



Catheter-Related Bacteraemia in Renal Replacement Therapy in Critically Ill Patients: Can We Use Femoral Access?

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Abstract

Purpose: To determine the incidence of catheter-related bacteraemia (CRB) in critically ill patients requiring renal replacement therapy and describe related factors.

Methods: Prospective analysis was conducted in critically ill patients with haemodialysis catheters between 25 October 2009 and 7 December 2010. We gathered data on: demographic characteristics, risk factors, extracorporeal therapy, mortality and microbiological results. CRB was detected through quantitative blood and catheter cultures. We assessed differences between aseptic and non-aseptic catheter insertion ($p < 0.05$).

Results: Overall, 71 catheters were placed in 53 patients with a median age of 71 years (range, 20-84), and median APACHE II score of 25 (range, 10-40). Extracorporeal purification was indicated for acute renal failure in 92.37% of patients (83% with multiorgan failure) and continuous techniques predominated. Overall, 55 catheters were placed in the femoral and 16 in the jugular vein. The median number of connections/catheter was 6 (r 1-50) and catheter days 7 (r 1-33). We found one bloodstream infection related to a permanent jugular catheter, 1.53/1000 days of catheter exposure and 3 catheters were culture positive that did not meet CRB criteria (*E. faecalis* was isolated from two catheters and *S. Aureus* from one). Femoral puncture was not associated with a higher risk of catheter colonization or CRB (RR 1.06 95% CI (0.1-10.94)).

Conclusions: Haemodialysis catheter-related bloodstream infections are uncommon, despite frequent femoral insertion.

Keywords

Bacteraemia, Catheter, Haemodialysis

Introduction

As many as 78% of critically ill patients require at least one central venous catheter (CVC) for carrying out haemodialysis, measuring central venous pressure, placing transvenous pacemakers or administering vesicants or parenteral nutrition [1]. The complication associated with placement of these catheters that has the greatest

impact on mortality rates and costs [2,3] is catheter-related bacteraemia (CRB) with a predominance of Gram-positive cocci [4-7]. Although it is assumed that this complication will develop in between 1 and 15% of CVCs [1,2], prevention and surveillance programmes for nosocomial infection have reduced the rates of CRB, from 7.4 to 4.89 cases per 1000 days of catheter exposure in Spanish intensive medicine units [4], which are very focused on aseptic measures and avoiding femoral vascular access [8] given the greater risk of faecal contamination [7-10].

Despite extracorporeal blood purification systems having been widely used in intensive care units (ICUs) for more than 15 years [11,12], and patients with acute renal dysfunction having a higher risk of developing nosocomial bacteraemia [13], few studies have analysed the risk of CRB during renal replacement therapy (RRT) in critically ill patients. Studies that have been published have focused on patients that require ICU admission and undergo RRT due to worsening of chronic kidney failure [13], and have provided controversial recommendations regarding its management [5,13]; moreover, the results cannot readily be extrapolated to other critically ill patients, in whom femoral vascular access for removal and return of blood for RRT has the advantage of being technically easy and associated with lower rates of mechanical complications [10,13].

The objective of our study was to determine the incidence of CRB in our critically ill patients receiving RRT and evaluate associated factors.

Material and Methods

Patients

We conducted a prospective, observational study of all the patients admitted to our ICU, a tertiary hospital multipurpose unit with 17 beds, who had one or more catheters for extracorporeal blood purification, between 25 October 2009 and 7 December 2010. We collected data on the following variables: demographic characteristics, patient diagnoses, 24-hour severity scores (Acute Physiology and Chronic Health Evaluation II [APACHE II] [14], and

Simplified Acute Physiology II Score [SAPS II] [15]), personal history suggesting a higher risk of CRB (chronic renal failure, hypertension, diabetes mellitus, immunosuppression, any type of carcinoma, previous microbiological colonisation, permanent haemodialysis catheter, immunosuppressive treatment) and certain high-risk clinical conditions, such as femoral catheterisation in abdominal surgery and jugular catheterisation in tracheostomized patients. Further, for each patient, we recorded the time catheters were placed, number and type of devices used, insertion site and dwell time. We also recorded deaths and RRT data, the microbiological results of blood and catheter tip culture and the diagnosis of haemodialysis CRB.

Catheter insertion and care

We used 13.5 Fr Niagara® non-radiopaque dual lumen polyurethane catheters that were 20 cm long for femoral access and 15 cm for jugular access (Bard, Salt Lake City, USA). In patients admitted with a long-term haemodialysis catheter, a so-called permanent haemodialysis catheter (placed by the nephrology unit under aseptic conditions, according to the usual protocol), we inserted a temporary catheter at a different site in the event of malfunction of the existing catheter.

The protocol for managing the catheters during the study period was as follows:

1. Placement: Devices were placed by ICU staff doctors and doctors in training with the unit with the following aseptic and sterile barrier measures: sterile drapes completely covering the patient, cleansing of the site with water and antibacterial soap, handwashing with a 2% chlorhexidine-alcohol solution, and the use of sterile surgical caps, gloves, gowns and masks. The doctor placing the venous access device decided on the site for catheter insertion. A 2% chlorhexidine solution was used to disinfect the site and 2% mepivacaine as a local anaesthetic. The catheters were inserted percutaneously using the Seldinger technique and secured with 2/0 silk sutures. After placement of the catheter, the site was cleaned with a chlorhexidine solution and covered with a sterile dressing.

2. Nursing care: Catheters were exclusively used for RRT and a procedure was established for cleaning the insertion site every day with saline and 2% chlorhexidine solution. The catheter hubs and caps were handled under aseptic conditions, and both lumens were locked between dialysis sessions with 2 ml of heparin sodium (200 IU/mL). The system was purged and managed in accordance with the usual technique, and lines were connected under aseptic conditions in the presence of a doctor.

3. Treatment: The need for RRT was determined by the patient's doctor, who also decided on the treatment to be given, and hence, a given patient may have had different therapeutic modalities at different time points, with the effluent flow rate adjusted depending on the indication and treatment goals. The anticoagulation protocol for the system was also chosen by the prescribing doctor considering potential contraindications.

4. Sample collection: Blood samples were taken for culture directly from peripheral vessels, using the usual aseptic technique, and in the event of suspected CRB when a permanent device was in place, blood was also drawn through the haemodialysis catheter itself. Further, samples were collected from the catheter tip during catheter removal with an aseptic technique. All samples were processed and cultured using standard diagnostic methods.

5. Catheter removal: The decision to remove a device was based on whether or not RRT was needed, and in event of device malfunction when access was needed, a new device was placed at a different site.

6. Digestive decontamination: Patients under mechanical ventilation for more than 48 hours received selective digestive decontamination based on amphotericin B, polymyxin, gentamicin and excipients, as well as 2 g/day of IV ceftriaxone for 3 days.

Definition of CRB

In the event of catheter removal: Patients were considered

to have a positive catheter culture if 10^3 colony forming units/ml were found by the Brun Buisson technique [16] and were assigned a diagnosis of CRB if they met criteria for sepsis [17], the catheter culture was positive, and there was significant isolation of the same bacteria in one or more cultures of peripheral blood taken between 48 hours before and 48 hours after catheter removal. Patients in whom the catheter culture was positive but blood cultures were negative were classified as having catheter colonisation or contamination during sampling and/or processing of the sample.

With no catheter removal [16]: Patients were assigned a diagnosis of CRB if they met criteria for sepsis and there was quantitative difference in colony number of $\geq 5:1$ (between cultures from blood extracted through the haemodialysis catheter and that collected directly from a peripheral vessel), or in growth time (with a positive result ≥ 2 hours earlier from blood extracted through the haemodialysis catheter than that collected directly from a peripheral vessel).

Measures of incidence and relative risk

To calculate incidence, we counted the total number of days haemodialysis catheters were in place for devices placed during the study period and days of admission in the ICU for permanent catheters (placed before admission to the ICU).

We estimated both cumulative incidence and incidence density. Cumulative incidence was calculated by dividing the number of cases of haemodialysis CRB by the number of patients who met inclusion criteria and expressed as a percentage. Incidence density was calculated by dividing the number of cases of haemodialysis CRB by the number of days of exposure to risk (haemodialysis catheter days) and expressed as cases per 1000 days of exposure.

We calculated relative risk (RR) of CRB or catheter colonisation in patients with femoral catheters undergoing abdominal surgery and RR of CRB.... (confidence interval 95%).

Data analysis

Statistical analysis was performed using SPSS 21 (SPSS Inc., Chicago, Illinois, USA). Qualitative data were expressed as a frequency and continuous data as a mean \pm standard deviation (SD) or median (P_{50}) and percentile 25-75, as appropriate given their distribution. Results were compared between patients with possible catheter-related infections (diagnosis of CRB or a catheter that was colonised or contaminated) and those classified as free of CRB with Fisher's exact, chi-squared, Student's t or Mann-Whitney U tests, as appropriate. P values < 0.05 were considered significant.

The study complied with the ethical requirements for the handling of data and medical records stipulated by the committee for research and clinical trials of our hospital. Written informed consent was obtained from patients' families before collection of blood samples for culture.

Results

Study population

The characteristics of the study population are summarised in table 1. A total of 71 catheters were placed in 53 patients, 12 of them requiring 2 or more catheters due to malfunctioning of a previous device, with no suspicion of CRB, or due to RRT being prescribed again after a previous catheter had been removed. RRT was indicated for acute renal failure (according to the RIFLE criteria [18]) in more than 90% of patients, and 83% of these patients also had multiorgan failure including renal failure. Most patients needed changes in their treatment during the course of their illness, generally including continuous intravenous haemodiafiltration and haemofiltration, with effluent rates tuned to attempt to achieve the clinical goals. The median of the maximum haemodialysis dose (effluent flow rate) used was 52 ml/kg/h (r 20-80).

55 catheters were placed in femoral vein (77.5%) and 16 in jugular

Table 1: Characteristics of the study population.

Characteristics	All patients N = 53	Patients with sterile catheter and without CRB N = 49	Patients with CRB or catheter colonisation/contamination N = 4	p
Age (years)	66.5 (14.7)	66.4 (14.2)	67.5 (12.3)	0.7
Sex (M; F)	36;17	33; 16	3;1	0.82
APACHE II score	25 (21.5-32)	25 (20.5-33.2)	24 (21.5-34)	0.84
SAPS II	60 (49-73.5)	60 (45.7-70)	66 (48-75)	0.45
MODS N (%)	44 (83)	41 (83.6)	3 (75)	0.54
Maximum SOFA score	12 (11-15.75)	12 (10-15)	13 (12-14)	0.31
Hypertension N (%)	12 (22.6)	11 (22.4)	1 (25)	0.81
Diabetes mellitus N (%)	26 (49)	24 (48.9)	2 (50)	0.69
Cancer N (%)	14 (26.4)	13 (26.5)	1 (25)	0.23
Immunosuppression N (%)	6 (11.3)	6 (12.2)	0	0.78
Permanent catheter N (%)	1 (1,8)	0	1 (25)	0.0004

CRB: Catheter Related Bacteraemia. Age is expressed as media (standard deviation). Other variables as median (percentile 25-75) and N (number of patients and %). Comparison with Mann-Whitney U test, p value (level of significance of 95%). Sex expressed as the total number of male (M) and female (F) patients. APACHE: Acute Physiology and Chronic Health Evaluation; SAPS: Simplified Acute Physiology Score; MODS: Multiple Organ Dysfunction Syndrome and the maximum score (range) in the Sequential Organ Failure Assessment (SOFA). Cancer: all types of carcinoma. Immunosuppression: previous diagnosis of clinically-relevant humoral or cellular immunosuppression.

Table 2: Risk factors for haemodialysis catheter-related bacteraemia.

