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Major article

Usefulness of endoluminal catheter colonization surveillance cultures to reduce catheter-related bloodstream infections in hemodialysis

Patricia Brañas PhD [a], Enrique Morales MD [b], Francisco Ríos MD [c], Francisca Sanz MD [a], Eduardo Gutiérrez MD [b], Nuria Quintanilla MD [c], M. Angeles Orellana MD, PhD [a], Mercedes Sánchez MD [c], Almudena Rodríguez-Aranda PhD [a], Fernando Chaves MD, PhD [a,*]

[a] Department of Clinical Microbiology, Hospital Universitario 12 de Octubre, Madrid, Spain
[b] Department of Nephrology, Hospital Universitario 12 de Octubre, Madrid, Spain
[c] Centro de Diálisis San Luciano, Madrid, Spain

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Background: To evaluate the use of surveillance cultures (SCs) to prevent catheter-related bloodstream infections (CRBSIs) in asymptomatic hemodialysis (HD) patients.

Methods: In 2011-2012, we conducted a prospective study of HD patients with tunneled cuffed central venous catheters (TCCs). Colonization of the catheter lumen was assessed every 15 days by inoculating ~5 mL endoluminal blood into aerobic culture bottles. Individual patients were triaged based on SC results: group 1 (negative); group 2 (coagulase-negative *Staphylococcus* [CoNS] with time-to-positivity (TTP) >14 hours); group 3 (CoNS with TTP ≤14 hours); and group 4 (any microorganism other than CoNS and any TTP).

Results: We studied 104 patients (129 TCCs). Median follow-up was 262.5 days (interquartile range [IR], 135.0-365.0). A total of 1,734 SCs were collected (median, 18 per patient; IR, 10.0-24.0), of which 1,634 (94.2%) were negative (group 1) and 100 (5.8%) were positive (group 2: 79; group 3: 12, group 4: 9). In groups 2 and 3, 19 TCCs required antibiotic lock therapy (ALT). In group 4, all patients received intravenous therapy and ALT. Under this protocol, there were 0.27 episodes of CRBSI per 1,000 catheter days compared with 1.65 ($P < .001$) prior to its implementation.

Conclusion: SCs based on easily accessible samples proved useful in triaging HD patients at a high risk of infection.

Hemodialysis (HD) requires repeated access to systemic circulation, preferably via arteriovenous fistulas or grafts. However, for a variety of reasons, including old age and comorbidities, the proportion of patients who undergo HD with a tunneled central venous catheter (TCC) is growing, and these patients are at increased risk of infection.[1-3]

Colonization intraluminal surface of the catheter occurs in a high percentage of HD cases.[4] Endoluminal colonization is a step in the pathogenesis of catheter-related bloodstream infections (CRBSIs) and precedes many symptoms of peripheral bacteremia and sepsis.[5] The microorganisms adhere to the catheter material and form biofilms, allowing sustained infection and hematogenous dissemination.[6] Coagulase-negative *Staphylococcus* (CoNS) and *Staphylococcus aureus* are frequently reported in these infections.[7,8]

CRBSI is associated with high morbidity and treatment cost and represents the second most common cause of death in the HD population.[9] The incidence of CRBSI in HD ranges between 0.6 and 6.5 episodes per 1,000 catheter days.[10] Measures have recently been introduced to decrease CRBSI rates, including review of protocols for connection and disconnection of lines and adoption of universal hygiene precautions in nursing care.[11,12] Antimicrobial

* Address correspondence to Fernando Chaves, MD, PhD, Servicio de Microbiología Clínica, Hospital Universitario 12 de Octubre, Avenida de Córdoba s/n, Madrid 28041, Spain.
E-mail address: fernando.chaves@salud.madrid.org (F. Chaves).

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lock therapy (ALT) at the end of each HD session has also led to lower rates of infection,[13] although continuous interdialysis ALT has been shown to increase the prevalence of antibiotic-resistance in *S aureus* and other microorganisms.[14]

Exit-site surveillance cultures have been investigated in several studies as part of catheter-care protocol. However, the high false-positive rates make to discourage it as a CRBSI preventive strategy.[15] Few studies have examined the usefulness of endoluminal surveillance culture (SC) to prevent CRBSI.[16,17] Heparin solution is commonly used to lock the catheter to prevent thrombosis, and there is some controversy over whether or not to include heparin in blood culture samples. Previous studies have shown no interference of heparin with the growth of microorganisms[18,19] and the usefulness of the blood-heparin mixture culture to predict CRBSI.[20-22] We thereby conducted a study in a cohort of HD patients with the aim of evaluating SCs of readily accessible endoluminal samples to prevent infection with the goals of decreasing the rate of CRBSI and avoiding widespread administration of ALT postdialysis.

MATERIALS AND METHODS

Study population

We conducted this prospective quasi-experimental study between April 2011 and April 2012 at the Hospital Universitario 12 de Octubre in Madrid, Spain, with the approval of the ethics committee of the institution. We enrolled patients >18 years of age with end-stage renal disease who underwent HD with a dual-lumen tunneled cuffed central venous catheter and who attended the hospital or an affiliated dialysis center. We included patients carrying a permanent TCC since the start of treatment and patients who underwent TCC insertion during the study period. Patients left the study when their TCCs were permanently removed (because of implementation of an arteriovenous fistula or renal transplantation), when they were transferred to another HD center, for prolonged hospitalization (>15 days), or because they died. Demographic and clinical information were collected prospectively on all patients. An adjusted Charlson comorbidity index was calculated for each patient.[23]

In the absence of a control group in our study population, a historical cohort of HD patients with TCCs from our institution was used for comparison.[22] This cohort was composed by 51 patients with similar demographic and clinical characteristics to those of the present study population. There were no major changes in the essential elements of the catheter care protocol for the 2 studies.

Measures for infection control in HD

Infection control measures during HD sessions were in accordance with written internal procedures and were based on Infectious Diseases Society of America and European Renal Best Practice guidelines.[24,25] Patients were treated with HD sessions 2 or 3 times a week. The dialysis equipment was connected directly to the catheter hub, and the catheter was opened for the shortest time possible to minimize the risk of intraluminal infection. The catheter hub was closed with heparin (5,000 International Unit/mL, full luminal volume) after each dialysis session. Chlorhexidine was used as an antiseptic agent, and maximum sterile barriers (sterile gloves, masks, hair caps) were used during connection and disconnection of lines.

Catheter exit sites were inspected for infection during every HD session. Cultures from the skin insertion sites were performed whenever infection was suspected because of purulent discharge, redness, or signs of inflammation. Topical and systemic antibiotics were started immediately after collecting samples for culture. *S aureus* nasal carriage was also investigated, and topical mupirocin was prescribed in cases of colonization.

Colonization of the inner catheter lumen was assessed every 15 days by SCs performed on ~5 mL of a 3:2 blood:heparin mixture that was withdrawn from the arterial catheter lumen and inoculated into aerobic culture bottles, which were incubated for 5 days in an automated blood culture system (BacT/Alert, bioMèrieux, Durham, NC). This blood and heparin mixture is readily accessible and is normally withdrawn and discarded by the nursing staff just prior to connecting the patient to the HD machine. Time-to-positivity (TTP), defined as the duration between the start of culture incubation and the start of the alert signal (as documented by the monitoring system), was recorded. A previous study conducted by our group showed the usefulness of this type of sample to investigate endoluminal catheter colonization and predict the risk of developing CRBSI.[22] Based on our results, we designed an algorithm based on SC results to triage individual asymptomatic HD patients (Fig 1). Different treatment strategies were adopted based on the presence or absence of microbial growth, organism identification, and TTP. When SCs were negative (group 1), we considered these patients at no risk of infection; therefore, no special measures were followed. When CoNS was recovered with TTP >14 hours (group 2), we determined whether it was caused by TCC colonization or culture contamination by performing a fresh SC after 1 week. If the same organism was recovered the second time, ALT was implemented. If CoNS was recovered with TTP ≤14 hours (group 3), we assumed it was colonizing the catheter, and ALT was also administered. Antibiotics used for ALT were either vancomycin (5 mg/mL) or daptomycin (5 mg/mL) with heparin, administered after each dialysis session for 2 weeks from the time the positive culture result was reported. Endoluminal catheter colonization samples were obtained after ALT to ensure that the line was successfully sterilized. Recovery of microorganisms other than CoNS (*S aureus, Enterococcus* spp, gram-negative bacteria, *Candida* spp) was considered significant, and a diagnosis of CRBSI was suspected (group 4). In these cases, blood cultures from a peripheral vein and the catheter were setup, and patients were managed according to therapeutic guidelines.[24,25] Intravenous and locking antibiotics were also administered, and the TCC was either left in place or removed based on clinical decision criteria.

Definitions

CRBSI was defined as the isolation of the same microorganism (identical biotype and antibiotic susceptibility pattern) from both the TCC and peripheral blood cultures, provided that the TTP from the catheter was ≥120 minutes less than that from peripheral blood.

Tunnel infection was defined as tenderness, erythema, and induration >2 cm from the catheter exit site, along the subcutaneous tract of a tunneled catheter, with or without concomitant bloodstream infection.[21]

Statistical analysis

The rate of CRBSI was calculated as a density of incidence and was reported per 1,000 catheter days. The rate of CRBSI observed during this study was compared with that obtained in a historical cohort from 2007-2008. CRBSI and non-CRBSI groups were compared using a 2-tailed χ^2 test or Fisher exact test for categorical variables and Mann-Whitney *U* test for continuous variables. Data were stored and analyzed using SPSS software version 15.0 (SPSS, Chicago, IL). The comparison of rates was performed using Epidat software 4.0 (Pan American Health Organization, Washington, DC).