Infection and Drug Resistance

Dovepress
open access to scientific and medical research

Open Access Full Text Article

LETTER

A Response to Research Article "Cefmetazole Resistance Mechanism for *Escherichia Coli* Including ESBL-Producing Strains" [Letter]

Novaria Sari Dewi Panjaitan*, Christina Safira Whinie Lestari*

Center for Biomedical Research, Research Organization for Health, National Research and Innovation Agency (BRIN), Cibinong Science Center, Bogor, West Java, Indonesia

*These authors contributed equally to this work

Correspondence: Novaria Sari Dewi Panjaitan, Center for Biomedical Research, Research Organization for Health, National Research and Innovation Agency (BRIN), Genomic Building, Cibinong Science Center, Jl. Raya Bogor No. 490, Cibinong– Bogor Km. 46, Bogor, West Java, Indonesia, Email nova014@brin.go.id

Dear editor

The work performed by Ito et al was much appreciated since the authors addressed a novel and important issue in antibiotic rational uses, particularly the resistance of Cefmetazole in ESBL-producing *E. coli* and the involved gene regulations. Cefmetazole have been used as an alternative to carbapenems in addition to the use of quinolone and trimethoprim or sulfamethoxazole in infection cases caused by ESBL-producing *E. coli*.[1,2] In their study, 14 ESBL-producing and 12 ESBL-non-producing *E. coli* from 63 *E. coli* strains in total were isolated clinically.[3] The ESBL-producing ability of those *E. coli* isolates did not determine their behavior against Cefmetazole treatment in this study, since the MIC of either ESBL-non producing or ESBL-producing *E. coli* isolates vary (still relatively low at 1–4 μg/mL) in the first culture. Eleven strains of total 25 isolate gained resistance after being cultured with Cefmetazole at a low dose. Interestingly, after passage culture with the antibacterial-free medium, only 4 strains from these 11 isolates remain resistant to Cefmetazole, while the others gained susceptibility. The purpose of the authors was to unravel the mechanisms involved in the resistance acquisition against Cefmetazole in ESBL-producing *E. coli* clinical isolates, with the use of ESBL-non-producing isolates as the controls.

The previous study, reported more than thirty years ago, addressed the potential mechanism of action of Cefmetazole in methicillin and cephem-resistant (MR) strains of *Staphylococcus aureus*.[4] However, the progression in this particular issue is relatively slower than the mechanism study of other type of antibiotic, especially in ESBL-producing *E. coli*. In this study, authors tried to explore the mechanism of how Cefmetazole resistance acquisition occurred in ESBL-producing *E. coli* isolates. Therefore, the transcription (mRNA) levels of porin encoding genes (*ompF*, *ompC*, *phoE*), chromosomal β–lactamase AmpC encoding genes (*acrA*, *yhiV*, *mdfA*), and drug efflux pump were detected in this particular study. However, as also discussed well in their discussion section, these mechanisms were not the novel part.

Moreover, the authors also combined the use of Relebactam (the β–lactamase inhibitor) in observing the effects obtained in Cefmetazole use in *E. coli* isolates, which resulted in alteration in Cefmetazole susceptilbity. The addition of Relebactam suppressed the resistance toward Cefmetazole. However, the remaining question is, while β–lactamase was inhibited, what mechanism was underlying the suppression of Cefmetazole resistance acquisition? Is the effect caused by inhibiting β–lactamase alone enough to suppress antibiotic resistance? Should the upstream regulators be checked for details of their mechanisms, since the authors themselves mentioned that the Relebactam probably caused the porin deficiency. Novel regulation and details of the mechanisms involved probably could be unraveled if any transcription factors or specific motifs in DNA level were to be predicted and proven.[5,6] If there are any predicted TFs, which is unique in ESBL-producing *E. coli*, then we recommend that this issue be unraveled in future studies.

Received: 14 October 2022
Accepted: 18 October 2022
Published: 21 October 2022

Disclosure

The authors report no conflicts of interest in this communication.

References

1. Takemura W, Tashiro S, Hayashi M, et al. Cefmetazole as an alternative to carbapenems against extended-spectrum beta-lactamase-producing Escherichia coli infections based on in vitro and in vivo pharmacokinetics/pharmacodynamics experiments. *Pharm Res*. 2021;38(11):1839–1846. doi:10.1007/s11095-021-03140-7
2. Tamma PD, Aitken SL, Bonomo RA, et al. Infectious Diseases Society of America Guidance on the treatment of extended-spectrum β-lactamase Producing Enterobacterales (ESBL-E), Carbapenem-Resistant Enterobacterales (CRE), and Pseudomonas aeruginosa with Difficult-to-Treat Resistance (DTR- P. aeruginosa). *Clin Infect Dis*. 2021;72:1109–1116. doi:10.1093/cid/ciab295
3. Ito R, Kawamura M, Sato T, Fujimura S. Cefmetazole resistance mechanism for Escherichia coli including ESBL-producing strains. *Infect Drug Resist*. 2022;15:5867–5878. doi:10.2147/IDR.S382142
4. Utsui Y, Ohya S, Magaribuchi T, Tajima M, Yokota T. Antibacterial activity of cefmetazole alone and in combination with fosfomycin against methicillin- and cephem-resistant Staphylococcus aureus. *Antimicrob Agents Chemother*. 1986;30:917–922. doi:10.1128/AAC.30.6.917
5. Figueroa-Cuilan WM, Howell M, Richards C, et al. Induction of AmpC-Mediated β-Lactam resistance requires a single lytic transglycosylase in agrobacterium tumefaciens. *Appl Environ Microbiol*. 2022;88:1–17. doi:10.1128/aem.00333-22
6. Pandey P. b -Lactam resistance in azospirillum baldaniorum Sp245 is mediated by lytic transglycosylase and b –lactamase; 2022: 1–18.

https://doi.org/10.2147/IDR.S393500