Differences in Clinical Characteristics of Third Generation Cephalosporin Resistance and Treatment Outcomes in *Escherichia coli* and *Klebsiella pneumoniae* Bacteremia in Patients with Liver Cirrhosis

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Background

This study aimed to identify characteristics of third-generation cephalosporin (3GC) resistance in *Escherichia coli* and *Klebsiella pneumoniae* bacteremia (EC-KPB) in patients with LC, and to differentiate the clinical characteristics between the strains.

Materials/Methods

We retrospectively collected demographic, clinical and microbiological information on all EC-KPB episodes in LC patients ≥ 18 years of age hospitalized to a tertiary-care teaching hospital in South Korea from 2007 to 2018. Clinical characteristics associated with 3GC resistance and treatment failure were analyzed using a multivariate logistic regression model. Treatment failure was defined as persistent bacteremia for ≥ 7 days, or relapsed bacteremia ≤ 30 days, or all-cause mortality ≤ 30 days.

Results

3GC resistance rates of *E. coli* (EC) were 30.3% overall and increased significantly during the study period (*P*=0.001), while the rates of *K. pneumoniae* (KP) were not changed (24.3% overall) (P=0.994). Of total 356 EC-KPB episodes, 112 were caused by 3GC resistant strains. The factor associated with 3GC resistance was isolation of 3GC resistant strain ≤ 1 year in both EC (OR, 7.754; 95% CI, 2.094~28.716) and KP (OR, 2.774; 1.318~5.838) bacteremia (Figure 1). However, in EC bacteremia, beta-lactam or fluoroquinolone treatment ≤ 30 days was another factor associated with 3GC resistance (OR, 2.774; 95% CI, 1.318~5.838). The factor associated with treatment failure was high MELD score in both EC (OR, 1.193 at 1 increase; 95% CI, 1.118~1.272) and KP (OR, 1.163; 95% CI 1.083~1.250) bacteremia (Figure 2). Additionally, in EC bacteremia, non-alcoholic LC (OR 3.262; 95% CI 1.058~10.063), high Charlson Comorbidity Index (OR, 1.285; 95% CI 1.066~1.548), and inappropriate empirical antibiotic treatment (OR, 3.194; 95% CI 1.207~8.447) were associated with treatment failure.

Table 1. Factors for 3GC resistance in multivariate analysis

Associated factors	*E. coli*		*K. pneumoniae*	
	aOR*	95% C.I	aOR	95% C.I
MELD score	0.975	0.936-1.015	1.049	0.986-1.117
PITT bacteremia score	1.037	0.908-1.185	0.982	0.807-1.194
Male sex	1.299	0.647-2.608	0.381	0.115-1.265
Non-alcoholic LC	1.716	0.834-3.533	0.952	0.227-3.993
Location of bacteremia onset	2.390	0.982-5.818	2.711	0.296-24.798
Immunosuppressive agent	1.301	0.432-3.917	5.034	0.995-25.456
ICU admission≤30d	0.571	0.095-3.435	2.699	0.212-34.318
TACE≤1yr	1.506	0.749-3.026	0.735	0.212-2.541
Central catheter	0.787	0.140-4.408	0.081	0.004-1.504
Urinary catheter	4.794	0.940-24.449	7.830	1.104-55.557
Beta-lactam or Fluoroquinolone treatment≤30days	2.774	1.318-5.838	3.353	0.921-12.208
Previous identification of Cefotaxime resistance *Enterobacteriacea*	7.754	2.094-28.716	5.113	1.010-25.878

*aOR; adjusted OR

Table 2. Factors for treatment failure in multivariate analysis

Associated factors	*E. coli*		*K. pneumoniae*	
	aOR	95% C.I	aOR	95% C.I
Age	0.981	0.937-1.027	1.024	0.961-1092
MELD score	1.193	1.118-1.272	1.163	1.083-1.250
Charlson comorbidity index	1.285	1.066-1.548	1.027	0.810-1.303
Removal of infection focus	1.945	0.311-12.164	0.690	0.142-18.773
Male sex	0.711	0.277-1.823	0.831	0.249-2.776
Non-alcoholic LC	3.262	1.058-10.063	3.058	0.926-10.098
Appropriateness of empirical antibiotics	3.194	1.207-8.447	0.435	0.042-4.534
Location of bacteremia onset	3.721	0.704-19.661	1.929	0.516-7.215
Immunosuppressive agent	1.827	0.439-7.603	0.977	0.120-7.949
Neutropenia	24.326	0.380-1558.472	35.524	2.325-542.745

Conclusion

During the study period, 3GC resistant rate increased significantly in EC bacteremia, but not in KP bacteremia. In EC bacteremia, the severity of the underlying disease and the appropriateness of empirical antibiotics were associated with treatment failure, but there was no correlation in KP bacteremia. In *E. coli* bacteremia of LC patients, the appropriateness of empirical antibiotics was a factor associated with treatment outcome, and is the only correctable factor in the clinical setting. Since the same Enterobacteriaceae showed different clinical characteristics for 3GC resistance, empirical antibiotics should be selected in consideration of the individual characteristics of each strain.

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