O115
2-hour Oral Session
MDR Enterobacteriaceae: clinical epidemiology and outcomes

Comparative study on the impact of quinolone therapy on colonization by ESBL(+) pathogens in non-ICU population

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Background: Quinolones are often used in the management of non-ICU patients with bacterial infections. While drug exposure has been associated with clinical and bacteriological outcome, the impact of quinolone treatment on the emergence of antimicrobial resistance pathogens in the gut flora is unknown. We therefore correlated ciprofloxacin and levofloxacin exposure with development of new colonization by ESBL(+) pathogens in non-ICU patients.

Material/methods: Patients hospitalized in medical and surgical wards of three centers and treated with ciprofloxacin (N=228) or levofloxacin (N=206) for more than 3 days were screened during treatment for ESBL(+) pathogens using rectal swabs and selective chromogenic medium. Patients colonized before treatment were excluded. Drug exposure was calculated for each patient using the KinFun1.07 Software (Medimatics, Maastricht, Netherlands) and previously published 2-compartment population pharmacokinetic models for ciprofloxacin (Forrest et al AAC 1993) and levofloxacin (Preston et al AAC 1998) with age, weight, race and creatinine clearance as covariates. The PK parameters fCmax, fCmin and fAUC were calculated for each patient and associated with the colonization rate by ESBL(+) pathogens using classification regression tree analysis (CART), Chi square test and multivariate logistic regression analysis.

Results: The colonization rates among patients treated with ciprofloxacin and levofloxacin were 25% and 13%, respectively. The median (range) dose of cirprofloxacin was 500 (100-1000) mg dosed every 12h (4h-24h) for 12 (3-136) doses with fAUCs, fCmax, fCmin 21 (3.3-64) mg.h/ml, 1.7 (0.5-6.7) mg/l, 0.22 (0.001-1.4) mg/l. The median (range) dose of levofloxacin was 500 (125-750) mg dosed every 24h (12h-24h) for 7 (3-43) doses with fAUCs, fCmax, fCmin 53 (16-183) mg.h/ml, 6.3 (2.2-13.3) mg/l, 0.8 (0.1-5) mg/l. Significant association was found between colonization and fAUC for both

drugs. For ciprofloxacin, the colonization rates in patients with fAUC >6.8 and <6.8 were 23% and 63%, respectively (p =0.009) whereas for levofloxacin the colonization rates for patients with fAUC >45.6 and <45.6 were 5% and 17%, respectively (p=0.016). The other PK parameters were significantly associated with colonization only for patients treated with levofloxacin. Multivariate logistic regression analysis showed that the PK parameters were significant independent risk factors together with other factors (center, age and ward).

Conclusions: A significant association was found between quinolones exposure and colonization by ESBL(+) pathogens. Levofloxacin was associated with lower colonization rates. Quinolones exposure can be optimized in order to reduce emergence of resistance.