

Effects of ciprofloxacin concentrations on the resistance of uropathogen Escherichia coli: in vitro kinetics and dynamics simulation mode

Title	Effects of ciprofloxacin concentrations on the resistance of uropathogen Escherichia coli: in vitro kinetics and dynamics simulation mode
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Abstract	<p>Ciprofloxacin is recommended for complicated urinary tract infection (UTIs) caused by multidrug-resistant pathogens included Escherichia coli. However, its optimum dose for UTIs remains uncertain that may cause the bacterial resistance. This study was conducted to evaluate the effects of ciprofloxacin concentrations on the resistance of E. coli. The in vitro pharmacokinetic/pharmacodynamic (PK/PD) models of ciprofloxacin 750 mg oral dose twice a day for one day was compared to that dose of 500 mg twice a day for three days. Pharmacokinetic parameters i.e. AUC₀₋₂₄ and C_{max}. and pharmacodynamic parameter i.e. MIC of ciprofloxacin against E. coli which previously had MIC of 0.5 $\mu\text{g/mL}$ were determined. The PK/PD parameters combination of ciprofloxacin included AUC₀₋₂₄/MIC, C_{max}/MIC, and T>MIC ratio were used to evaluate its antimicrobial activities which was measured based on kill and re-growth rates of bacterial colony after the ciprofloxacin administration. The result showed that MIC value against E. coli increase to 8-16 and 32-64 $\mu\text{g/mL}$ after ciprofloxacin 750 and 500 mg administration, respectively, indicating the emergence of resistance. Both doses of ciprofloxacin were able to reduce the number of bacterial colony in the first two hours administration. However, after two hours administration, those both doses could make re-growth of bacterial colony. The value of AUC₀₋₂₄/MIC (120.42 \pm 1.27 vs. 92.62 \pm 9.36), C_{max}/MIC (4.75 \pm 0.21 vs. 3.26 \pm 0.30), and (T>MIC 89.58 \pm 7.22 vs. 76.39 \pm 9.39) after ciprofloxacin administration at dose of 750 mg were higher than those at dose of 500 mg. The increase of AUC₀₋₂₄/MIC and C_{max}/MIC values could reduce the number of bacteria colony, however could not for T>MIC value. In conclusion, the AUC₀₋₂₄/MIC and C_{max}/MIC parameters of ciprofloxacin can be used to evaluate its activity. In addition, ciprofloxacin twice per day at dose 500 mg for three days and 750 mg for one day are not different in the inhibition of E. coli resistance emergence.</p>
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