Treatment of catheter-related bacteraemia with an antibiotic lock protocol: effect of bacterial pathogen

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Abstract

Background. The standard therapy of dialysis catheter-related bacteraemia involves both systemic antibiotics and catheter replacement. We reported recently that instillation of an antibiotic lock (highly concentrated antibiotic solution) into the catheter lumen after dialysis sessions, in conjunction with systemic antibiotics, can successfully treat many episodes of catheter-related bacteraemia without requiring catheter removal. The present study evaluated whether the likelihood of achieving a cure with this protocol depends on the type of pathogen.

Methods. This was a historically controlled interventional study of an antibiotic lock protocol for the treatment of catheter-related bacteraemia. We analysed prospectively the likelihood of clinical cure (fever resolution and negative surveillance cultures) with an antibiotic lock protocol among patients with dialysis catheter-related bacteraemia. In addition, infection-free catheter survival was evaluated for up to 150 days, and compared with that observed among patients managed with routine catheter replacement.

Results. Overall, the antibiotic lock protocol was successful in 33 of 47 infected patients (70%) with catheter-related bacteraemia. The likelihood of a clinical cure was 87% for Gram-negative infections, 75% for Staphylococcus epidermidis infections, and only 40% for Staphylococcus aureus infections (P = 0.04). The median infection-free catheter survival with the antibiotic lock protocol was longer than that observed among patients with routine catheter replacement (154 vs 71 days, P = 0.02).

Conclusions. The clinical success of an antibiotic lock protocol in eradicating catheter-related bacteraemia while salvaging the catheter is highly dependent on the bacterial pathogen. Thus, the overall success rate in an individual dialysis programme will depend on the relative frequencies of different bacterial pathogens.

Keywords: antibiotic; bacteraemia; dialysis catheter; haemodialysis; infection

Introduction

Bacteraemia is a frequent complication among haemodialysis patients using a tunnelled dialysis catheter [1–6]. K/DOQI guidelines recommend treating catheter-related bacteraemia with systemic antibiotics, as well as catheter replacement [7]. This approach, while effective, requires the patients to undergo burdensome and expensive radiologic procedures. Several investigators have documented a biofilm on the inner surface of most indwelling central vein catheters [8,9], and this biofilm is considered the source of most cases of catheter-related bacteraemia. If the biofilm could be eradicated pharmacologically, it might be possible to treat many patients with catheter-related bacteraemia without replacing the catheter. Instillation of an antibiotic lock (concentrated antibiotic solution with anticoagulant) into the catheter lumen eradicates the biofilm in vitro [10]. Moreover, a few small clinical studies have reported that instillation of antibiotic locks into central vein catheters used for chemotherapy, parenteral nutrition or dialysis can effectively treat catheter-related bacteraemia without requiring catheter replacement [11–13]. On the basis of such studies, an infectious diseases panel recently advocated treatment of uncomplicated bacteraemia due to tunnelled catheters with an antibiotic lock [14].

We reported recently our experience with treatment of dialysis catheter-related bacteraemia using an antibiotic lock, in conjunction with systemic antibiotics. This approach produced a bacteriologic and clinical cure in about two-thirds of cases, thereby obviating the need for catheter replacement [6]. That study did not explore specific factors affecting the likelihood of cure. The goal of the present study was to evaluate prospectively whether the infecting organism affects...
the success rate with an antibiotic lock protocol among patients with catheter-related bacteraemia.

Subjects and methods

Patient population

The University of Alabama at Birmingham (UAB) provides chronic dialysis to approximately 600 in-centre haemodialysis patients. About 20% of the patients dialyse with tunnelled dialysis catheters. Catheters were inserted preferentially in the right internal jugular vein, followed by the left internal jugular vein and the subclavian vein. The catheter exit site was cleaned with a topical iodine solution at the initiation and termination of each dialysis session, and covered by a dry sterile gauze during the interdialytic period. No topical or systemic antibiotic prophylaxis was used in catheter-dependent dialysis patients. All patient hospitalizations, surgical procedures and radiologic procedures were done at UAB Hospital.

