Effect of qnr gene on MIC's of Newer Flouroquinolones in Gram-negative Bacteria

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Abstract

Introduction: Antibacterial resistance is a global public health care concern that is impacted by both human and non human antimicrobial use. The consequences of antimicrobial resistance are particularly important when disease is caused by pathogens that are resistant to antimicrobials considered critically important in the treatment of human disease by the WHO. Fluoroquinolones have been classified as the highest priority drugs by WHO for management of infections due to Enterobacteriaceae.

Fluoroquinolones with expanded spectrum of action, excellent tissue penetration and ease of administration (oral) have made them economical and important drugs for OPD practice. Hence study of resistance mechanism is of great importance in the fight against the spread of resistance genes of this class of drugs.

The mechanism of Fluoroquinolone resistance is not completely understood and until recently the conventional understanding is that clinically relevant resistance to quinolones in Enterobacteriaceae is always considered to be chromosomal in origin caused by mutation(s) in topoisomerase genes (target enzymes) or affecting drug permeation and transmitted only vertically. Recently the discovery of novel plasmid mediated quinolone resistance (PMQR) mechanism has threatened the diagnostic capabilities of routine diagnostic laboratories and increased the chances of possible spread of resistance by horizontal gene transfer. There is paucity of data regarding PMQR mediated qnr gene in India. Hence the present study was undertaken to study the presence of qnr A and S in Indian isolates and the effect of qnr gene on MIC of various Fluoroquinolones.

Material and methods

Clinical isolates of E.Coli (n=8)with high level resistance to Fluoroquinolones were screened for qnr A and S. Plasmid DNA was extracted from positive strains and cloned them in pGEMT Easy vector. The cloned plasmid DNA was then transformed into DH10B strain of E.Coli (which were susceptible to Fluoroquinolones).. The plasmids were then isolated from these transformed colonies (to confirm cloning) and PCR screening done. Both DH10B strain of E.Coli and transformed E. coli DH10B with qnr A and B were subjected to MICs against quinolones and newer fluoroquinolones using E-test .

Results

Both qnrA and S conferred only low level resistance to Fluoroquinolones but remained susceptible to nalidixic acid (NA), suggesting that high level resistance in parent strains was mediated by other mechanisms. Hence NA screening (routinely done for detection of low level resistance for Fluoroquinolones according to CLSI guidelines) cannot be recommended for screening for qnr mediated resistance. Further, the resistance conferred by qnr S was twofold higher than qnr A to all Fluoroquinolones tested.

Conclusion

Fluoroquinolone resistance is mediated primarily by mutation in target enzymes or permeability is not true and that plasmid mediated mechanisms are prevalent and result in non-classical resistance, which is not detected by phenotypic tests i.e. NA resistance screening and hence under reported. As these elements are spread through plasmid there is an urgent need to detect them by performing MIC to Fluoroquinolones. Further prevention of spread through rational antibiotic use is critical to save this important and useful antibiotic.