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Journal of Medical Microbiology and Immunology Research 2022

Vol 8, No. S2

Emergence of tigecycline-resistant Klebsiella pneumoniae ST11 clone in patients without exposure to tigecycline

Babak Asghari

Tabriz University of Medical Sciences, Iran

Abstract

Introduction: Tigecycline is a unique class of semi-synthetic glycylcyclines developed to treat infections caused by multidrug-resistant Klebsiella pneumoniae. In the past decades, eight tigecycline-resistant Acinetobacter baumannii isolates have been identified in Tehran and no Klebsiella pneumoniae has been reported.

Methodology: To elucidate the mechanism of K. pneumoniae efflux pump-mediated resistance, the expression of efflux pump genes (oqxA, oqxB, acrA, acrB, tolC) and regulators (acrR, ramA, marA, soxS, rarA, rob) was investigated by real-time RT-PCR. Multilocus sequence typing (MLST) of tigecycline-resistant strains was also performed.

Results: Compared to the tigecycline sensitive strain K32 (negative control), all resistant strains showed higher expression levels of efflux genes and regulatory factors. Three tigecycline-resistant strains (K53, K67, K79) showed higher levels of rarA expression (38.1-fold, 41-fold and 24-fold, respectively) and oqxB pump gene (48.2-fold, 60-fold and 58-fold, respectively). The increased expression of acrB was associated with the expression of ramA. However, to the best of our knowledge, studies on the mechanisms of resistance of K. pneumoniae strains to tigecycline are limited, especially in developing countries such as Iran.

Conclusions: In the present study, we found that both AcrAB-TolC and OqxAB efflux pumps may play an important role in tigecycline resistance in K. pneumoniae isolates. Finally, the emergence of ST11 molecular type of resistant isolates should be monitored in hospitals to identify factors leading to tigecycline resistance.

Received: July 05, 2022; Accepted: July 13, 2022; Published: July 20, 2022

Biography

Babak Asghari, Ms, PhD(2009-2014) of Medical Bacteriology, Department of Medical Microbiology, School of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran.