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Case Report

Linezolid lock prophylaxis of central venous catheter infection

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Central venous catheter (CVC)-related infections are a major problem for patients requiring long-term venous access and may result in frequent hospital admissions and difficulties in maintaining central venous access. CVC-related blood stream infections are associated with increased duration of inpatient stay and cost approximately €13 585 per patient [Blot, S. I., Depuydt, P., Annemans, L., Benoit, D., Hoste, E., De Waele, J. J., Decruyenaere, J., Vogelaers, D., Colardyn, F. & Vandewoude, K. H. (2005). *Clin Infect Dis* **41**, 1591–1598]. Antimicrobial lock therapy may prevent CVC-related blood stream infection, preserve central venous access and reduce hospital admissions. In this paper, the impact of linezolid lock prophylaxis in a patient with short bowel syndrome is described.

Case report

A 42-year-old man with short bowel syndrome was admitted to our hospital suffering from recurrent central venous catheter (CVC)-related infections. A quarry accident 15 years earlier had necessitated excision of the vast majority of his small and large intestine. He has required central venous access for total parenteral nutrition ever since. For 2 years prior to this admission, he had experienced frequent CVC-related infections, which presented with raised temperature, elevated white cell count and positive blood cultures from the line. Repeated CVC-related infections and venous occlusions necessitated multiple line changes resulting in a diminishing number of available access sites. Suboptimal sites such as femoral veins were eventually used until these too became infected. The line infections were due predominantly to coagulase-negative staphylococci (CNS), uniformly susceptible to vancomycin, teicoplanin and linezolid. Episodes of CNS CVC-related infection were treated by line removal and systemic antimicrobials (vancomycin or linezolid) or, alternatively, with both systemic antibiotics and 2 weeks of lock therapy, as recommended in the Infectious Diseases Society of America CVC-related infection treatment guidelines (Mermel *et al.*, 2001). A radiolabelled white cell scan and transoesophageal echo excluded the presence of an ectopic focus of infection. Central venous access was via a tunnelled single lumen Hickman line into the inferior vena cava, which had been inserted 5 weeks earlier. After five short courses of linezolid lock therapy for recurring CNS line infections in the preceding 10 months, it was decided to use linezolid lock prophylaxis indefinitely. The linezolid lock solution was prepared by the hospital pharmacy and the patient kept the supply at home in a dedicated refrigerator at 4 °C. The patient used a new bag daily and the excess from each 600 mg bag was discarded. He was trained to administer it himself using aseptic technique. He availed of the 16 h when the line was free and instilled 3 ml of a 2 g linezolid l^{-1} solution (without heparin) into the lumen after 8 h of nocturnal total parenteral nutrition. In order to minimize manipulation of the line, the lock solution was not removed after the 16 h period. He was monitored routinely by regular blood culture, line swabbing and testing of platelet levels and inflammatory markers.

Prior to linezolid lock prophylaxis, the patient had 18 admissions for CVC-related infections, 28 positive blood cultures and eight CVC changes. He had spent 180 of the preceding 632 days in hospital. In 7 months of linezolid lock prophylaxis, he had one line change and one admission for 7 days due to CVC-related infection and a deep vein thrombosis in the common and external iliac veins. The tunnelled femoral line was removed and temporary venous access was achieved via a collateral vein. CVC-related infection was confirmed by culture of CNS from peripheral blood, a line culture and from the line tip. The patient had 44.3 infections per 1000 days (28 line

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Abbreviations: CNS, coagulase-negative staphylococci; CVC, central venous catheter.

infections in 632 days) prior to lock prophylaxis and 4.5 infections per 1000 days (one infection in the subsequent 221 days) during prophylaxis. The mean time to infection increased from 22.57 to 221 days when linezolid lock prophylaxis was used.

Prophylactic antibiotic lock solutions are only advised in special circumstances, such as recurrent catheter-related blood stream infections in a tunnelled line despite optimal aseptic technique (O'Grady *et al.*, 2002). Although the infecting organisms and the antibiotics used were different, Onder *et al.* (2007) also showed that antibiotic lock prophylaxis reduced CVC-related infections and inpatient hospital stay in children with short bowel syndrome or intestinal transplantation, supporting the role of antibiotic lock prophylaxis in this patient group. Preventive lock therapy using vancomycin was shown to reduce line-infection rates in several prospective randomized controlled trials and a meta-analysis (Carratala *et al.*, 1999; Garland *et al.*, 2005; Safdar & Maki, 2006). Linezolid was selected for this study based on surprising *in vitro* results that demonstrated more rapid bacterial killing (approaching a 3-log reduction) than vancomycin or gentamicin against an established CNS biofilm in a model of catheter infection (Curtin *et al.*, 2003). Although linezolid is bacteriostatic for planktonic-phase bacteria, this study suggests that it may be more effective in CNS biofilms. Linezolid was reported to be bactericidal in an *in vitro* model of endocarditis (Cha *et al.*, 2003). Recent *in vitro* work suggests that bactericidal daptomycin is another excellent candidate for antibiotic lock prophylaxis (LaPlante & Mermel 2007; Raad *et al.*, 2007). Concerns surrounding the long-term prophylactic use of antimicrobial therapy relate to selection of resistance and drug toxicity. Only 6 mg linezolid was administered per day and none of the adverse effects of systemic linezolid therapy were observed. Linezolid lock therapy has been used successfully in the treatment of catheter-related infection both in this patient and with systemic linezolid therapy in a similar patient (Castagnola *et al.*, 2006). Resistance to linezolid was never observed in any of the cultures from our patient, despite 7 months of linezolid lock prophylaxis (MICs 0.25–1.5 mg ml^{-1}).

The expense of linezolid lock prophylaxis must be balanced against the cost of repeated hospital admissions, central line changes and therapeutic antibiotics. This patient has since left our care and is being assessed for an intestinal transplant. In patients with recurrent central line infections and long-term intravascular access problems where line removal is not feasible, linezolid lock prophylaxis should be considered but line surveillance, education and adherence to evidence-based guidelines for catheter insertion and manipulation (Centers for Disease Control and Prevention, 2005; Pronovost *et al.*, 2006) remain the basis for the successful prevention of CVC-related infections.

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