Factor	Total haemodialysis catheters N = 71	Sterile catheters with no catheter-related bacteraemia N = 67	CRB or catheter colonisation/contamination N = 4	p
Catheter (F/J)	55/16	54/13	1/3	0.03
Number of catheter days	7 (1-33)	7 (1-33)	1 (2-26)	0.65
Placement day	1 (0-48)	1 (0-48)	0.5 (0-22)	0.72
Number of connections	6 (1-50)	6 (1-50)	4.5 (3-21)	0.54
Maximum haemodialysis dose (ml/kg/h)	42 (20-80)	42 (20-80)	39.5 (35-50)	0.74
Indication for catheter:				
Acute renal failure	66	63	3	0.25
Chronic renal failure	1	1	0	1
Guillain-Barré syndrome	1	1	0	1
Negative water balance	3	2	1	1
Therapies				
CVVH	30	27	3	0.14
CVVHDF	24	21	3	0.07
IVVHDF	45	44	1	0.13
SCUF	4	4	0	1
PP	1	1	0	1
CVVHD	2	2	0	1

P: 95% significance level, Catheter (F/J): Catheter Location Femoral/Jugular, N: Number of catheters, CVVH: Continuous Venovenous Hemofiltration, CVVHDF: Continuous Venovenous Hemodiafiltration, IVVHDF: Intermittent Venous-Venous Hemodiafiltration, SCUF: Slow Continuous Ultrafiltration, PP: Plasmapheresis, CVVHD: Continuous Venovenous hemodialysis.

Variables expressed as absolute numbers of catheters, median (range), or percentage of catheters used for each indication in at least one connection. Comparisons performed using Mann-Whitney U and Fisher's exact tests. P value (95% significance level).

vein. Overall, 56.3% of catheters were placed within the first 24 hours and were kept in place for a median of 7 days (r 1-33), with a median of 6 filter changes (r 1-50) per catheter. In one patient, a permanent catheter malfunctioned after 5 days and a temporary catheter was required.

CRB and catheter colonisation

We diagnosed one case of CRB due to *S. aureus* of nosocomial origin; this was found in a permanent haemodialysis catheter (placed more than two years earlier) used for five days in the ICU, and the criterion for diagnosis was the differential growth of bacterial colonies. The incidence density of haemodialysis CRB in our study was 1.53 per 1000 days of catheter exposure, with a cumulative incidence of 0.018 haemodialysis CRB per patient during the 652-day follow-up period. We obtained positive catheter tip cultures that did not meet criteria for CRB in three patients, *E. faecalis* being isolated from two and *S. aureus* from one. Microbiological culture was not carried out for 21 catheters, in 85% of cases due to patient death with no suspicion of CRB and in the other cases due to catheters not being removed in our unit, patients recovering renal function and having no diagnosis of systemic inflammatory response syndrome [17].

Bacteraemia was not diagnosed in relation to any of the other catheters placed in any other patients in our series.

Risk factors

We found zero CRB among femoral catheter and we only found significant differences in the percentage of femoral and jugular catheters between the group in which microorganisms were isolated in catheter tip cultures and the others (Table 2). Three out of the four catheters from which cultures were positive had been placed in the jugular vein (in patients without severe sialorrhoea or tracheostomy; RR: 3.87, 95% CI: 1.83-8.16) versus one in the femoral vein. Out of the 55 femoral catheters, 17 had been used in patients undergoing abdominal surgery and bacteria was isolated from culture in one case, and hence, our data provide no evidence of a higher risk of CRB or catheter colonisation in this subset of patients (RR: 1.06, 95% CI: 0.10-10.94).

Discussion

This was a prospective observational study of the most severe complication associated with the use of haemodialysis catheters. According to our results, the incidence of this complication is very low (1.53 CRB per 1000 days of catheter exposure). Despite numerous consensus statements and clinical guidelines on CRB prevention having advised against femoral central venous access, our results suggest that this approach is safe for performing RRT in critically ill patients.

Catheter-related bacteraemia

Out of the complications associated with central venous catheterisation (bleeding, pneumothorax, fat embolism, haemothorax, thrombosis and infection), CRB is the most severe with high associated mortality and costs [2,3]. In Spain, the incidence is around 4.89 episodes per 1000 days of catheter exposure [4], and published mortality figures vary between series and microbiological findings from 12 to 25.9% [6-8,10-12,19]. These figures have motivated the development of safety policies, leading to the establishment of measures for the prevention and control of nosocomial bloodstream infections based on the recommendations of the programme developed in Michigan [8]. In our multi-purpose medical unit, the rate of bacteraemia cases related to CVCs was 0.97 cases per 1000 catheter days during 2009, with 1.1 catheters per patient, and 0.16 per 1000 days of catheter exposure during 2010, with 1.2 catheters per patient. We believe that these figures can be explained by our staff tending to opt for subclavian central venous access, and inclusion in the calculation of catheters placed in arteries, which tend to be associated with lower rates of infection.

Bacteraemia associated with haemodialysis catheters

Despite an increase in blood urea levels causing humoral and cellular immune dysfunction [20] and RRT to compensate for renal failure increasing the risk of infection, few studies have focused on haemodialysis CRB in critically ill patients. Published data are from studies on patients with chronic kidney failure requiring ICU admission and RRT, but with different vascular access sites, and often with permanent catheters and with arteriovenous fistula. In these samples, the rate of asymptomatic catheter colonisation has ranged from 10 to 55% [21], and the incidence of CRB from 3.8 to 6.5 cases per 1000 short-term non-tunnelled catheter days and from 1.6 to 5.5 cases per 1000 permanent tunnelled catheter days [6-22]. We have not found data in the literature regarding other groups of critically ill patients requiring RRT; in our series, the incidence density of CRB associated with haemodialysis catheters was only 1.53 cases per 1000 catheter days. These results may be attributable to adherence to a strict protocol for inserting and maintaining the catheter, the culture of safety and the nosocomial infection surveillance programmes in our unit.

Diagnosis of catheter-related bacteraemia

Various consensus statements and studies related to the diagnosis of CRB have been published [16,23,24], with a certain degree of variability in the classification and criteria used. In our study, we have used the classification of Sabatier, et al. [3], and adopted criteria for the diagnosis of CRB and catheter colonisation in accordance with several published studies [5,13,22], allowing the diagnosis to be reached with or without removing the catheter [16,23-28]. There is controversy over whether catheters should be systematically removed when CRB is suspected [21,27] given the complications associated with other catheter insertion sites and the variable usefulness of cultures, while it is not essential to establish a diagnosis. In our series, bacteria were isolated from three catheters from patients who did not meet criteria for a CRB, and the only diagnosis of CRB was made without removing the catheter (tunnelled catheter placed more than 2 years earlier), with significant differential colonies counts and no tip culture, as the patient died following a decision to withhold life support.

No culture was performed for a further 21 catheters which were removed from clinically stable patients with no sepsis attributable to potential CRB, and for the purposes of analysis, they were considered to be free of infection. Some of these catheters may have been colonised, and hence, the haemodialysis catheter colonisation rate obtained may be an underestimate. On the other hand, the fact that we recorded permanent catheter days from ICU admission until they were removed (rather than from when they were placed) means that our calculations would tend to overestimate the incidence density in our series. We did not diagnose any cases of primary bacteraemia or bacteraemia associated with other types of CVC during the study period.

Risk factors for CRB and type of central venous access

The incidence of CRB varies according to the type of catheter, placement site, dwell time, hospital size, place where insertion procedure was performed, and medical unit involved [22]. Lorente, et al. [2] reported incidence rates of 1.57 to 15.83 cases per 1000 days of catheter exposure, with higher rates for femoral and lower rates subclavian access. A recent study on CVCs placed by specialised nursing teams [29] found a significantly lower incidence rate (1.3 compared to 7.2 per 1000 days of catheter exposure, 95% CI: 0.03-7.3), which may be attributable to adherence to a catheter insertion protocol by the nurses, the catheter placement sites selected (in particular subclavian and antecubital access), and the comparison with historical controls (inserted by specialists and trainee doctors). Since the publication of a list of measures to avoid CRB by Pronovost, et al. [8], it has been proposed that femoral access should be avoided for the placement of CVCs. In the light of our results, in which the incidence of CRB was very low despite femoral access being used in the majority of cases, long dwell times, large numbers of connections and different types of therapies, we believe that the aforementioned recommendation should be interpreted with caution in the case of RRT. The conditions inherent to these therapies, such as the continuous blood flows, the type of catheter (polyurethane and with larger lumens than for other treatments) and a detailed protocol for maintaining aseptic conditions, makes this a safe alternative in terms of infection, as well as it being easier in terms of access and having a lower incidence of mechanical complications [2], which can be minimised by placing the catheter with ultrasound guidance [30-32].

Although femoral access has been associated with a higher rate of catheter colonisation [1], our review does not support this finding. This is probably because in some cases catheters may have been colonised but culture was not performed, as when haemodialysis catheters were removed there was no suspicion of CRB. This may also explain the higher rate of bacterial isolation in jugular catheters. Some authors have associated the risk of CRB with physical constitution in patients requiring acute renal replacement therapy [13] and recommend avoiding femoral and jugular access in patients with a body mass index (BMI) above 28.2 and below 24 kg/m², respectively. We did not find any association between BMI and the risk of infection as a function of the type of venous access in our patients; the only case of bacteraemia being related to a permanent jugular tunnelled catheter in a patient who underwent abdominal surgery with a BMI > 30 kg/m².

There has been discussion in the literature about whether CVCs should be changed regularly given the rate of colonisation of these devices [2] and the development of endo- and extraluminal biofilms [5,6,20,22] which have a role in the pathogenesis of CRB. In a study on critically ill patients with acute renal failure published in 2002, changing the catheter used for continuous arteriovenous hemodiafiltration every 5 days was associated with a lower incidence of secondary sepsis than that observed in historical controls [30]. These results cannot easily be extrapolated, however, to current therapies based on venovenous access. In our group, we do not routinely replace haemodialysis catheter if there is no clinical suspicion of infection or malfunctioning of the device, and we consider that if catheter replacement is required, a different access site should be used (in another anatomical location), given the risk of contamination during the process of placing the catheter.

Microbiological aspects

The most common microbiological agents involved in CRB in haemodialysis patients are Gram-positive cocci, especially *S. aureus* and coagulase-negative staphylococci [6,20-22]. The epidemiology of CRB and primary cases of bacteraemia is similar in critically ill patients [4]. Studies assessing the distribution of bacteria as a function of catheter site have shown a higher rate of Gram-negative bacilli and fungi in femoral access sites [7]. In our series, the bacteria isolated were consistent with published data, with one CRB due to *S. aureus* and three cases of positive catheters, *E. faecalis* being isolated in two and *S. aureus* in one.

Local antiseptics and antibiotic-coated catheters

Although various methodologically well designed studies and some meta-analyses have evidenced a decrease in the rate of CRB using antiseptic or antibiotic-coated CVCs [1,19,33], their use has not become widespread given that they are more expensive than standard catheters and the potential development of microbiological resistance [33-35], the emergence of which has been controversial [36-39]. Antibiotic-coated devices may be recommended in adults requiring CVCs for more than 5 days, if the use of a CRB control protocol fails to achieve the objectives set [1] or in the presence of CRB rates of over 3.3 cases per 1000 catheter days [40,41]. According to our results, neither the use of this type of catheter nor antibiotic lock therapy recommended in permanent catheter carriers [6,20,35] seem to be necessary for the treatment of critically ill patients with acute renal failure. Chlorhexidine-impregnated dressings for covering the catheter [42-44], the use of tunnelled catheters [10] and *S. Aureus* nasal decolonisation [6,20] are not standard practices in critically ill patients in general or in our unit. The antiseptic used during the placement of the catheter is 2% chlorhexidine, the current antiseptic of choice in CVC insertion protocols and for CVC placement in chronic patients [20].

Study limitations

The limitations of our study include the fact that catheter insertion sites were not randomly assigned and we have not performed multivariate analysis controlling for confounding factors. We did not assess the effect of selective digestive decontamination of patients on mechanical ventilation for more than 48 hours. We did not use antibiotic-coated catheters, and hence, have no data to clarify related issues. Catheters were not cultured after their removal if patients did not meet clinical criteria for infection, and this may have reduced the percentage of haemodialysis catheters classified as colonised but without CRB criteria.

Conclusions

In our cohort of patients receiving RRT, CRB was a rare complication. In the light of our results, we suggest that femoral access should not be avoided for the placement of central venous catheter for extracorporeal blood purification in critically ill patients, in the context of the use of a protocol for catheter placement and care under aseptic conditions. Further research should be conducted to confirm these results.

Authors have no conflicts of interest to declare in relation to this study.

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