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Faropenem Disks for Screening of *Klebsiella pneumoniae* Carbapenemase-Producing *Enterobacteriaceae*

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Carbapenemase-producing *Enterobacteriaceae* (CPE) demonstrate a wide range of carbapenem susceptibility, and while most isolates are nonsusceptible to carbapenems, some isolates, especially *Escherichia coli*, may test susceptible to them (1, 2). Day et al. recently reported the utility of using disks of faropenem, an oral penem, in the screening of CPE (3). The authors demonstrated that disks containing up to 10 μg faropenem had 99% sensitivity and 94% specificity when tested against 166 CPE isolates producing various carbapenemases and 82 isolates producing other β-lactamases.

In the United States and several other countries, *Klebsiella pneumoniae* carbapenemase (KPC) is by far the most common carbapenemase found in *Enterobacteriaceae* (4). In this study, we tested the ability of faropenem disks as well as carbapenem disks to predict KPC production using 62 unique KPC-producing *Enterobacteriaceae* isolates, including *K. pneumoniae* (n = 31), *Escherichia coli* (n = 20), and *Enterobacter* spp. (n = 11). The presence of the KPC gene was confirmed by PCR. Seventy-three isolates producing extended-spectrum or AmpC β-lactamases were used as controls (5, 6). Only one isolate was included from a given patient. The disk diffusion testing was performed with ertapenem, imipenem, meropenem (disks obtained from BD, Sparks, MD), tebipenem, and faropenem (disks obtained from Eiken Chemical Co., Tokyo, Japan) using the standard methodology endorsed by the Clinical and Laboratory Standards Institute. Tebipenem is an oral carbapenem which is approved for clinical use in Japan. All disks contained 10 μg of the agent, except the faropenem disks, which contained 5 μg of the agent.

The ranges of zone diameters for faropenem and the four carbapenems against KPC-positive or -negative *Enterobacteriaceae* are shown in Table 1. All 62 KPC-positive *Enterobacteriaceae* showed confluent growth up to the edge of the 5-μg faropenem disk, to generate a zone diameter of 6 mm. In contrast, none of the KPC-negative isolates showed growth up to the edge of faropenem disks, with all zone diameters of faropenem being greater than or equal to 10 mm. The data show that a zone diameter of 6 mm (i.e., no inhibition) for faropenem predicted a KPC producer with 100% sensitivity and specificity for the set of isolates studied. The other four carbapenems generated zone diameters of 6 to 22 mm and 14 to 32 mm for KPC-positive and KPC-negative *Enterobacteriaceae*, respectively.

Our data confirm the potential utility of faropenem disks in predicting the KPC production reported by Day et al. and extend their findings to a large set of KPC-producing isolates, including *K. pneumoniae*, *E. coli*, and *Enterobacter* spp. Unlike in the aforementioned study, we did not observe any false-positive tests among either extended-spectrum β-lactamase- or AmpC β-lactamase-producing isolates, though this may be due to the overall smaller number of isolates investigated in our study. Faropenem is not currently approved for clinical use in the United States, but it may have a diagnostic role in sensitive prediction of KPC production among *Enterobacteriaceae* clinical isolates.

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TABLE 1 Ranges of inhibition zone diameters produced by six carbapenems against *Enterobacteriaceae* with or without *Klebsiella pneumoniae* carbapenemase

Isolate type and organism(s) (no. of isolates [*n* = 135])	Median (range of) inhibition zone diam (mm)				
	Imipenem	Meropenem	Ertapenem	Tebipenem	Faropenem
KPC positive					
E. coli (20)	16 (12–20)	15 (10–21)	13 (6–20)	16 (8–22)	6 (6)
K. pneumoniae (31)	11 (6–22)	9 (6–20)	8 (6–16)	10 (6–21)	6 (6)
Enterobacter spp. (11)	15 (7–23)	14 (7–20)	12 (6–17)	16 (7–22)	6 (6)
KPC negative					
E. coli (23)	26 (22–30)	26 (25–30)	26 (22–30)	28 (26–32)	19 (10–24)
K. pneumoniae (36)	26 (23–30)	26 (19–30)	26 (13–28)	28 (20–30)	19 (12–23)
Enterobacter spp. (14)	23 (19–25)	25.5 (16–28)	24.5 (14–28)	27 (19–29)	16.5 (10–22)

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