Management of dialysis catheter-associated bacteraemia

The antibiotic lock treatment protocol was evaluated prospectively during the study period from 10/1/01 to 3/31/02. All catheter-dependent dialysis patients with fever or chills on dialysis had two sets of blood cultures drawn from a peripheral vein if possible (61% of the time) or from the catheter lumen when a peripheral vein could not be used (39% of the time). Empiric therapy was then initiated with broad-spectrum antibiotics (vancomycin and ceftazidime). Because outpatient dialysis was performed at freestanding facilities without ready access to a hospital or clinical laboratory, it was not possible to perform routine diagnostic studies to evaluate for non-catheter sources of infection. However, the dialysis nurse elicited questions regarding other potential sources of infection (cough, shortness of breath, dysuria, foot infection, diarrhea, etc.), and performed a brief physical examination. In the absence of evidence for an alternate source of infection, it was presumed that the bacteraemia arose from the dialysis catheter.

The clinical antibiotic lock protocol was modified in two ways from the one we described previously [6]. First, our original protocol required the routine administration of gentamicin for empiric Gram-negative coverage. In spite of individualized weight-based dosing of gentamicin, some patients developed aminoglycoside ototoxicity. To alleviate this problem, ceftazidime was substituted for gentamicin as the initial antibiotic for Gram-negative coverage. Secondly, patients with catheter-related bacteraemia due to Enterococcus exhibited a low clinical success rate and high frequency of secondary Candida infections with the original protocol. For this reason, patients whose blood cultures grew Enterococcus were excluded from the antibiotic lock protocol in the current study and referred instead for routine catheter exchange.

In the modified antibiotic lock protocol, patients with suspected dialysis catheter-associated bacteraemia received loading doses of vancomycin (20 mg/kg) and ceftazidime (1 g), followed by maintenance doses of antibiotics during each of the next eight consecutive dialysis sessions. The maintenance dose was 500 mg for vancomycin [15], and 1 g for ceftazidime. Vancomycin was infused during the last hour of dialysis, and ceftazidime was given immediately after completion of the dialysis session. The antibiotics were discontinued if the initial blood cultures had no growth after 5 days, but continued for 3 weeks in patients with positive blood cultures. The antibiotic regimen was modified on the basis of type of pathogen grown from the blood cultures and its antibiotic sensitivities. (The changes usually involved stopping either the vancomycin or ceftazidime, and switching to cefazolin 1 g after each dialysis session when possible [16].) The dialysis catheter was removed promptly if fever or haemodynamic instability persisted 48 h after initiation of antibiotics. Surveillance blood cultures were obtained routinely from the patients a week after completing the antibiotic lock protocol.

Antibiotic lock. We have documented previously the in vitro compatibility of vancomycin (2.5 mg/ml) and cefazolin (5 mg/ml) with heparin (2500 U/ml) when incubated for up to 72 h at 37°C [6]. We have subsequently confirmed the compatibility of cefazidime (5 mg/ml) with heparin under similar conditions. The stability and bioactivity of these three antibiotics in heparin solutions instilled into implantable venous ports has also been reported by others [17,18]. All the antibiotic–heparin locks were prepared by the dialysis nurses from the antibiotic solutions used for systemic administration (Table 1). If the systemic antibiotic was modified on the

Table 1. Preparation of the antibiotic lock solutions

<table>
<thead>
<tr>
<th>Type of lock solution</th>
<th>Volume of solution (ml)</th>
<th>Vanc&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Ceftaz&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Cefazolin&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Heparin&lt;sup&gt;c&lt;/sup&gt;</th>
<th>NS&lt;sup&gt;d&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vancomycin/ceftazidime</td>
<td>1.0</td>
<td>0.5</td>
<td>–</td>
<td>–</td>
<td>0.5</td>
<td>–</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>1.0</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>Cefazidime</td>
<td>–</td>
<td>1.0</td>
<td>–</td>
<td>–</td>
<td>0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>Cefazolin</td>
<td>–</td>
<td>–</td>
<td>1.0</td>
<td>–</td>
<td>0.5</td>
<td>0.5</td>
</tr>
</tbody>
</table>

The antibiotic–heparin lock solutions were prepared from the following solutions used for systemic administration of antibiotics. The final drug concentrations in the antibiotic lock solutions were: vancomycin, 2.5 mg/ml, ceftazidime, 5 mg/ml, cefazolin 5 mg/ml and heparin, 2500 U/ml.

<sup>a</sup>Vancomycin, 5 mg/ml (in NS).
<sup>b</sup>Ceftazidime and cefazolin, 10 mg/ml (in NS).
<sup>c</sup>Heparin, 10 000 U/ml.
<sup>d</sup>NS, normal (0.9%) saline.
basis of culture sensitivities, the antibiotic lock was modified accordingly. The antibiotic locks were instilled into both lumens of the dialysis catheter after each dialysis session, and withdrawn immediately before the next dialysis session. Standard heparin locks were resumed, once the course of systemic antibiotics had been completed.

Data analysis. The UAB Institutional Review Board approved review of the patients’ medical records for research purposes. Two full-time Access Coordinators (D.C. and L.B.) tracked all blood culture reports, use of antibiotics, and patient and catheter events, and maintained this information in a prospective, computerized database [19]. We defined a protocol success as catheter salvage with resolution of symptoms within 48 h of initiation of the antibiotic lock protocol and negative surveillance cultures 1 week after completing the antibiotic regimen. A protocol failure was defined as: (i) persistent fever or haemodynamic instability > 48 h after initiation of the antibiotic lock protocol or (ii) post-treatment surveillance cultures positive for any organism. Catheters removed electively due to a mature access or due to catheter malfunction before completion of the antibiotic lock protocol were excluded from this analysis. In addition, we compared the likelihood of protocol success or failure for patients with catheter-related bacteraemia caused by Gram-negative rods, Staphylococcus epidermidis and Staphylococcus aureus, using the \( \chi^2 \) test.

To evaluate the longer-term success rate of the antibiotic lock protocol, we also evaluated episodes of bacteraemia or distant metastatic infections in the patients for up to 150 days after the initial bacteraemic episode. Infection-free catheter survival was modelled using survival analysis techniques. Patients whose catheter was electively removed (due to a mature access or catheter malfunction) or who died of a non-infectious cause with a functioning catheter were considered censored. Catheter survival with this protocol was compared with that reported previously from our institution for all patients who had catheter-related bacteraemia diagnosed in 1997–1998. This non-concurrent, historical patient group was managed with routine catheter replacement [20]. The control group had never been treated with an antibiotic lock protocol. There was no patient overlap between the group treated with the antibiotic lock and the historical controls. Survival distributions were plotted for the two treatment groups using Kaplan–Meier curves, and compared with each other by the log rank test.

Results

Catheter-related bacteraemia was suspected clinically on 141 occasions in our haemodialysis population during the study period. The blood cultures grew an organism in 83 of the episodes, for an overall dialysis catheter-related bacteraemia rate of 4.6/1000 patient-days. The likelihood of positive blood cultures tended to be higher if the patient presented with chills (with or without fever) than if the patient had fever alone (72 vs 54%, \( P = 0.07 \)). Nineteen patients, or 23% of patients with catheter-related bacteraemia, had a concurrent exit site infection, which grew the same organism as the blood culture. A single Gram-positive coccus grew in 64% of the cases, a single Gram-negative organism grew in 20% of the cases, and 16% of positive cultures yielded two or more organisms (Table 2). Of the 97 pathogens grown from blood cultures, 72% were Gram-positive cocci, and 28% were Gram-negative rods. About 79% of the Staphylococcal species were methicillin-resistant. None of the Gram-positive infections was vancomycin-resistant. Among the 25 episodes with Gram-negative bacteraemia, the bacteria were sensitive to ceftazidime in 92% of the cases; two infections with Pseudomonas were ceftazidime-resistant.

Of the 83 episodes of catheter-related bacteraemia, 15 were excluded from the protocol by design because their blood cultures grew Enterococcus, and the patients referred for routine catheter exchange. The remaining 68 patients with other bacterial pathogens were initiated on the antibiotic lock protocol with systemic vancomycin and ceftazidime, in conjunction with a vancomycin-ceftazidime antibiotic lock (Table 1). The demographics of the patients treated with the antibiotic lock protocol are summarized in Table 3. Fifteen patients (or 22% of the total) had experienced one or more previous episodes of catheter-related bacteraemia (eight with Gram-negative rods, nine with Staphylococcus epidermidis, and one with S.aureus). The infected catheter was placed in the right internal jugular vein in 69%, the left internal jugular vein in 22%, and the subclavian vein in 9% of the study patients.

Among the 68 patients with catheter-related bacteraemia enrolled in the antibiotic lock protocol, the outcome was indeterminate in 21 patients, either because of elective catheter removal due to a mature

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Catheters (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single organism</td>
<td>70</td>
</tr>
<tr>
<td>Single Gram-positive cocci</td>
<td>53</td>
</tr>
<tr>
<td>Staphylococcus</td>
<td>44</td>
</tr>
<tr>
<td>MRSE</td>
<td>29</td>
</tr>
<tr>
<td>MSSE</td>
<td>0</td>
</tr>
<tr>
<td>MRSA</td>
<td>5</td>
</tr>
<tr>
<td>MSSA</td>
<td>10</td>
</tr>
<tr>
<td>Enterococcus</td>
<td>7</td>
</tr>
<tr>
<td>Other</td>
<td>2</td>
</tr>
<tr>
<td>Single Gram-negative rods</td>
<td>17</td>
</tr>
<tr>
<td>Klebsiella</td>
<td>2</td>
</tr>
<tr>
<td>Enterobacter</td>
<td>6</td>
</tr>
<tr>
<td>Serratia</td>
<td>1</td>
</tr>
<tr>
<td>E.coli</td>
<td>3</td>
</tr>
<tr>
<td>Pseudomonas</td>
<td>4</td>
</tr>
<tr>
<td>Haemophilus</td>
<td>1</td>
</tr>
<tr>
<td>≥2 organisms</td>
<td>13</td>
</tr>
<tr>
<td>Two Gram positive</td>
<td>5</td>
</tr>
<tr>
<td>Two Gram negative</td>
<td>2</td>
</tr>
<tr>
<td>One Gram positive + one Gram negative</td>
<td>5</td>
</tr>
<tr>
<td>One Gram positive + two Gram negative</td>
<td>1</td>
</tr>
</tbody>
</table>

MRSE, methicillin-resistant St.epidermidis; MSSE, methicillin-sensitive St.epidermidis; MRSA, methicillin-resistant S.aureus; MSSA, methicillin-sensitive S.aureus.
fistula or graft, catheter replacement due to malfunction, non-infectious death, or transfer to a non-participating dialysis unit (Figure 1). Of the remaining 47 episodes of catheter-related bacteraemia, the protocol was successful (the patient remained asymptomatic with negative surveillance cultures and the catheter was salvaged) in 33 cases (70%), and failed in 14 cases (30%). The likelihood of protocol success was similar between those patients with a previous episode of catheter-related bacteraemia and those without a previous episode (85% vs 69%, $P = 0.28$ by the $\chi^2$ test).

Six of the study patients had an infection with human immunodeficiency virus (HIV). Two of these patients grew *S. epidermidis* from their blood cultures, one grew *S. aureus*, two grew a Gram-negative rod, and one grew two different pathogens. The antibiotic lock protocol was successful in two patients, failed in one, and was indeterminate in three (one death, one transfer to an outside facility and one elective catheter removal).

The protocol failed in seven patients due to fever persisting longer than 48 h after antibiotic initiation, and in seven patients who became asymptomatic but had positive surveillance cultures 1 week after completing the antibiotic lock protocol (Figure 1). The patients with positive surveillance cultures grew a bacterial pathogen in six cases, and *Candida* in one patient. In five cases, the same organism grew from the initial and
surveillance cultures, indicating a bacteriologic failure (three had *S.epidermidis*, one had *S.aureus* and one had *Pseudomonas*). In the other two cases (one with *S.epidermidis* and one with *Enterobacter*) the organism grown from the surveillance cultures differed from the initial organism, suggesting a new infection. The overall frequency of secondary *Candida* infections was \~2% in the patients who completed the antibiotic lock protocol.

The success rate of the protocol differed substantially by type of organism, being 87% for Gram-negative infections, 75% for *S.epidermidis*, but only 40% for *S.aureus* infections (\(P=0.04\) for the comparison between the three pathogens) (Table 4). The clinical failures among patients with *S.aureus* infections were largely due to patients with persistent fever. Six patients with polymicrobial catheter-related bacteraemia (two with two different Gram-negative rods, two with *S.epidermidis* and a Gram-negative rod, one with *S.aureus* and a Gram-negative rod and one with *S.aureus* and *S.epidermidis*) were treated with the antibiotic lock protocol. Four of these patients had a protocol success, one failed and one was indeterminate, yielding an 80% success rate for this small sample.

Serious infectious complications occurred in three of 47 patients (6.4%) with catheter-associated bacteraemia who completed the antibiotic lock protocol. These complications included septic shock (one patient), empyema (one patient) and an infected superior vena cava thrombus (one patient). There were two additional serious complications among the 21 patients enrolled in the antibiotic lock protocol who had incomplete follow-up (Figure 1): one patient had septic shock and one had septic arthritis. Thus, the overall rate of serious complications among all 68 patients enrolled in the antibiotic lock protocol was 7.3%. Among the patients with serious complications, three had blood cultures positive for *S.aureus*, one grew *S.epidermidis* and one grew *Klebsiella*.

To evaluate the long-term results with the antibiotic lock protocol, we plotted infection-free catheter survival for all 68 patients enrolled in the antibiotic lock protocol. These outcomes were compared with those observed previously in a group of 69 non-concurrent control patients from our institution whose catheter-related bacteraemia was managed with routine catheter replacement. Although this was not a randomized control group, the patients in the two treatment groups were similar in their age, sex, race and frequency of diabetes (Table 3). The distribution of pathogens was similar between the two groups, except that *S.epidermidis* infections were more common in the group treated with the antibiotic lock protocol. The median catheter survival without infection following the initial episode of catheter-related bacteraemia was about twice as long among the group treated with the antibiotic lock protocol, as compared with the group treated with routine catheter replacement (154 vs 71 days, \(P=0.02\)) (Figure 2).

### Discussion

During the study period we documented catheter-related bacteraemia in our haemodialysis population at a rate of 4.6/1000 days. This infection rate is comparable with the 5.4/1000 patient-days observed previously at our centre [6], and at the higher range of 2–5.5/1000 patient-days reported from other institutions [1–5]. The modified antibiotic lock protocol was successful (absence of symptoms and negative surveillance blood cultures) in about two-thirds of the patients in the current study, without requiring catheter replacement. The protocol failed in the remainder, either because of persistent fever or due to positive surveillance blood cultures. The success rate varied markedly according to the type of organism, being quite good for Gram-negative and *S.epidermidis* infections, and quite poor for *S.aureus* infections (Table 4). Importantly, the protocol was frequently successful in high-risk groups, including those with previous catheter-related bacteraemia, polymicrobial infections or co-existing HIV infection. Failure to eradicate some catheter infections with the antibiotic lock protocol suggests that certain bacterial strains are refractory to even high bactericidal antibiotic concentrations when the bacteria are incorporated into a biofilm [21].

