

A Retrospective Analysis of Catheter-Related Infections in a Hemodialysis Population

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ABSTRACT

Objectives: To promote optimal use of vancomycin and reduce selective pressures for development of vancomycin-resistant enterococci in our hemodialysis units, we conducted a retrospective study to a.) characterize catheter-related infections (CRI) in our hemodialysis population, and b.) review vancomycin usage to treat these infections.

Methods: A retrospective analysis of hospital and dialysis charts was performed for patients receiving chronic hemodialysis (>1 month) in our University-affiliated teaching hospital. Data was collected by a single investigator for all episodes of suspected or documented catheter-related infection (bacteremia) for the 24-month period beginning May 1, 1994 and ending April 30, 1996. Management of each confirmed CRI was also recorded.

Results: Of 135 suspected CRIs, 74 were confirmed using Centre for Disease Control criteria. Permanent and temporary subclavian catheters had the highest rate of infection. Pus at the catheter site was most commonly associated with confirmed CRI (75%). Of the 74 confirmed CRIs, the most commonly isolated pathogens were *S. epidermidis* (47/74, 63.5%) and *S. aureus* (23/74, 31%). Twenty-six percent of confirmed CRIs involved *S. epidermidis* or *S. aureus* isolates that were resistant to all antibiotics commonly-used to eradicate gram-positive organisms, e.g. cefazolin, cloxacillin, clindamycin, but remained sensitive to vancomycin.

Conclusions: After one empiric dose of vancomycin, cefazolin should be considered

for the remainder of therapy in all episodes where in vitro susceptibility of the organism to cefazolin has been established.

Keywords: *hemodialysis, catheter, infection, antibiotics, vancomycin.*

RÉSUMÉ

Objectifs : Promouvoir l'usage optimal de la vancomycine et réduire les risques sélectifs d'apparition d'entérocoques résistants à la vancomycine dans nos unités d'hémodialyse. Nous avons mené une étude rétrospective pour a) établir les caractéristiques des infections liées à l'utilisation d'un cathéter (CRI) dans notre population d'hémodialysés, et b) évaluer l'utilisation de la vancomycine pour traiter ces infections.

Méthode : Une analyse rétrospective des dossiers hospitaliers et d'hémodialyse a été réalisée pour les patients sous hémodialyse chronique (> 1 mois) dans notre centre hospitalier associé à une université. Les données ont été recueillies par un seul investigateur pour tous les épisodes d'infection par cathéter soupçonnés ou documentés (bactériémie) durant la période de 24 mois commençant le 1er mai 1994 et se terminant le 31 avril 1996. Le traitement de chaque CRI confirmée a également été consigné.

Résultats : Des 135 cas soupçonnés de CRI, 74 ont été confirmés en utilisant les critères du Centre for Disease Control. Les cathéters sous-claviers permanents et temporaires étaient associés au plus haut taux d'infection. La présence de pus au point d'insertion du cathéter a été le plus souvent associée à

une CRI confirmée (75%). Des 74 cas de CRI confirmés, l'agent pathogène le plus fréquemment isolé était *S. epidermidis* (47/74, 63,5 %) et *S. aureus* (23/74, 31 %). Vingt-six p. cent des cas confirmés de CRI présentaient des isolats de *S. epidermidis* ou de *S. aureus* résistants à tous les antibiotiques couramment utilisés pour éradiquer les microorganismes gram-positifs, comme la céfazoline, la cloxacilline et la clindamycine, mais sont demeurés sensibles à la vancomycine.

Conclusions : Suite à l'administration d'une dose empirique de vancomycine, l'administration de céfazoline devrait être envisagée pour le reste du traitement dans tous les épisodes où une sensibilité in vitro du micro-organisme à la céfazoline a été établie.

Mots clés : *hémodialyse, cathéter, infection, antibiotiques, vancomycine.*

INTRODUCTION

Hemodialysis is a life saving treatment for patients with acute or chronic renal failure. Initial establishment of a venous access site may involve the insertion of a catheter into a subclavian, internal jugular, or femoral vein if a fistula is not present.¹ A serious complication of introducing central venous catheters (CVCs) is the development of infection. Fifty to 80 percent of bacteremias in hemodialysis patients originate from the access site.¹ In turn, life-threatening complications including endocarditis, meningitis, osteomyelitis and sepsis may develop.²

To prevent these complications, patients with a CVC *in situ* presenting with fever and chills and no other obvious source of infection, are commonly treated empirically with vancomycin +/- gentamicin. Routine use of vancomycin may increase the risk of developing vancomycin-resistant enterococci (VRE).^{3,4} The National Nosocomial Infections Surveillance Program in the United States reported that a review of enterococcal isolates showed an increase in the incidence of hospital-acquired VRE from 0.3% in 1989 to 7.9% in 1993.³ Several outbreaks of VRE have occurred in specialty populations including hemodialysis.⁴⁻⁷ There is also preliminary evidence that VRE is capable of transferring vancomycin-resistance to other Gram-positive bacteria including *Staphylococci*, which are common pathogens in the hemodialysis population.⁸ Therefore, as an initial step to promote optimal use of vancomycin and reduce selective pressures for development of VRE, we conducted a retrospective study to a.) characterize catheter-related infections (CRI) in our hemodialysis population, and b.) review vancomycin usage to treat these infections.

METHODS

A retrospective analysis of hospital and dialysis charts was performed for patients receiving chronic hemodialysis (>1 month) in our University-affiliated teaching hospital. Two dialysis units at the Health Sciences Centre currently provide service to over two hundred hemodialysis patients, primarily from Manitoba and Northwestern Ontario. A list of all patients undergoing chronic hemodialysis in these units during the study period was obtained from the nephrology program. All charts were reviewed by a single investigator and pertinent data were collected for all episodes of suspected or documented CRI for the 24-month period beginning May 1, 1994 and ending April 30, 1996. Patients who

had catheters inserted prior to May 1, 1994, but experienced an episode of CRI during the study time frame were included in the analysis.

Patient demographics including gender, age, weight, date of initial hemodialysis, cause of end-stage renal disease, and other concurrent disease states were collected. Catheter histories were also documented for each patient including type and location of the access, type of catheter, date of insertion and removal, and the reason for removal when available. Charts were analyzed for signs and symptoms associated with CRI including fever $\geq 38^{\circ}\text{C}$, chills, rigors, hypotension, and redness/pus around the catheter site. Blood culture data were also recorded including the location from which the sample was drawn (arterial, venous, or peripheral sites). All organisms isolated were documented along with corresponding antibiotic sensitivities. Data regarding the management of each infectious episode, including type of antibiotic(s) and duration of therapy were collected. Patients were included more than once if they had recurrent CRIs over the course of the study.

A "suspected" catheter-related bloodstream infection (bacteremia) was defined as: a patient with a catheter *in situ* and a.) signs and symptoms including fever ($\geq 38^{\circ}\text{C}$) or chills with no other obvious source of infection, or b.) signs and symptoms present with no obvious source of infection, blood cultures drawn, +/- antibiotics ordered, or c.) signs and symptoms present with no other obvious source of infection and antibiotics ordered.

A "confirmed" catheter-related bloodstream infection was defined by Center for Disease Control (CDC) criteria pertinent to the time frame in which the infections occurred and included: a.) signs and symptoms including fever ($\geq 38^{\circ}\text{C}$), chills or hypotension and, b.) a common skin contaminant isolated from blood culture from a patient with an intravascular access device, and c.) the physician institutes appropriate antimicrobial therapy.⁹

Permanent catheters were defined as cuffed, tunneled, dual lumen catheters and temporary catheters were defined as dual-lumen catheters inserted percutaneously into the subclavian, intrajugular, or femoral veins. Permanent and temporary catheters were most commonly made of polyurethane (Vascath®).

Statistical analysis of qualitative differences between catheter location or clinical presentation and confirmed CRI were conducted with the chi square statistic and Yates correction for expected values less than five.

RESULTS

The retrospective analysis included 177 patients on chronic hemodialysis. Ninety-three (52.5%) were male and 84 (47.5%) female. The average age was 55 years (range: 17–87 yrs). Between May 1, 1994 and April 30, 1996, 135 suspected CRIs occurred in 107 patients. The most common causes of renal disease in these 107 individuals were diabetic nephropathy (39%) and glomerulonephritis (15%). The most significant co-morbid diseases included anemia (76%), diabetes mellitus (51%), hypertension (46%), congestive heart failure (6%), and ischemic heart disease (3%).

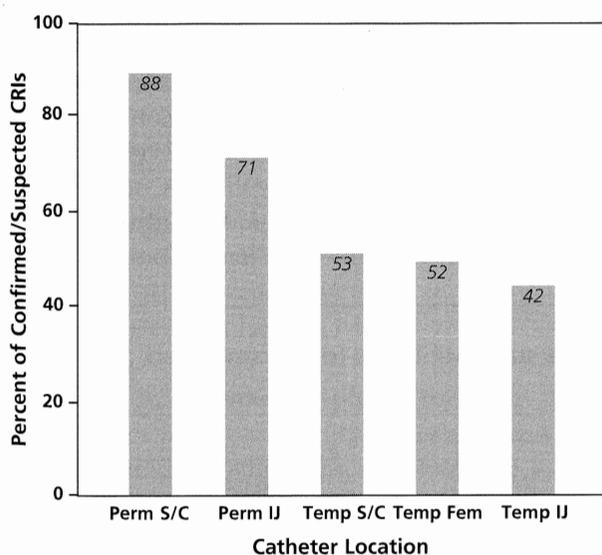
Of the 135 suspected CRIs, 74 (55%) were confirmed in 42 patients using CDC criteria.⁹ Permanent subclavian catheters had the highest rate of confirmed CRI (14/16 catheters inserted over 24 months, 88%) followed by permanent intrajugular catheters (18/26, 69%). Temporary subclavian catheters had the highest rate of confirmed CRI of all temporary catheters inserted, i.e. 20/72 (28%) temporary subclavian catheters inserted over the 24 month study period, compared with 10/53 (19%) of temporary intrajugular catheters and 12/85 (14%) of temporary femoral catheters. There was a significant difference in the rate of infection of permanent versus temporary subclavian catheters (88% vs 28% respectively, $\chi^2= 18.18$ for 1 df, $p<0.001$) and permanent versus temporary intrajugular catheters

(69% vs 19% respectively, $\chi^2=20.4$ for 1 df, $p<0.001$).

An attempt was also made to identify predictive factors in the 135 cases of suspected CRIs, 74 of which were later confirmed. Specifically, the location of the catheter and clinical presentation were analyzed. The specific catheter location and the percentage of suspected CRIs later confirmed are shown in Figure 1. Suspected permanent subclavian and intrajugular catheter infections were most commonly confirmed (88% and 71% respectively), compared with suspected temporary subclavian, femoral or intrajugular infections (53%, 52%, 42%, and respectively). The presenting signs and symptoms along with the percentage of suspected CRIs later confirmed are shown in Figure 2. Pus at the catheter site was the most common presentation associated with confirmed CRI (75%), compared to redness at the catheter site (58%), rigors (55%), fever (53%) and chills (53%).

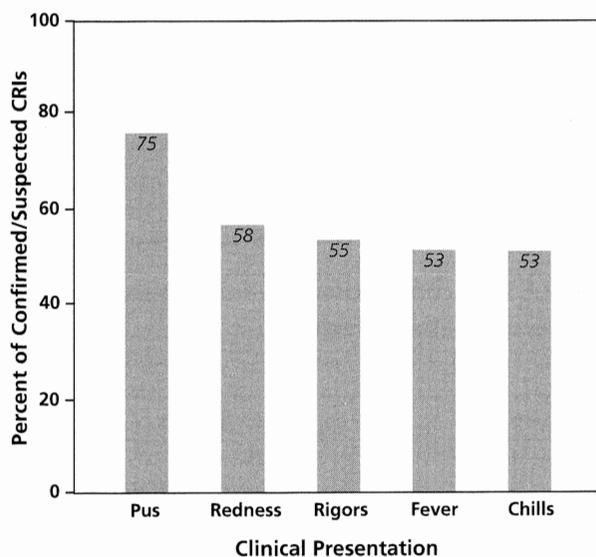
Empiric treatment of the 135 suspected CRIs was initiated with vancomycin in 50 cases (37%), vancomycin and gentamicin in 55 cases (41%), gentamicin alone in 7 cases (5%) and a variety of other antibiotics in the remaining cases. Thus, vancomycin either alone or in combination was used empirically in 105/135 (78%) of suspected CRIs. The most commonly isolated pathogens in the 74 confirmed cases included *S. epidermidis* (47/74, 63.5%), *S. aureus* (23/74, 31%), *E. coli* (5/74, 6.8%), *E. cloacae* (4/74, 5.4%),

FIGURE 1: Incidence of confirmed catheter-related infections in specific catheter locations



Perm = Permanent, Temp = Temporary, S/C = subclavian, IJ = intrajugular, Fem = femoral

FIGURE 2: Incidence of confirmed catheter-related infections with specific presenting signs and symptoms



P. aeruginosa (3/74, 4.1%), and *E. faecalis* (1/74, 1.4%). VRE were not isolated. Sensitivities of these gram-positive and gram-negative organisms to selected antibiotics are shown in Tables 1 and 2.

Antibiotic sensitivities reported in the 74 confirmed cases indicate that isolates of *S. epidermidis* and *S. aureus* were sensitive to antibiotics commonly used to treat gram-positive infections (e.g. cefazolin, cloxacillin, clindamycin) in all but 19 cases. Therefore, 19/105 (18%) of empiric vancomycin used to treat suspected CRIs was supported by laboratory susceptibility data. Vancomycin may also be required in cases of penicillin allergy; however vancomycin was commonly ordered even in the absence of allergies to other antibiotics.

In 20/74 (27%) of cases, vancomycin therapy was continued when organisms were reported susceptible to cefazolin or cloxacillin. Ten of the infections were due to *S. epidermidis*, 5 were due to *S. aureus*, and 5 were mixed infections with both organisms. Vancomycin was continued in 5 cases, despite the culture being sensitive to alternate antibiotics, because of documented penicillin allergy.

DISCUSSION

Catheter-related infections cause significant morbidity and mortality in the hemodialysis population.^{10,11} Although CRIs have been studied extensively in the

intensive care setting (ICU) and in patients receiving total parenteral nutrition (TPN), CRIs in the hemodialysis population are not as well characterized.¹²⁻¹⁴

Our retrospective analysis indicated that 42/177 (24%) of patients treated in our hemodialysis centres over a 24 month period experienced at least one CRI. Depending on several factors, including the location of the catheter, duration of use, rates of nasal carriage of *S. aureus*, and techniques used for catheter care, the reported incidence of catheter-related bacteremia in the literature varies from 2–25%.¹⁵

Some of the variability may be explained by the use of varying definitions of CRI. The CDC criteria used to define a CRI in this study have not been used consistently in previous studies and are not as stringent as those defined by the current Canadian IV guidelines (Health Canada, <http://www.hc-sc.gc.ca>). Current definitions of a “definite intravascular device related bacteremia” require a “single positive peripheral blood culture from a patient with clinical and microbiological data disclosing no other source of the bacteremia, in the presence of a semiquantitative culture of a device segment (proximal or distal), from which the same organism (species, antibiogram) was isolated” (Health Canada, <http://www.hc-sc.gc.ca>). Catheter tip cultures were not consistently obtained during the study period, precluding the opportunity to determine the incidence of bloodstream infections in our study using these criteria. However, we estimate that the incidence of bloodstream infections in our sample would be reduced using these more stringent criteria.

Our results suggest that permanent catheters have a higher rate of infection than temporary catheters (permanent subclavian (88%) versus temporary subclavian (28%)). In addition, temporary femoral catheters showed a lower rate of infection (14%) compared with temporary subclavian catheters (28%), ($\chi^2=3.95$ with 1 df, $p<0.05$). A recent review by the CDC suggests that subclavian catheters used for hemodialysis have elevated bloodstream infection rates compared with

TABLE 1: *S. epidermidis* and *S. aureus* blood culture susceptibilities for documented catheter-related infections.

Organism	Number of susceptible isolates			
	Cefazolin	Vancomycin	Clindamycin	Oxacillin
<i>S. epidermidis</i> (n=46)	19 (41%)	46 (100%)	35 (76%)	21(46%)
<i>S. aureus</i> (n=22)	21(95%)	22 (100%)	22 (100%)	22 (100%)

TABLE 2: *E. coli*; *E. cloacae*, and *P. aeruginosa* blood culture susceptibilities for documented catheter-related infections.

Organism	Number of susceptible isolates				
	Ciprofloxacin	Gentamicin	TMP/SMX	Cefotaxime	Ceftazidime
<i>E. coli</i>	5/5 (100%)	3/5 (60%)	5/5 (100%)	5/5 (100%)	—
<i>E. cloacae</i>	4/4 (100%)	4/4 (100%)	4/4 (100%)	4/4 (100%)	—
<i>P. aeruginosa</i>	3/3 (100%)	3/3 (100%)	—	—	3/3 (100%)

TMP/SMX = trimethoprim / sulfamethoxazole



subclavian catheters used for other indications, e.g. ICU, TPN.¹²⁻¹⁴ However, it is currently unclear whether subclavian hemodialysis catheters have a higher bloodstream infection rate than femoral or intrajugular hemodialysis catheters. Studies over a short duration (5 dialysis sessions/catheter) reported similar low rates of septicemia (<5%) associated with either temporary femoral or temporary subclavian catheter access.^{16,17}

Rates of bloodstream infections are commonly compared based on episodes per 1000 catheter days. Due to limitations of a retrospective analysis and the extent of documentation available, we were not able to determine an accurate measurement of total catheter days. Without an accurate measure of infections per 1000 catheter days, rates cannot be accurately compared using this method, i.e. permanent catheters may have a higher rate of infection compared with temporary catheters in our study because of their long duration of use. Similarly, temporary femoral catheters may have been used for a shorter duration and subsequently appeared to have a lower infection rate than temporary subclavian catheters. Currently, a prospective pilot project by the Canadian Nosocomial Infection Surveillance Program (CNISP) is underway to collect this information and further characterize CRIs.

Fever, chills, rigors and redness at the catheter site in patients with a suspected CRI were associated with confirmed CRI in approximately 50% of cases (Figure 2). Hemodialysis patients frequently experience temperature fluctuations and chills on dialysis which must be distinguished from fever and chills associated with an infectious process.¹⁸ However, pus at the catheter site was associated with a confirmed CRI in 75% of cases.

The organisms isolated from blood cultures were consistent with published literature indicating that gram-positive organisms including *S. epidermidis* and *S. aureus* are most commonly isolated.^{19,20} Forty-one percent of our *S. epidermidis* isolates and 95% percent of our *S. aureus* isolates were reported sensitive to cefazolin. There is some limited data indicating that the *in vitro* sensitivity of *S. epidermidis* to cefazolin does not always correlate well with *in vivo* eradication of the organism.²¹ In addition, the pharmacokinetics of cefazolin are not well studied in the hemodialysis population. Despite these limitations, our institution uses one dose of empiric vancomycin followed by cefazolin in all episodes where *in vitro* sensitivity of the organism to cefazolin has been established. Although vancomycin has an extended half-life in renal failure and may allow dosing every 4-6 days, it should not be used

to complete the course of treatment when the isolated organism is sensitive to other commonly used antibiotics. This approach should help to minimize selective treatment pressures for the development of VRE, especially when the organisms are susceptible to other antibiotics. Our results will be used to assist in drafting prescribing criteria to optimize management of CRIs in our population, including the increased utilization of alternative antibiotics such as cefazolin when appropriate. A second review of vancomycin usage should be conducted to assess the impact of these criteria on future vancomycin usage.

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