentrated in the Americas, eight in the United States, four in Canada and two in Brazil. The extensive participation of the United States may be explained by the fact that they have two data collection systems the *United States Renal Data System*, that analyzes information on renal injury at terminal stage and the *Dialysis Surveillance Network*, initiated by the Centers *for Disease Control and Prevention* (CDC) in 1999 to monitor data of patients submitted to dialysis in specialized centers.[42,43] In Canada, three works involved common researchers.[16,19,23] Brazilian studies were carried out by the same principal authors.[36,40]

France was the European country with the largest participation of four articles, three of them of the same researchers.[10,11,15] Next came Turkey with two publi-

cations, Belgium, Serbia and Montenegro, Scotland, Portugal and Italy with one article each. In the Asiatic continent India, Saudi Arabia, Israel, Taiwan Japan and Iraq contributed with one article each and Oceania, with two works from Australia.

There was a higher concentration of publications from 2001 to 2005, with a tendency to increase, since in the latter three years practically the same number of articles was polished as in the five prior years.

Regarding the type of study, 31 were cohort trials (93%) and of these three were retrospective[27,28,41] and other three conducted in parallel, case control studies for identification of risk factors.[13,16,23] In addition to these 31 studies, two analyzed existing databases (*United States Renal Data System* and *Dialysis Surveillance Network*), totaling 33 articles.[14,25] No clinical randomized trial was found.

More than one center participated in 33.3% of studies (ranging from 3 to 109). Of the studies that mentioned the place of performance of hemodialysis, 89.6% were in clinics or hospital units specialized in nephrology and only 10.4% in the ICU. Mean time of follow-up was of 18.8 months (ranging from six to 67 months).

Regarding the population under study, there was no uniformity, sometimes patients under hemodialysis were studied, sometimes sessions of hemodialysis. Two abstracts did not cite this information and two studies worked with more than one type of population (Table 1).

Table 1- Presentation of the selected works according to country, sample (patients, hemodialysis sessions, patients-day, patients-month), place of study and factor under study. São Paulo, 2008.

Country	Sample	Place of performance	Factor under study
		Out patient dialysis center (number)	
France[10]	203	27	IG and VARI in the different types of access*
France[11]	607	13	IG not stratified by type of access
India[12]	84	1	IG not stratified by type of access
France[15]	988	19	VARI not stratified by type of access
USA[18]	796	7	VARI not stratified by type of access
Canada[23]	527	9	VARI in the different types of access *
Serbia and Montenegro[34]	107	1	VARI in temporary venous catheters
Brazil[40]	64	1	VARI in temporary venous catheters
Brazil[36]	62	1	VARI in temporary venous catheters
USA[17]	38,096[(a)]	3	VARI in the different types of access*
USA[21]	111,383[(a)]	6	VARI in the different types of access*
USA[4]	75,535[(c)]	109	IG and VARI and in the different types of access*
Portugal[29]	4,501[(c)]	5	VARI in the different types of access*
		Hospitals	
USA[13]	365	Patients with CRI (1 hospital)	IG not stratified by type of access
Canada[16]	80	1 dialysis unit	VARI not stratified by type of access
Saudi Arabia[20]	183	1 dialysis unit	VARI in the different types of access*
Scotland[28]	265	1 dialysis unit	VARI in the different types of access*
Taiwan[30]	135	1 dialysis unit	VARI in temporary venous catheters
Australia[31]	52	1 dialysis unit	VARI in temporary venous catheters
Canada[32]	218	1 dialysis unit	VARI in temporary venous catheters
Turkey[35]	70	1 dialysis unit	VARI in temporary venous catheters
Iraq[37]	103	1 dialysis unit	VARI in temporary venous catheters
USA[22]	951	10 dialysis units	VARI not stratified by type of access
	142,525[(a)]		

Continued

Table 1- Continuation

Country	Sample	Place of performance	Factor under study
Canada[19]	133,158[(a)] 316,953[(b)]	11 dialysis units	VARI in the different types of access*
Israel[26]	2568[(c)]	1 dialysis unit	VARI in the different types of access*
Australia[27]	14,528[(b)]	1 dialysis unit	VARI in the different types of access*
France[38]	170	1 ICU	VARI in temporary venous catheters for hemodialysis and other central catheters
Japan[39]	54	1 ICU	VARI in temporary venous catheters
Belgium[41]	406	3 ICU	IG in patients submitted to RRT
Turkey[33]	67	Not cited	VARI in temporary venous catheters
Italy[24]	Not cited	Not cited	VARI in the different types of access*
USA[25]	321,519[(c)]	Not cited	Retrospective analysis of the database *Dialysis Surveillance Network*
USA[14]	Not cited	Not cited	Retrospective analysis of the *United States Renal Data System* and of largas coortes

