Ertapenem for multiple β-lactamases producing Gram-negative bacteria causing urinary tract infections in HIV patients

Sir,

Extended-spectrum β-lactamases (ESBLs) and AmpC β-lactamases (AmpC) are responsible for β-lactam antibiotic resistance among *Escherichia coli*.[1] Metallo-β-lactamases (MBLs) hydrolyze virtually all drugs in the class of carbapenems. This study was aimed to detect the ESBLs, MBLs, and AmpC production among Gram-negative bacteria from HIV patients. A total of 128 bacterial isolates were collected from urine samples of HIV patients having the symptoms of urinary tract infections (UTIs), attending Y. R. Gaitonde Centre for AIDS Research and Education (YRG CARE), South India. The Gram-negative bacterial isolates were screened for ESBLs production using cefotaxime (30 μg) and ceftazidime (30 μg) alone and in combination with clavulanic acid (10 μg), for MBL production using imipenem (10 μg) alone and in combination with ethylenediaminetetraacetic acid (EDTA) (750 μg), and for AmpC production using cefoxitin (30 μg) alone and in combination with cloxacillin (200 μg) by combination disc method. Of the 128 urinary isolates, 73 (50.7%) were *E. coli*, 19 (13.2%) *Klebsiella pneumoniae*, 17 (11.8%) *Klebsiella oxytoca*, 9 (6.3%) *Proteus mirabilis*, 2 (1.4%) *Proteus vulgaris*, and 8 (5.5%) *Pseudomonas aeruginosa*. Out of 128 bacterial isolates, 120 belonged to *Enterobacteriaceae* family and 8 to *Pseudomonas aeruginosa*. Among the bacterial isolates of *Enterobacteriaceae*, 63 (52.5%) showed positive for ESBLs, 62 (51.66%) for MBLs, and 60 (50%) for AmpC, and among the bacterial isolates of 8 *Pseudomonas aeruginosa*, 4 (50%) showed positive for ESBLs and 5 (62.5%) for both MBLs and AmpC. It was also observed that ESBLs producing isolates showed minimum inhibitory concentration (MIC) values ranging

Table 1: The percentage of antibiotic resistance and β-lactamases production of the Gram-negative bacteria from HIV patients

	Organisms						Total (β-lactamases producing bacteria, *n*=113)
	E. coli (%)	*K. penumoniae* (%)	*K. oxytoca* (%)	*P. aeruginosa* (%)	*P. vulgaris* (%)	*P. mirabilis* (%)	
Antibiotics							
Aztreonam	66.3	11.2	10.2	4.7	0.9	6.5	94.6% (*n*=107)
Cefpodoxime	67.9	13.2	12.3	NA	0.9	5.6	93.8% (*n*=106)
Nalidixic acid	66	14.1	13.2	NA	0	6.6	93.8% (*n*=106)
Cefoperazone	68.9	8.7	9.7	5.8	1.9	4.8	91.3% (*n*=103)
Cefoxitin	65.7	15.7	12.7	NA	1	4.9	90.3% (*n*=102)
Ampicillin	62	14	13	5	1	5	89% (*n*=100)
Cefotaxime	67	13	11	3	1	5	89% (*n*=100)
Imipenem	76.5	8.6	11.1	2.5	0	1.2	72% (*n*=81)
Piperacillin-tazobactam	81.7	7	7	2.8	0	1.4	62.8% (*n*=71)
Piperacillin	82.8	6.2	7.8	1.6	0	1.6	56.6% (*n*=64)
Ceftazidime	86.2	6.9	6.9	0	0	0	51.3% (*n*=58)
Gentamicin	52.6	18.4	15.8	7.9	0	5.3	33.6% (*n*=38)
Amikacin	62.5	16.7	12.5	4.2	0	4.2	21.2% (*n*=24)
Chloramphenicol	73.9	13	8.7	NA	0	4.3	20.3 (*n*=23)
Ertapenem	31.2	25	18.7	6.2	0	18.7	14.1% (*n*=16)
β-lactamases production							
ESBLs	56.7	17.9	11.9	6	1.5	6	52.3% (*n*=67)
MBLs	61.2	16.3	9	7.5	0	6	52.3% (*n*=67)
AmpC	55.4	18.5	13.8	7.7	0	4.6	50.8% (*n*=65)

E. coli = *Escherichia coli*; *K. pneumoniae* = *Klebsiella pneumoniae*; *K. oxytoca* = *Klebsiella oxytoca*; *P. aeruginosa* = *Pseudomonas aeruginosa*; *P. vulgaris* = *Proteus vulgaris*; *P. mirabilis* = *Proteus mirabilis*; ESBLs = Extended spectrum β-lactamases; MBLs = Metallo β-lactamases; AmpC = AmpC β-lactamases; NA = Not applicable

from <0.125 to >16 μg/ml to the combination of three antibiotics, namely, cefotaxime, ceftazidime, and cefepime without clavulanic acid and from 0.094 to >4 μg/ml to the combination of cefotaxime, ceftazidime, and cefepime with clavulanic acid by Etest. Furthermore, AmpC-positive isolates showed MIC values ranging from <0.125 to >16 μg/ml using the combination of cefotaxime, ceftazidime, and cefepime without cloxacillin and from 0.125 to >4 μg/ml for cefotaxime, ceftazidime, and cefepime with cloxacillin and MBLs producing isolates showed MIC values ranging from 16 to 256 μg/ml for meropenem without EDTA and from 2 to > 64 μg/ml for meropenem with EDTA by Etest. In this study, β-lactamases producing bacteria had shown resistance to aztreonam (94.6%), cefpodoxime (93.8%), nalidixic acid (93.8%), cefoperazone (91.3%), cefoxitin (90.3%), cefotaxime (89%), ampicillin (89%), and imipenem (72%). About 86.04% of isolates showed sensitivity to ertapenem, followed by chloramphenicol (79.7%) and amikacin (79%) [Table 1]. Cotton *et al.*[2] reported that 50% of *Enterobacteriaceae* produced ESBLs. The findings of our study were slightly higher than that of Cotton *et al.* showing 60% of *Enterobacteriaceae* produced ESBLs. In this study, 55.3% of *E. coli* from HIV patients produced AmpC, and these results contrasted with that of Padmavathy *et al.*[3] who reported that about 72.7% of the *E. coli* from HIV patients showed AmpC production. This study also revealed that about 82% of *E. coli* showed TMP-SMX drug resistance, which was slightly higher than that of Vignesh *et al.*[4] who reported that 80.6% of *E. coli* from UTIs among HIV patients showed resistance to TMP-SMX. They recommended imipenem as a drug of choice for treating UTIs caused by multi-drug resistant bacteria, but to our surprise, we found that 72% of the isolates showed resistance to imipenem. Gutiérrez-Gutiérrez *et al.*[5] reported that ertapenem appears as effective as other carbapenems for empirical and targeted therapy of bloodstream infections due to ESBLs producing *Enterobacteriaceae*. In our study, ertapenem exhibited good sensitivity not only to ESBL-producing bacteria but also to MBLs and AmpC producers causing UTIs in HIV patients. Based on this study, we suggest ertapenem as the drug of choice for treating multiple β-lactamases producing bacteria from HIV patients.

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Conflicts of interest

There are no conflicts of interest.

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