Letter to editor:

Cefepime/tazobactam-a promising BL-BLI combination against multidrug resistant Gram negative bacteria

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Sir,

Antimicrobial resistance among the gram-negative bacteria (GNB) including β-lactam antibiotics is increasing because of the production of various enzymes like Extended spectrum β–lactamases (ESBLs) and AmpC β-lactamases leaving carbapenems as the only therapeutic option\(^1\). Excessive use of carbapenems has resulted in emergence of newer and dangerous bugs like NDM1 and MBL producers. The need of the hour is to reduce use of Carbapenems. Hence new combinations of β lactams and β lactamase inhibitors have being investigated as a therapeutic option to treat moderately severe infections due to ESBL producers\(^2\). Such a carbapenem sparing and restriction strategy may be beneficial in reducing the carbapenem usage and carbapenem resistance rate.

Cefepime/tazobactam is a new promising β-Lactam/β-Lactam inhibitor combination (BL/BLI) for the treatment of moderate-to-severe infections. Cefepime, a ‘fourth-generation’ cephalosporin is bactericidal in action against Gram-negative and Gram-positive pathogens and is stable against both AmpC and OXA but lacks activity against ESBLs. Tazobactam inactivates ESBLs. Thus Cefepime/tazobactam should effectively cover all the three mechanism of resistance\(^3\).

No significant clinical data is available on this drug and limited number of in vitro studies are published till now.

In the present study, we compared the sensitivity pattern of GNB to Cefepime/tazobactam as compared to cefepime, imipenem and other BL/BLI combination like Piperacillin/tazobactam, cefoperazone/sulbactam. We also analysed whether Cefepime/tazobactam combination can be used as an alternative to carbapenems.

Out of 480 clinically significant non-repetitive gram negative isolates tested 122 (25.4%) were *E.coli*, 113 (23.5%) were *K. pneumoniae*, 119 (24.8%) were other enterobacteriaceae (*Citrobacter spp.*, *entero bacter spp.*, & *Proteus spp.*) followed by *Pseudomonas spp.* 75 (15.6%) and *Acinetobacter spp.* 51 (10.6%). Amongst enterobacteriaceae 219 (62%) were ESBL producers. Gram negative bacteria showed maximum sensitivity to Cefepime/tazobactam (65.4%), followed by imipenem (53.7%), piperacillin/tazobactam (33.5%) and cefoperazone/sulbactam (29.7%).

Amongst the ESBLs excellent sensitivity was seen with Cefepime/tazobactam (94.1%) followed by imipenem (91.1%), cefoperazone/sulbactam (58.8%) and piperacillin/tazobactam (55.8%). Addition of tazobactam increased the susceptibility of GNB to cefepime from 12.8% to 65.4%.
Amongst the non-fermenters like Pseudomonas and Acinetobacter, Cefepime/tazobactam proved an excellent drug showing a higher sensitivity of 62.6% and 62.7% respectively as compared to imipenem sensitivity of 32% and 29.4% respectively. In the present study a combination of Cefepime/tazobactam appeared to be mere active against ESBLs and nonfermenters than cabapenems and other BL/BLI combinations like piperacillin/tazobactum and cefoperazone/sulbactum. It has been documented in other Indian studies that Cefepime/tazobactam performed equally well or better than the Carbapenems against ESBLs and non-fermenters. The findings of our study suggests that Cefepime/tazobactum appears to be very promising combination and can be used as an alternative therapeutic option to carbapenems for treatment of moderately severe infections due to ESBLs and nonfermenters.

REFERENCES: