Antimicrobial lock solutions and central line-associated bloodstream infections

Antimicrobial lock therapy is based on the principle of installation of a concentrated antibiotic solution into an intravascular catheter lumen and allowing it to dwell for a suitable period of time in order to sterilize or reduce bacterial colonization in the catheter lumen. The goal of antibiotic lock therapy is to reduce the incidence of central line-associated bloodstream infections (CLABSIs), catheter-related bloodstream infections (CRBSIs), and reduce the incidence of premature catheter removal. A recently published meta-analysis of randomized controlled trials looking at the efficacy of antimicrobial lock solutions in preventing CLABSIs [1] is the focus of this month’s newsletter.

The preceding meta-analysis critically reviewed a large number of randomized controlled trials that compared the efficacy and safety of antimicrobial lock solutions to heparin lock solutions. All studies eligible for inclusion in this meta-analysis met these 5 criteria: (1) randomized controlled trial study design; (2) use of an antimicrobial lock solution in the intervention group; (3) use of heparin in the control group; (4) use lock solutions the were allowed to dwell, rather than simply be flushed through the catheter; and (5) included an appropriate definition of CLABSI. The primary outcome of interest was the incidence of CLABSI. Secondary outcomes included the rate of catheter failure, exit site infections, and all-cause mortality.

The authors performed an extensive literature search that identified 2,371 possibly pertinent citations. A total of 23 studies met the above criteria. These 23 studies were published between 2002 and 2013 and reported outcome data on 2,896 patients with catheters in place for 383,710 catheter days. Antimicrobial lock therapy included the use of one or more of the following agents: gentamicin, vancomycin, minocycline, cefotaxime, cefazolin-gentamicin, linezolid, and amikacin.

The authors of this meta-analysis concluded that prophylactic use of antimicrobial lock solutions significantly reduced the rate of CLABSI (relative risk [RR] 0.31, 95% CI: 0.24-0.40). The authors acknowledged that a publication bias may have occurred as more studies showing an effect of antimicrobial lock solutions on CLABSI rates were published.
than studies showing no effect. However, antimicrobial lock solutions still reduced the rate of CLABSI (RR 0.36, 95% CI: 0.28-0.46) after adjustment was made for this presumed publication bias.

The authors also attempted to specifically examine the effect of antimicrobial lock solutions in patients from centers with low rates of CLABSI. Six studies were done at centers with pre-intervention CLABSI rates < 1.15 per 1000 catheter-days. All six centers had evidence of preexisting and ongoing good compliance with the use of full barrier precautions during catheter insertion, routine exit site care using antiseptic agents, and use of masks and sterile gloves when assessing catheter hubs or ports after insertion. A sub-analysis of intervention trials done at these 6 sites showed that a significant relative reduction in the CLABSI rate occurred following use of antimicrobial lock solutions (RR 0.32, 95% CI: 0.17-0.60). These findings suggest that antimicrobial lock therapy has additive protective benefits to optimal catheter care measures.

A number of secondary outcome measures were also assessed in this meta-analysis:

- Antimicrobial lock solutions were effective in reducing the rate of exit site infections (RR 0.68, 95% CI: 0.49 – 0.95).
- There was no difference in noninfectious complications necessitating catheter removal in the antimicrobial lock group and the heparin lock group (RR 0.83, 95% CI: 0.65-1.06).
- No statistically significant difference was observed on all-cause mortality among the 13 studies that provided extractable data on this outcome (RR 0.84, 95% CI: 0.64-1.12).
- Antimicrobial lock therapy reduced the rate of CRBSI (RR 0.12, 95% CI: 0.03-0.47).

We believe that this study provides good evidence that the use of antimicrobial lock therapy may be beneficial. The authors estimated that routine use of antimicrobial lock solutions could prevent 7 of 10 CLABSIs in patients who receive routine heparin lock therapy. However we believe that it is difficult to extrapolate these results to all patients with central vascular catheters for one key reason: the majority of the patients included in the above meta-analysis had indwelling catheters for hemodialysis access. Thus the benefit of routine use of antimicrobial lock therapy for patients with intravascular catheters placed for short duration in patients without renal failure remains unclear. The impact of the use of these solutions on overall rates of antimicrobial resistance remains an open issue.

**Summary:**

- Antimicrobial lock therapy when compared to heparin lock therapy may decrease the rate of CLABSIs by almost 70% in selected patients with long-term intravascular catheters.
- Instituting antimicrobial lock therapy can lead to a further reduction in CLABSI rates in facilities with preexisting low CLABSI rates.
• However, despite the above conclusions, antibiotic lock therapy cannot yet be recommended for all patients with intravascular catheters.

References: