aqueous or alcohol formulations) is most effective in decreasing the incidence of SSIs.[3]

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Controversies on Antibiotic Lock Technique Duration: Experience with a 3-Day Course for Hematological Patients

To the Editor—We read with much interest the recent article by Polgreen and colleagues[1] that emphasizes the wide variability existing among clinicians in the use of the antibiotic lock technique (ALT). Central venous catheter (CVC)–related infections (CRIs) are frequently observed among patients with hematological diseases.[2,3] Systemic antibiotic therapy in combination with the ALT for the treatment of localized CVC colonization-related infection (LCC-CRI) and bloodstream CVC-related infection (BS-CRI)[2] is recommended. Many studies, conducted both in vitro and in vivo, showed the validity of this approach and provided the rationale for ALT approval in guidelines.[5-7] The suggested treatment duration is 14 days;[2] however, this impairs CVC usability for a period sometimes too long for critical or high-risk patients undergoing chemotherapy with or without stem cell transplantation. Moreover, the duration of the ALT is controversial, and in vitro studies have demonstrated that shorter periods may be sufficient.[4] Also, the recent article by Sauer et al[8] suggests that a shorter ALT may be as effective as a longer-duration technique.

Between September 2003 and December 2005, we treated in our center patients affected by uncomplicated BS-CRI or LCC-CRI (based on 2 sets of CVC cultures with evidence of infection at least 2 hours earlier than peripheral blood cultures for BS-CRI or peripheral blood culture results negative for LCC-CRI) due to coagulase-negative staphylococci or gram-negative bacilli and with systemic symptoms of infection (body temperature > 38°C and/or chills) with a new short-course (3-day) ALT, to allow broad CVC usage for intensive

treatment (such as hemopoietic stem cell transplantation or chemotherapy). Informed consent was obtained.

The ALT consisted of the instillation of antibiotic solution inside CVC lumen without anticoagulant for a total period of 72 hours. Solution remained in CVC lumen during a locking period of 12 hours every 24 hours; at the end of the locking period, the solution was removed and the lumen opened to allow infusions. In the case of 2-lumen CVC, locking was alternated every 12 hours so that one lumen was available for use during the 72-hour ALT.

Antibiotic solutions were chosen according to the type of infection. Teicoplanin at a concentration of 22 mg/mL was used for susceptible gram-positive non-*Staphylococcus* hemolyticus infections, vancomycin at a concentration of 10 mg/mL was used for *Staphylococcus haemolitycus* infection or other teicoplanin-resistant gram-positive bacteria, and amikacin at a concentration of 20 mg/mL was used for gram-negative bacteria. The volume of the solution to be instilled was chosen according to the lumen volume declared by the manufacturer.

Response was defined by blood cultures performed after the end of treatment and clinical evaluation of infection signs. Resolution was defined as sterilization of both peripheral blood and CVC cultures and disappearance of systemic signs of infection.

A total of 26 infectious episodes in 20 patients were treated (*Staphylococcus episermidis* in 19, *S. haemolyticus* in 3, other gram positive in 3, and gram negative in 1). Resolution was obtained in 21 (81%) of 26 CRIs. Reinfection incidence of the 21 successful CRIs was 54% and 66% at 100 and 180 days from ALT, respectively. CRI-related removal probability was 22% and 33% at 100 and 180 days from ALT and 11% and 28% at 100 and 180 days from the day of placement, respectively. The CRI-related removal probability of successful cases was 7% and 20% at 100 and 180 days from ALT, respectively.

The success rate of the ALT in reported studies varies from 57% to 100%, with a mean of 82.6%, significantly improving the historical control rate of 66.5% with systemic antibiotics alone.[5-7] ALT procedures may differ for a number of parameters, such as the type of antibiotic, the use of heparin, or the duration of the ALT procedure.[5]

The results obtained in our study are similar to those reported in other studies, although the lack of a control arm is a limit. However, no randomized studies are available in the literature, and control arms usually are only historical control groups, so that statistical evidence of the superiority of a recommended 14-day ALT is still lacking.

Two main advantages of a short-course antibiotic lock were noted: (*a*) the infusion discontinuation for a short interval allows a greater availability of devices, crucial in a high proportion of patients and more advantageous than CVC removal and replacement, which requires not less than 7–10 days for the completion of the procedure,[2] and (*b*) CVC manipulation during any ALT increases the risk of second infections. A shorter ALT course could reduce both the number of reinfections and the cost of the procedure, compared with either a longer ALT course or CVC removal and replacement.