Some clinical failures could have been due to inappropriate antibiotics. In fact, two patients with ceftazidime-resistant *Pseudomonas* infections would fall into that category. Another possibility is that the protocol failed in some patients due to subtherapeutic antibiotic levels. We did not measure serum vancomycin levels in our patients, as this test is not readily available at the freestanding dialysis facilities.

### Table 4. Outcome of catheter-related bacteraemia treated with the antibiotic lock protocol, sorted by type of organism

<table>
<thead>
<tr>
<th>Type of organism</th>
<th>Infections (n)</th>
<th>Success (n) (%)</th>
<th>Failures (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Persistent fever</td>
<td>Positive survival cultures</td>
</tr>
<tr>
<td>Gram negative</td>
<td>15</td>
<td>1 (87%)</td>
<td>1</td>
</tr>
<tr>
<td><em>S.epidermidis</em></td>
<td>16</td>
<td>1 (75%)</td>
<td>1</td>
</tr>
<tr>
<td><em>S.aureus</em></td>
<td>10</td>
<td>4 (40%)</td>
<td>5</td>
</tr>
</tbody>
</table>

Analysis of outcomes was restricted to episodes in which the initial blood cultures grew a single organism. \(P=0.04\) by \(\chi^2\) test for the comparison between the pathogens.
Moreover, the pharmacokinetics of vancomycin are complex in dialysis patients, with negligible elimination between dialysis sessions, and variable removal during dialysis sessions. However, a previous investigation in dialysis patients has documented therapeutic vancomycin levels in most patients receiving the doses administered in the current study [15]. Persistent fever at 48 h may have been too restrictive a criterion for clinical failure in some patients, especially if they had S.aureus bacteraemia, but was chosen to optimize patient safety. Finally, some patients grew a different organism from their surveillance cultures than from their initial blood cultures, suggesting a new, rather than persistent, infection. All these factors may have resulted in some patients being erroneously classified as clinical failures. Thus, the success rate of the antibiotic lock may be higher than that obtained using our conservative definition.

In our previous vancomycin–gentamicin antibiotic lock protocol we observed secondary Candida infections in the surveillance cultures of 14% of patients enrolled in the protocol [6]. The likelihood of a secondary Candida infection depended greatly on the pathogen: it was 42% among patients whose initial cultures grew Enterococcus, but only 8% for infections with all other pathogens. Because attempts to salvage the catheter in Enterococcus infections resulted in a high rate of Candida infection, we excluded Enterococcus infections from the antibiotic lock protocol in the current study. As a result, there was a gratifying reduction in secondary Candida infections to just 2% in the present study.

It is not possible to definitively exclude the possibility that some episodes of bacteraemia were unrelated to a catheter infection. Ideally, we would have liked to perform an extensive diagnostic evaluation in each febrile patient to exclude alternative sources of infection. In practice, this is not usually feasible, because the patients dialyse in freestanding units that are geographically remote from a hospital or clinical laboratory. The dialysis nurses screened symptomatic patients for potential sources of infection by a focused history and physical examination, both at the time of the febrile illness, and on subsequent dialysis sessions thrice weekly. Thus, it appears unlikely that the bacteraemia in this patient group was due to an alternate source.

There are four potential clinical management strategies for patients with catheter-related bacteraemia. Treatment with systemic antibiotics alone cures the infection in only ~30% of patients [1–3,5,22]. Removal of the infected catheter with delayed placement of a new tunnelled catheter is more effective, but requires multiple access procedures, including use of a temporary dialysis catheter. Exchange of the infected catheter over a guidewire in patients whose fever resolves within 48–72 h of initiation of systemic antibiotics reduces the burden of access procedures required [4,5,20,23]. In the two largest series reporting on this approach, the patients achieved an 81–88% infection-free catheter survival at 45 days, after excluding patients with persistent fever [4,5]. In the current study the use of an antibiotic lock protocol resulted in a 75% infection-free catheter survival at 45 days. However, after exclusion of those patients in whom the protocol failed due to persistent fever (seven of 68 patients, or 10% of the total), the catheter survival would increase to 85%, quite comparable with the outcomes with catheter exchange. The chief virtue of the antibiotic lock strategy is that it permits catheter salvage in the
majority of patients, with selective catheter exchange in the subset in whom the protocol fails.

The relative distribution of pathogens in patients with catheter-related bacteraemia varies considerably among different reports. In four recent series [3–5,23] the frequency of S. aureus ranged from 13 to 44%, S. epidermidis from 14 to 31%, Gram-negative rods from 17 to 44%, and Enterococcus from 5 to 13%. Only two previous reports evaluated the effect of the bacterial organism on the outcome. Using systemic antibiotics alone, Marr et al. observed a 23% success rate with Gram-positive cocci and a 50% success rate with Gram-negative rods [3]. Using catheter exchange, Saad reported an 83% success rate with Gram-positive cocci and 100% success rate with Gram-negative rods [5]. Unfortunately, both studies lumped together all infections due to a Gram-positive coccus. Differences in pathogen frequencies among series may contribute to differences in cure rates of catheter-related bacteraemia. Thus, for example, the higher frequency of S. epidermidis bacteraemia in the current study (Table 3) may account for the superior infection-free catheter survival as compared with the historical control group (Figure 2).

Serious systemic complications occurred in 7% of cases treated with the vancomycin–ceftazidime antibiotic lock protocol. The close outpatient follow-up of haemodialysis patients thrice weekly by dialysis nurses largely precludes missing metastatic infections. The reported frequency of serious complications with dialysis catheter-related bacteraemia ranges widely, from 3 to 22%, in several recent series [3–6,20]. Some publications are retrospective and others prospective, and they are not consistent in their definition of serious complication. Nevertheless, the frequency of serious complications in the present report is within the expected range, so it does not appear that attempting to salvage the catheter with an antibiotic lock protocol increases the risk of serious complications from catheter-related bacteraemia. Serious complications occurred more frequently with infections due to S. aureus (20%), as compared with those due to S. epidermidis (3.5%) or Gram-negative rods (6%). This finding is in keeping with the high virulence of S. aureus.

The high frequency of catheter-related bacteraemia in haemodialysis patients necessarily requires frequent administration of antibiotics in this patient population. Furthermore, vancomycin is used commonly, because many of the Staphylococcus infections are methicillin-resistant. Unfortunately, this has led to the emergence of vancomycin-resistant S. aureus in the haemodialysis population [24,25]. Given that there will always be a subpopulation of haemodialysis patients with catheters, there is an urgent need for effective chemoprophylaxis of catheter-related bacteraemia that does not involve the use of antibiotics.

In conclusion, our modified vancomycin–ceftazidime antibiotic lock protocol was successful in about two-thirds of episodes of dialysis catheter-associated bacteraemia without requiring replacement of the infected catheter. The success rate was quite high when the infection is due to a Gram-negative rod or S. epidermidis, but disappointingly low with S. aureus. The overall success rate of implementing an antibiotic lock protocol for management of dialysis catheter-related bacteraemia in an individual dialysis programme will depend on the relative frequencies of different bacterial pathogens.

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Conflict of interest statement. None declared.

References
22. Pourchez T, Moriniere P, Fournier A, Pietri J. Use of Perm cath (Quinton) catheter in uremic patients in whom the creation of conventional vascular access for hemodialysis is difficult. Nephron 1989; 53: 297–302

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