USA – United States of America; VARI- vascular access related infection (local and/or bloodstream infection); IG – infections in any topography; CRI –Chronic renal injury; ICU – intensive care unit.
*Temporary central catheter, tunneled catheters, arteriovenous grafts and arteriovenous fistulas
(a) –hemodialysis sessions; (b) – patients-day; (c)- patients-month

Of the studies, 63.3% only focused on infection incidence in patients submitted to hemodialysis. The others, also included identification of risk factors, the impact of infection on mortality, access complications, creation of a surveillance system, updating of an already exhibiting national network and strategies to prevent infection.

Definition of infection

Criteria to define different infection topographies varied, 15 (44.5%) used their own criteria,[(4,10-12,15,18,28,30,31,34-38,40)] 12 (36.4%) CDC criteria ,[(13,16,17,20-22,25,26,29,32,33,39)] 3 (9.1%) nationally set criteria [(19,23,27)] and 3 (9.1%) did not cite the criteria used.[(14,24,41)]

Regarding VARI, authors who used their own criteria defined, for infection on the access site, the presence of pus and phlogistic signs surrounding insertion. For the BSI, criteria varied, such as presence of signs and symptoms, hemoculture (HMC) and positive catheter tip, positive HMC without another apparent cause or only positive HMC. Two trial studied related bacteremia (signs and symptoms, HMC and positive catheter tip) and possible fever, without other cause and insufficient microbiological criteria to relate.

Notwithstanding the similarity between definitions, use of own criteria leads to divergences in study results which may jeopardize their comparison.

Incidence of infection

In the majority of articles the most often identified infection was BSI.

Different infection topographies were studied in five articles.[(4,10-13)] Three identified higher rates of VARI. One identified pneumonia and the other, urinary tract infection (UTI) as the most frequent topographies among chronic patients submitted to hemodialysis.[(12,13)]

Sixteen articles used different denominators to calculate incidence of VARI stratified by type of access in outpatients (Table 2).[(14-29)] Only two articles also included patients with ARI, but excluded the procedures carried out in the ICU.[(16,27)]

In general, data disclosed that the highest rates are related with temporary catheters, when compared to tunneled catheters, fistulas or grafts. However there was a higher incidence of bacteremia with tunneled catheters when the denominator was dialysis sessions. In the study in question, authors admit that data, besides disagreeing from the findings in literature were not significant and could be explained by the possibility of inappropriate collection of blood samples for HMC in patients with a temporary catheter, resulting in underreporting.[(17)]

One study conducted in nine hemodyalisis centers, found higher rates of access-related infection in tunneled catheters.[(23)] Authors argue that theoretically the cuff promotes a protective barrier against migration of bacteria along the catheter towards the bloodstream. There was

Table 2 – Incidence of hemodialysis-related infection according to site of infection, access way for procedure and type of denominator used in the calculation for infection rate froms January 1990 to March 2008 . São Paulo, 2008.

	Access-related infection*	Infection on the access site	Bacteremia
For 1,000 hemodialysis sessions			
Temporary catheter	19.92 to 29.2	16.75	1.4 to 5.2
Tunneled catheter	3.93 to 12.2	8.3	3.1 to 4.55
Graft/fístula	0.9 to 4.23	2.06	0.2 to 0.6
For 10,000 hemodyalisis sessions			
Temporary catheter	40.26	-	-
Tunneled catheter	45.26	-	-
Graft/fístula	7.97	-	-
For 100 patients-month			
Temporary catheter	42.85	3.5	8.73 to 10.1
Tunneled catheter	12.6	0.36	2.17 to 4.84
Graft/fístula	0.95 to 1.6	0.05	0.16 to 0.6
For 1000 pacients-day			
Temporary catheter	-	-	20.2
Tunneled catheter	-	-	4.02
Graft/fístula	-	-	2.86

*Access related infection includes local infection and bloodstream infection

no statistical difference between the two types of catheters and possibly, the institutional policies and severity of patients may have contributed to the results.

All studies elected worked with infection incidence. Furthermore of the nine works about infection incidence in chronic patients with temporary catheter, six, in parallel, studied risk factors.[30,37,40] The identified risk factors were low creatinine serum level, immunocompromise, number of hemodialysis sessions, inadequate hygiene of the patient, time of catheter; insertion in the jugular and femoral vein, diabetes mellitus, use of intravenous drugs, number of puncture attempts and hypoalbuminemia. Reported rates range from 8 to 42.2% for access-related infections 13.8% to 49% for BSI. Another utilized denominator was catheter-day with a rate of 3.8% to 9.8%.

Only two articles and one abstract studied patient in the ICU. In the abstract[41] of 406 patients followed, 87% developed different types of infections with the rate of 5.9% patient-day. In another two articles, rates of UTI were reported ranging from 1.0 and 2.7% catheter-day.[38,39]

A study[38] that compared colonization rates and infection between temporary catheters for hemodialysis and central catheters for intravenous therapy in critically ill patients did not find statistically significant differences.

Colonization and infection rates of 4.8% and 2.7% dialysis catheters-day respectively were observed in another study, where the authors stressed that in the critically ill patient it is difficult to control infections associated to hemodialysis separately from other topographies.[39]

Differences in defining criteria and use of denominators hindered comparison of rates between different centers. Diversity of institutional policies for infection prevention and control, the type of analyzed population and the economic differences between countries also hindered comparison.

Analysis of articles led to the conclusions that publications on the subject had progressed. Initially, incidence of different topographies of infection in patients submitted to hemodialysis was studied and it was found that the more evident infections were related to vascular access. Thereafter, studies began to investigate infections stratified by different types of vascular accesses. Currently, publications of patients with CRI, submitted to hemodialysis in specialized centers, vascular access-related infection incidence in temporary catheters, followed by tunneled catheters, grafts and fistulas are more in evidence.[43,44] For patients undergoing hemodialysis in the ICU, were located only three articles.

CONCLUSIONS

With the increased life expectancy, technological advances in the care of critically ill patients in the ICU and considering that use of temporary central catheters is a rather common practice in this population, not only because it represents immediate access to circulation for hemodialysis, for management of ARI, but also when other accesses are not available in patients with CRI, the need for studies on the incidence of infection in the patient under dialysis in the intensive care unit, seems mandatory.

In addition to scarcity of articles on the subject, patients in the ICU and those in the hemodialysis treatment present a high risk of mortality by the primary disease itself. They are further submitted to other invasive procedures such as central accesses for intravenous therapy for diagnosis and parenteral nutrition, demanding considerable effort to establish a causal relation between hemodialysis and BSI and the possible risk factors related to the procedure to establish adequate prevention and control measures.

RESUMO

Objetivos: Os procedimentos dialíticos para a correção da lesão renal têm a infecção como uma das principais complicações, com impacto significante na morbi-mortalidade em pacientes dialíticos crônicos e agudos críticos. O objetivo deste trabalho foi revisar a literatura sobre infecções em pacientes submetidos a procedimentos hemodialíticos.

Métodos: Foi realizado levantamento das publicações de 1990 a março de 2008 nas bases eletrônicas COCHRANE, PubMed/MEDLINE, Literatura Latino-Americana e do Caribe em Ciências da Saúde, Banco de dados de Enfermagem. Foram utilizados os descritores em Ciências da Saúde (DeCS) e o *Medical Subject Headings Section* (MeSH) do PubMed/MEDLINE: infecção; infecção hospitalar; bacteremia; diálise renal; insuficiência renal crônica; insuficiência renal aguda; hemofiltração; hemodiafiltração; terapia de substituição renal.

Resultados: Foram selecionados 33 artigos. A maioria das publicações era americana, concentrou-se entre os anos 2001 e 2005 e a principal topografia foi infecção relacionada ao acesso vascular. Os estudos divergiram na definição de infecção e denominadores utilizados, comprometendo a comparação dos mesmos. Cinco artigos trabalharam com diferentes topografias de infecção, 16 estudaram infecção relacionada ao acesso vascular nos diferentes tipos de acessos vasculares, nove focaram especificamente nos cateteres centrais temporários para hemodiálise e apenas três estudaram infecções em pacientes de unidade de terapia intensiva. A realização de hemodiálise por cateteres centrais temporários foi o principal fator de risco identificado.

Conclusão: Evidenciou-se a necessidade de estudos sobre a incidência de infecção no paciente crítico, que dialisa por cateter temporário devido à lesão renal aguda, na tentativa de estabelecer relação causal e fatores de risco, com a finalidade de direcionar medidas de prevenção e controle adequadas.

Descritores: Infecção; Infecção hospitalar; Bacteremia; Diálise renal; Insuficiência renal aguda; Insuficiência renal crônica

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