Bacterial colonization of chronic hemodialysis catheters: Evaluation with endoluminal brushes and heparin aspirate

M. KOCH¹, D. COYNE¹, J. HOPPE-BAUER², T. M. VESELY³

¹ Department of Internal Medicine, Division of Nephrology, Washington University School of Medicine
² Department of Laboratory Medicine, Washington University School of Medicine
³ Mallinkrodt Institute of Radiology, Washington University School of Medicine, St. Louis - USA

ABSTRACT: Tunneled catheters serve as interim access during maturation of a graft or fistula, or as a permanent vascular access in those patients who have exhausted their traditional access sites. However, bacteremia rates are high in patients with chronic catheters and indiscriminate removal of catheters during bacteremia increases morbidity and costs. A method to identify whether a catheter was colonized with the offending bacteria, without requiring catheter removal is desirable.

We compared endoluminal brushing and heparin aspiration, to detect catheter colonization, in 24 asymptomatic patients undergoing elective tunneled hemodialysis catheter removal. The incidence of catheter colonization was highly correlated with catheter duration of ≥ 30 days (p=0.03). Staphylococcus epidermidis represented 68% of the organisms isolated. No other organism accounted for more than 7% of the total. Fifteen (62.5%) of the 24 catheters had positive cultures. Eleven of the catheters were positive by culture of heparin aspirate and eight were positive by endoluminal brush. Only four of the catheters were positive by both methods. The arterial lumen was more likely to have positive cultures than the venous lumen using either method.

In this prospective investigation of tunneled hemodialysis catheters in asymptomatic patients we have demonstrated that a heparin aspirate sample is more likely to detect colonizer catheter than a sample obtained using an endoluminal brush. Furthermore, 75% of catheters present for more than 30 days were colonized. Further study is needed to determine if the heparin aspirate method could be used in patients with bacteremia to accurately identify catheters that need removal. (The Journal of Vascular Access 2002; 3: 38-42)

KEY WORDS: Hemodialysis, Central venous catheter, Bacterial colonization, Bacteremia

INTRODUCTION

Tunneled catheters continue to serve an important role as a vascular access for hemodialysis. Nearly 20% of all hemodialysis patients have a tunneled catheter as their vascular access two months after initiating hemodialysis (1). These catheters function as either an interim access during maturation of a graft or fistula, or as a permanent vascular access for those patients who have exhausted their traditional access sites.

Due to the inevitable problems and complications associated with chronic catheters, the National Kidney Foundation’s Disease Outcome Quality Initiative guidelines discourage the use of these devices as a permanent vascular access for hemodialysis. These problems include poor function with suboptimal hemodialysis treatment, thrombosis or injury of the central veins, and catheter-related infections. Although all of these complications are detrimental, catheter-related infections can be the most devastating and life-threatening. Catheter-related infections can be divided into several different categories based upon the location...
of the infection and associated clinical symptoms. Types of infections include exit site infections, tunnel infections, bacteremia, sepsis, and metastatic infection. Two recent studies demonstrated episodes of bacteremia occurring at rates of 3.9 and 5.5 per 1000 catheter days in tunneled hemodialysis catheters (2, 3). The appropriate management of catheter-related bacteremia continues to be a topic of debate. In many instances the catheter is assumed to be the source of infection and is immediately removed. However, in the growing number of patients with limited sites for vascular access, a policy of immediately removing all potentially infected catheters can have serious long-term repercussions. Therefore, clinical management should be based upon the results obtained following evaluation of the catheter as the source for the clinical infection.

An ideal method for the evaluation of a tunneled catheter as a source of infection would be rapid, sensitive, specific, inexpensive, and would not require removal of the catheter unnecessarily. Currently there is controversy regarding the optimal method to evaluate a catheter as a source of clinical infection. A common clinical practice is to remove the catheter and culture the tips. However, despite a high index of suspicion, the results from catheter tip cultures are not always consistent with those obtained from the patient’s peripheral blood (4). By requiring culture of the catheter tips the removal of the catheter may be premature. Therefore an accurate and sensitive method of evaluating the catheter that does not require removal of the catheter is desirable.

All of the current methods to evaluate the catheter as the source of infection have limitations. It is our belief that endoluminal samples obtained from the suspected catheter would be useful when evaluating the source of bacteremia or sepsis. This is especially true when the catheter has been in place for a prolonged period of time.

This investigation was performed to compare two different techniques for obtaining bacterial samples from the internal surface of tunneled hemodialysis catheters in asymptomatic patients. One technique utilized an endoluminal brush and the other involved aspiration and culture of the heparin lock solution. The use of the endoluminal brush has recently been described as both sensitive and specific in the evaluation of catheter related sepsis (5). The samples obtained using the two techniques were quantitatively cultured using standard microbiological methods. The data was analyzed to determine the incidence of bacterial colonization and to compare the two sampling techniques.

