

碳青霉烯類不敏感肺炎克雷伯菌的臨床特徵及β-內酰胺酶基因
— 聚焦於對窄效β-內酰胺類抗生素仍具感受性的菌株

Clinical Characteristics and Beta-lactamase Genes of Carbapenem-non-susceptible *Klebsiella pneumoniae* Strains Which Remains Susceptible to Beta-lactams of Narrower Spectra

I-Fan Lin (林怡汎)^{1,2,3}, Yu-ying Wu (吳祐穎)^{3,4}, Yi-Han Huang (黃意涵)³, Wei-Fang Chen (陳韋芳)², Chung-Hsu Lai (賴重旭)^{1,2,3*}

¹Division of Infectious Diseases, Department of Internal Medicine, E-Da Hospital (義大醫院內科部感染科) ²Department of Infection Control, E-Da Hospital (義大醫院感染管制部) ³School of Medicine, College of Medicine, I-Shou University (義守大學醫學院醫學系) ⁴Department of Neurosurgery, E-Da Hospital (義大醫院神經外科部)

Purpose

目的

- Some carbapenem-nonsusceptible *Klebsiella pneumoniae* (CnSKP) isolates are susceptible to β-lactams of narrower spectra.
- We aim to investigate their clinical significance and molecular characteristics.

Methods

方法

- CnSKP from clinical microbiology laboratory, from 2004 to 2019
- Patient characteristics and outcomes from medical records
- PCR for β-lactamases, and pulsed-field gel electrophoresis (PFGE)
- Risk factor and outcome analyses

Results

結果

197 CnSKP / 20465 *K. pneumoniae* isolates **0.96%** → 37 CnSKP isolates susceptible to β-lactams of narrower spectra → 34 CnSKP included

Antimicrobial agent	Carbapenemase genes detected (n=9)				Carbapenemase genes not detected (n=25)				p-value ^a
	Minimum inhibitory concentration, MIC (mg/L)			Susceptibility, n (%)	MIC (mg/L)			Susceptibility, n (%)	
	Range	50%	90%		Range	50%	90%		
amikacin	≤2-≥64	≤2	≥64	5 (55.6)	≤2-≥64	≤2	≥64	21 (84.0)	0.17
gentamicin	≥16-≥16	≥16	≥16	0	≤1-≥16	≥16	≥16	11 (44.0)	0.02
cefazolin	≥64-≥64	≥64	≥64	0	≤4-≥64	≥64	≥64	2 (8.0)	1.00
ceftriaxone	16-≥64	≥64	≥64	0	≤1-≥64	≥64	≥64	2 (8.0)	1.00
cefmetazole	≥64-≥64	≥64	≥64	0	≤1-≥64	≥64	≥64	4 (16.0)	0.55
cefepime	16-≥64	≥64	≥64	0	≤1-≥64	4	≥64	9 (36.0)	0.04
piperacillin-tazobactam	≥128-≥128	≥128	≥128	0	≤4-≥128	≥128	≥128	7 (28.0)	0.15
ertapenem	2-≥8	≥8	≥8	0	≤0.5-≥8	≥8	≥8	2 (8.0)	1.00
meropenem	≥16-≥16	≥16	≥16	0	2-≥16	4	≥16	0	NA
levofloxacin	≤0.12-≥8	1	≥8	6 (66.7)	≤0.12-≥8	1	≥8	16 (64.0)	1.00
ceftazidime-avibactam ^b	2->256	>256	>256	3 (33.3)	0.19->256	2	>256	19 (76.0)	0.04

^aComparison of the susceptibility rates between two groups. P-values ≤ 0.05 were marked in bold.

^bMICs for ceftazidime-avibactam were obtained by Etest.

Carbapenemase detected, 9 (26.5%)

- *bla*_{KPC}, 3 (33.3%)
- *bla*_{IMP-2}, 3 (33.3%)
- *bla*_{NDM}, 3 (33.3%)

- **91.2%** antibiotic inappropriateness
- **Site of infection** determined mortality (blood vs non-blood, odds ratio [OR] 18.0, *p* < .01), rather than antibiotic appropriateness (*p* = .38)
- Risk factors for carbapenemase and mortality:
 - **Hospital-acquired infection** (OR 1.7 and 17.9)
 - **Nonsusceptibility to cefepime** (OR 1.6 and 9.5)
 - **Meropenem MIC ≥ 16 mg/L** (OR 32.0 and 5.0)

Carbapenemase non-detected, 25 (73.5%)

- Extended-spectrum β-lactamase (ESBL) genes: 25, 100%

Mechanism of β-lactamase	No. of isolates	Meropenem MIC (mg/L)			
		2	4	8	≥16
ESBL					
<i>bla</i> _{SHV}	6	2	0	0	3
<i>bla</i> _{SHV} + <i>bla</i> _{TEM}	1	0	0	0	1
<i>bla</i> _{TEM} + <i>bla</i> _{CTX-M}	2	0	0	2	0
<i>bla</i> _{SHV} + <i>bla</i> _{TEM} + <i>bla</i> _{CTX-M}	2	0	2	0	0
ESBL + AmpC					
<i>bla</i> _{SHV} + <i>bla</i> _{DHA-1}	4	1	1	1	0
<i>bla</i> _{TEM} + <i>bla</i> _{DHA-1}	5	1	3	0	0
<i>bla</i> _{SHV} + <i>bla</i> _{TEM} + <i>bla</i> _{DHA-1}	3	0	2	0	0
<i>bla</i> _{SHV} + <i>bla</i> _{TEM} + <i>bla</i> _{CTX-M} + <i>bla</i> _{DHA-1}	1	0	1	0	0
<i>bla</i> _{TEM} + <i>bla</i> _{CMY} + <i>bla</i> _{DHA-1}	1	1	0	0	0

Conclusion

結論

- The composition of CnSKP is complicated.
- Characteristics of carbapenemase-producing *K. pneumoniae* (CPKP) are different from non-CPKP.