In conclusion, our limited study provides a look into the use of an alternative antibiotic lock therapy; advantages seem to emerge, but efficacy, safety, and cost evaluation need larger comparative trials.

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Gastrointestinal Selective Capacity of Doripenem, Meropenem, and Imipenem for Carbapenem-Resistant Gram-Negative Bacilli in Treated Patients with Pneumonia

To the Editor—Multidrug-resistant gram-negative bacilli (GNB) have emerged as major infectious threats and therapeutic challenges for physicians worldwide.[1,2] Infections with these multidrug-resistant pathogens have been associated with poor patient outcomes.[3,4] Data on the emergence of carbapenem-resistant (CR) GNB in gastrointestinal flora and the selective capacity of carbapenem exposure are limited. We conducted a feasibility trial to evaluate the gastrointestinal selective capacity of 3 carbapenems for CR *Acinetobacter baumannii*, CR *Pseudomonas aeruginosa*, and CR *Stenotrophomonas maltophilia* among patients treated for healthcare-associated pneumonia. These findings on the emergence of multidrug-resistant GNB contribute to the current understanding of the selective capacity of gastrointestinal flora after carbapenem exposure.

From October 31, 2009, through August 31, 2010, all patients who were admitted to the medical intensive care unit (ICU) at Thammasat University Hospital with healthcare-associated pneumonia were approached for study participation. Consecutive consenting adults were enrolled. By means of a computer-generated list, patients were randomly assigned at a 1 : 1 : 1 ratio to receive imipenem, meropenem, or doripenem at admission after enrollment. Clinical criteria for healthcare-associated pneumonia were the same as described elsewhere.[5] Rectal swab specimens for culture were obtained at admission, on day 14, and on day 28. Patients who tested positive for enteric CR-GNB at admission or patients who died before day 14 were excluded. Prestudy baseline ICU rates of CR *A. baumannii*, CR *P. aeruginosa*, and CR *S. maltophilia* colonization or infection were 0.85, 0.14, and 0.05 cases per 1,000 patient-days, respectively. Rectal swab specimens were transported and processed within 1 hour of procurement for culture on MacConkey agar plates. Bacterial colonies suspected of being *A. baumannii*, *P. aeruginosa*, or *S. maltophilia* were identified using standard microbiological techniques. The minimum inhibitory concentrations (MICs) of all representative isolates were determined for the 3 study drugs by E-test (AB bioMérieux), in accordance with the manufacturer's protocol. Susceptibility results were interpreted according to Clinical and Laboratory Standards Institute breakpoints.[6] Laboratory personnel were masked to treatment assignments.

During the study period, 69 patients were screened for study participation, and 60 met the study criteria for participation and follow-up (20 patients per drug group). Excluded patients included 4 who tested positive for enteric CR-GNB at admission (2 positive for CR *A. baumannii* and 2 positive

TABLE 1. Characteristics of 60 Study Subjects with Healthcare-Associated Pneumonia and the Emergence of Carbapenem-Resistant (CR) Enteric Flora after Exposure to Carbapenems

Variable	Imipenem (n = 20)	Meropenem (n = 20)	Doripenem (n = 20)
Characteristics			
Age, years	51 (31–65)	50 (25–69)	49 (28–67)
Male sex	12 (60)	13 (65)	13 (65)
Comorbid conditions			
Diabetes	6 (30)	5 (25)	6 (30)
COPD	5 (25)	4 (20)	5 (25)
Chronic liver disease	4 (20)	4 (20)	3 (15)
Chronic kidney disease	5 (25)	5 (25)	4 (20)
Neurological disease	3 (15)	3 (15)	2 (10)
APACHE II score, median	17	16	19
Duration of study therapy, days	7 (6–16)	6 (5–16)	7 (6–15)
Outcomes			
Day 14 after treatment			
CR *Acinetobacter baumannii*	4 (20)	4 (20)	3 (15)
CR *Pseudomonas aeruginosa*	6 (30)	6 (30)	0 (0)[a]
CR *Stenotrophomonas maltophilia*	1 (5)	1 (5)	1 (5)
Day 28 after treatment			
CR *A. baumannii*	4 (20)	4 (20)	3 (15)
CR *P. aeruginosa*	5 (25)	5 (25)	0 (0)[a]
CR *S. maltophilia*	1 (5)	1 (5)	1 (5)

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