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See related article, “Measured GFR Does Not Outperform Estimated GFR in Predicting CKD-Related Complications,” on pages 1931–1937.

Antimicrobial Catheter Locks: Searching for the Ideal Solution

Anthony J. Bleyer and Mariana Murea

Section on Nephrology, Wake Forest School of Medicine, Winston-Salem, North Carolina

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In this issue of *JASN*, Campos *et al.* report a well performed, prospective, randomized clinical trial demonstrating the benefit of an antimicrobial catheter lock solution (ACL) containing minocycline and EDTA (M-EDTA) in the prevention of hemodialysis catheter-related bacteremia.¹ It is unclear why most nephrologists do not use ACLs in this setting; a number of clinical trials consistently demonstrate their superiority to conventional solutions.^{2–7} Oddly enough, we have no trouble pursuing other kinds of treatments for which robust clinical benefit is lacking, such as moderately increasing dialysis dosage

in peritoneal and hemodialysis, using statins in dialysis patients, low protein diets in chronic kidney disease, or early asymptomatic initiation of dialysis.

ACLs are instilled into dialysis catheters at the end of a hemodialysis treatment. Small amounts of the ACL will enter the systemic circulation when instilled initially and through diffusion during the interdialysis interval. The ideal ACL should have the following properties: it should be nontoxic when administered systemically; it should prevent catheter thrombosis; it should be effective against a wide variety of microorganisms; it should be biocompatible with the catheter; it should not lead to antibiotic resistance; and it should be readily available and inexpensive.

A variety of solutions have been tried over the last decade, but there is no consensus on the ideal solution. Hypertonic sodium citrate is an effective and inexpensive catheter lock,³ but inadvertent systematic administration results in severe hypocalcemia and cardiac arrest.⁸ Ethanol may be an effective agent, but there are concerns about thrombosis and compatibility with catheter materials.⁹ ACLs containing gentamicin^{4,6,7} are extremely effective in preventing infection; the high concentrations achievable within the catheter are toxic to staphylococci. ACLs containing gentamicin are inexpensive and highly effective. Unfortunately, the use of these solutions has been discouraged because of the potential risk for antimicrobial resistance. The Interpretative Guidance for Conditions of Coverage state: “The CDC advises that prophylactic antibiotic lock solutions be reserved for use only in special circumstances, for example, in units where the rate of catheter-related bloodstream infection has not decreased despite optimal maximal adherence to aseptic technique.”¹⁰

Avoidance of antimicrobials in catheters seems at odds with the effective use of antimicrobials in the prevention of other infections. Antimicrobial prophylaxis is given routinely for many surgeries, dental procedures in individuals with cardiac valvular abnormalities, prevention of urinary tract infections, and prevention of infection in immunosuppressed transplant patients. In the dialysis center, gentamicin ointment is routinely applied to reduce peritoneal catheter exit site infection,¹¹ and a polyantibiotic ointment is often placed at the exit site of hemodialysis catheters.¹² The use of gentamicin as an antimicrobial catheter lock may lead to gentamicin resistance, an antibiotic for which alternative choices exist. However, the use of vancomycin in dialysis units is increased markedly without prophylactic antimicrobial catheter lock solutions, and this clearly has the potential to lead to *Staphylococcus aureus* that are resistant to vancomycin. Notably, some of the first vancomycin-resistant *Enterococci*¹³ and coagulase-negative *Staphylococcus epidermidis* species were found in dialysis patients.¹⁴ Vancomycin-intermediate *S. aureus* species have also been identified in dialysis patients.¹⁵

In the study by Campos *et al.*,¹ M-EDTA was very effective and well tolerated. The rate of catheter-related bacteremia was 4.3 per 1000 catheter-days in the control group receiving heparin dwells and 1.1 per 1000 catheter days in the M-EDTA group ($P = 0.005$). The rate of catheter removal due to dysfunc-

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Correspondence: Dr. Anthony J. Bleyer, Section on Nephrology, Wake Forest School of Medicine, Medical Center Boulevard, Winston-Salem, NC 27157-1053. Phone: 336-716-4513 Fax: 336-716-4318; E-mail: ableyer@wfubmc.edu

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tion was 4.6 per 1000 catheter-days for the M-EDTA group and 3.2 per 1000 catheter-days for heparin-filled catheters ($P = 0.31$). Thus, there were fewer infections and the rate of catheter thrombosis appeared similar. One concern in prior ACL trials has been high infection rates in the control group. Ideally, dialysis centers should have a catheter-related bacteremia rate less than 1 per 1000 catheter-days, and the rate in the control group in this study was much higher. However, in other studies of ACLs with control groups having lower rates of infection, a significant treatment effect has still been observed.^{2,16} In another prospective randomized trial using M-EDTA,¹⁷ catheter colonization was found to be far lower in the M-EDTA group.

Minocycline has fewer important clinical applications, and the authors postulate that resistance to minocycline would be less of a clinical problem compared with other antibiotics that have been used in ACLs, including gentamicin. This might be a distinct clinical advantage. However, two areas of concern remain: the cost of the solution and its pharmaceutical preparation. Although these compounds are easily synthesized and produced, market factors may make the cost of the mixture higher than the standard catheter locks used in dialysis centers. Compounding this solution is also a potential problem for dialysis centers.

Although none of the ACLs that have been tested to date are ideal, many vastly out-perform our current catheter-locking solutions. While we await the perfect solution, the mortality of patients on hemodialysis relating to catheter bacteremia remains high. What should nephrologists do? First, it is incumbent that we each be aware of the catheter-related bacteremia rate in our dialysis centers. This number is easily calculated by dividing the number of bacteremic events by the number of patient-days during the period under study. Optimal hygiene should be pursued in using access catheters. If bacteremic rates are elevated, one should consider the use of ACLs. In addition, in our opinion, patients at extremely high risk from infection—such as patients with dialysis catheters who have artificial heart valves, transvenous pacers, or defibrillators—should receive these solutions or at a minimum be informed of their availability and the reason they are not being used.

Catheter-related bacteremia is responsible for the deaths of approximately 2000 to 5000 hemodialysis patients each year.⁸ The time is right to translate the results of clinically robust trials into action, thereby preventing a large proportion of catheter-related bacteremia with associated morbidity, mortality, and higher healthcare costs.

DISCLOSURES

None.

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