METHODS

Our institutional review board approved this prospective clinical investigation. From August 2000 to March 2001 all asymptomatic patients who underwent elective removal of a tunneled hemodialysis catheter were included in the study. The indication for removal was that the catheter was no longer needed as a vascular access for hemodialysis.

An experienced interventional radiologist performed the hemodialysis catheter removal and obtained the samples for culture in the angiography suite. The catheter and the skin exit site on the chest wall were cleaned and draped using standard sterile technique. Following infiltration with 1% lidocaine the catheter cuff was removed using blunt dissection. The catheter was then transferred to a sterile table and the catheter hubs were sprayed with 70% isopropyl alcohol. Using a syringe, one milliliter of the heparin lock solution was separately withdrawn from the arterial and venous lumens and transferred to two microbiological culture containers. Although each lumen contained 1.8 to 2.3 ml of heparin lock solution, only one milliliter of fluid was collected to avoid the inclusion of blood in the sample. After regloving, an endoluminal brush (FAS Medical Limited, United Kingdom) was inserted into the arterial lumen and advanced towards the distal end of the catheter. The brush was removed and the tip of the brush was then cut and placed into a culture tube. The same brushing procedure was repeated for the venous lumen.

All four samples, two from each catheter lumen, were sent to the microbiology laboratory for quantitative cultures and microbial identification. The plate culture method involved adding one milliliter of sterile phosphate buffered saline to the vial holding the endoluminal brush tip. The solution was then vortexed for 15 seconds. Ten micro liters of this solution were then transferred to a blood agar plate and 100 micro liters were transferred to a second blood agar plate. The solution was then spread over the surface of the plate using a sterile plastic spreader. The same culturing procedure was repeated using the heparin aspirate sample. The culture plates were incubated at 37 degrees Celsius and were examined for growth of bacteria and yeast at 24 and 48 hours. For our analysis the cultures were considered positive if ≥ 100 colony-forming units/ml were present.

Statistical analysis was performed using SigmaStat statistical software version 2.03 (SPSS Inc. San Rafael, CA). Statistical correlations were assessed using the Spearman rank order correlation test.
RESULTS

Twenty-four asymptomatic patients with tunneled hemodialysis catheters were prospectively enrolled in this investigation. All 24 patients had an Ash Split catheter (Med Comp, Harleysville, PA) as their tunneled hemodialysis catheter. The average duration of catheter placement was 97 days (range 9 to 216 days). A total of 96 endoluminal samples were sent for quantitative culture. Fifteen (62.5%) of the 24 catheters had positive cultures. Eleven of the catheters were positive by culture of the heparin aspirate and eight were positive by endoluminal brushing. Only four of the catheters were positive by both methods (Tab. I). Four of the 11 catheters with a positive heparin aspirate culture were positive from both the arterial and venous lumens (Tab. II). Only one of the 8 catheters with a positive brushing culture was positive from both the arterial and venous lumens (Tab. III). Patients with positive cultures by any method were highly correlated with a catheter duration ≥30 days (p=0.03). All cultures were negative in the four patients with catheter duration less than 30 days. Staphylococcus epidermidis represented 68% of the organisms isolated. No other organism accounted for more than 7% of the total and these did not differ significantly between the aspirate and brushing cultures. Two of the heparin aspirate samples showed mixed growth and Staphylococcus epidermidis was present in both. Of the nine remaining catheters with positive heparin aspirate cultures, Klebsiella was present in one while the remaining eight catheters had Staphylococcus epidermidis. One of the endoluminal brushing cultures showed mixed growth and included Staphylococcus epidermidis. Again in only one catheter was an organism (Corynebacterium) other than Staphylococcus epidermidis present without mixed growth.

DISCUSSION

Infectious complications are common in patients with tunneled hemodialysis catheters. Electron microscopy has revealed that the external surface of a central venous catheter undergoes rapid bacterial colonization soon after insertion (6). Conversely, bacterial colonization of the endoluminal surface predominates after 30 days and appears to precede episodes of catheter related bacteremia (7). Previous studies using blood cultures drawn through hemodialysis catheters have demonstrated that catheter colonization occurs by 16 weeks with a mean time to colonization of 27 days and a range of 5 to 126 days (8). This is also consistent with the data from our study, where none of the catheters in place for less than 30 days had positive cultures using either the heparin aspirate or endoluminal brushing methods. Several methods have been described to determine if a central venous catheter is the source for a systemic infection while maintaining catheter placement. One method is to compare the results of quantitative cultures; one sample obtained from the catheter lumen and another sample obtained from the peripheral blood (9). A variation of this method, termed differential time to positivity, compares the time for a culture drawn through the catheter to turn positive to the time it takes for the peripheral blood culture to turn positive. This method has been reported to be as accurate but less expensive than quantitative culture methods (10). The gram stain and acridine orange leukocyte cytospin test has demonstrated excellent sensitivity and specificity in evaluating the

<table>
<thead>
<tr>
<th>TABLE I - POSITIVE AND NEGATIVE CULTURES BY HEPARIN ASPIRATE (HASP) AND ENDOLUMINAL BRUSHING (ELB), ARTERIAL AND VENOUS</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=24 Hasp negative</td>
</tr>
<tr>
<td>ELB negative</td>
</tr>
<tr>
<td>ELB positive</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>TABLE II - POSITIVE HEPARIN ASPIRATE CULTURES, ARTERIAL AND VENOUS</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=24 Hasp arterial negative</td>
</tr>
<tr>
<td>Hasp venous negative</td>
</tr>
<tr>
<td>Hasp venous positive</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>TABLE III - POSITIVE ENDOLUMINAL BRUSHING CULTURES, ARTERIAL AND VENOUS</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=24 ELB arterial negative</td>
</tr>
<tr>
<td>ELB venous negative</td>
</tr>
<tr>
<td>ELB venous positive</td>
</tr>
</tbody>
</table>
internal catheter lumen for the presence of bacteria and yeast. However, this test is sometimes limited by the inability to draw blood through an occluded catheter lumen (11).

Other microbiological methods, such as the Maki roll technique (external lumen culture) or the Cleri flush (internal lumen culture), require catheter sacrifice and have a high sensitivity but a low specificity (11). False positive cultures can occur, especially with methods that culture the external lumen, as this can be contaminated upon catheter removal (5).

Current methods for evaluating a catheter as a source of systemic infection require several days to obtain the results of the microbiological tests. Immediate decisions regarding appropriate treatment must be made based on the clinical context. The endoluminal brush and heparin aspirate cultures obviously have the same limitation of waiting for the culture results.

The endoluminal brush and the heparin aspirate methods have the potential to satisfy most of the desired criteria for assessment of a catheter as a source of systemic infection. Using either of these two methods, the endoluminal samples are easily obtained and do not require catheter removal. Heparin aspirate cultures can be obtained without the use of special equipment or procedures and therefore are relatively inexpensive. The endoluminal brush method has the added expense of both the brushing supplies and the procedure itself, usually performed in the interventional radiology department.

The predominance of *Staphylococcus epidermidis* in our study catheters is consistent with other studies reporting the results of blood cultures obtained from tunneled central venous catheters (8, 12). Although we defined a positive culture as one that had $\geq 100$ colony forming units, this value may vary depending upon the specific microbiological methods used to perform the quantitative cultures. In our investigation, the heparin aspirate sample was more likely to have a positive culture result than the samples obtained using the endoluminal brush. However, there was significant discordance with respect to the results using these two methods (Tab. I). The reason for this discrepancy is unclear. The endoluminal brushing method utilized in this study was in accordance with the recommendations of the manufacturer. However, inadequate biofilm sampling with the brush remains a possible explanation for the discrepancy. In theory, disruption of the biofilm by the endoluminal brush should have obtained a larger number of bacteria. While the heparin aspirate cultures would not be expected to obtain bacteria present in the biofilm, the endoluminal brush would have the potential to obtain bacteria present in the biofilm as well as bacteria present in the intraluminal fluid. It is possible that bacteria residing in the biofilm may not be as viable for growth in culture and that the bacteria cultured by heparin aspirate may represent more viable organisms that are more likely to grow in culture medium.

The release of significant numbers of proliferating bacteria from the biofilm into the heparin lock solution may not occur until a critical mass of organisms is present. If the majority of the positive cultures obtained by the endoluminal brush actually originate from the endoluminal fluid rather than from the biofilm, then the increased likelihood of obtaining positive cultures via heparin aspirate sampling may relate to the volume of luminal fluid obtained by heparin aspirate compared to endoluminal brushing.

Interestingly, the arterial lumen was more likely to have positive cultures than the venous lumen using either the heparin aspirate or the endoluminal brush method. The samples obtained from the venous lumen by either method provided only two positive cultures. In these two patients catheter colonization would not have been detected using samples from only the arterial lumen. It is unclear why this occurred, but it is of interest when evaluating studies comparing one culture method to the other. The arterial lumen was more likely to have positive cultures than the venous lumen.

Catheter colonization usually precedes the development of catheter-related sepsis (12). Surveillance cultures with the goal of intervening through catheter exchange or instillation of intraluminal antibiotic solutions (“antibiotic locks”) prior to the development of catheter related sepsis have been proposed. Antibiotic lock solutions provide a much higher intraluminal concentration of antibiotics than systemic administration and are a potential means of catheter salvage. However, the use of intraluminal antibiotics may not be effective if the bacteria within the endoluminal biofilm are metabolically inactive. Furthermore, the biofilm layer provides an effective barrier against antibiotic penetration (13, 14).

In this prospective investigation of chronic hemodialysis catheters in asymptomatic patients we have demonstrated that a heparin aspirate sample is more likely to detect catheter colonization than a sample obtained using an endoluminal brush. Furthermore, we have demonstrated that 75% of
catheters present for more than 30 days were colonized. If heparin aspirates can demonstrate catheter colonization with a reasonable degree of sensitivity and specificity, then this simple and inexpensive method could be used to prevent unnecessary catheter removal.

REFERENCES