Drug Exposure and Susceptibility of Pyrazinamide Correlate with Treatment Response in Patients with Multidrug-Resistant Tuberculosis

Authors

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Abstract

Background Understanding the impact of pyrazinamide exposure and susceptibility on treatment response will help to optimize the treatment of multidrug-resistant tuberculosis (MDR-TB). This study aimed to investigate the association between pyrazinamide exposure, susceptibility, and response to MDR-TB treatment as well as find clinical thresholds of drug exposure for pyrazinamide.

Methods A prospective multi-center cohort study of participants with MDR-TB was conducted in three TB-designated hospitals in China. Univariate and multivariate analyses were applied to investigate the impact of pyrazinamide exposure and susceptibility on treatment responses. The Classification and Regression Tree (CART) analysis was used to identify clinical thresholds, which were further evaluated by multivariate analysis and receiver operating characteristic (ROC) curves.

Results The study included 143 patients with MDR-TB. The exposure/susceptibility ratio of pyrazinamide was associated with two-month culture conversion (adjusted risk ratio (aRR), 1.1; 95% confidence interval (CI), 1.07-1.20), six-month culture conversion (aRR, 1.1; 95% CI, 1.06-1.16), treatment success (aRR,1.07; 95% CI, 1.03-1.10), as well as culture conversion time (adjusted hazard ratio (aHR) 1.18; 95% CI,1.14-1.23). The threshold for optimal improvement in sputum culture results at month sixth of treatment was determined to be a pyrazinamide $AUC_{0\text{-}24h}$/MIC ratio of 7.8.

Conclusions In conclusion, the exposure/susceptibility ratio of pyrazinamide is associated with the treatment response of MDR-TB, which may change in different Group A drug-based regimens.