

doi: 10.3978/j.issn.2095-6959.2020.08.023

View this article at: <http://dx.doi.org/10.3978/j.issn.2095-6959.2020.08.023>

老年反复呼吸道感染产 ESBLs 细菌调查及耐药性分析

于群¹, 黄伟英², 李晓明³

(青岛市第九人民医院 1. 门诊部, 2. 供应室, 3. 消化内科, 青岛 266002)

[摘要] 目的: 研究老年人群(>60岁)反复呼吸道感染(recurrent respiratory tract infection, RRTI)产ESBLs细菌调查及耐药情况, 为老年人群RRTI的防治提供临床指导。方法: 统计分析2018年1月至2019年1月青岛市第九人民医院老年RRTI患者ESBLs细菌感染发生情况及其耐药性。结果: 384例RRTI老年患者共分离124株肺炎克雷伯菌及76株大肠埃希菌。产ESBLs总检出率为40.50%(81/200), 其中肺炎克雷伯菌产ESBLs检出率48.39%(60/124), 大肠埃希菌产ESBLs检出率27.63%(21/76); 老年RRTI细菌培养产ESBLs菌株对氨苄西林、头孢噻肟、头孢他啶、庆大霉素、左氧氟沙星、环丙沙星、复方新诺明、阿米卡星、哌拉西林耐药率均超过50%, 非产ESBLs菌株耐药率均低于50%, 产ESBLs菌株对氨苄西林、头孢噻肟、头孢他啶、头孢吡肟、庆大霉素、左氧氟沙星、环丙沙星、复方新诺明、哌拉西林耐药率均高于非产ESBLs菌株, 差异有统计学意义($P<0.05$)。结论: 了解老年人群RRTI产ESBLs细菌发生情况及耐药性有助于指导临床抗生素的合理使用, 提高老年人群RRTI的治疗效果。

[关键词] 老年人群; 反复呼吸道感染; 产ESBLs细菌; 耐药

Investigation on the ESBLs bacteria and analysis of drug resistance in elderly patients with recurrent respiratory tract infection

YU Qun¹, HUANG Weiyin², LI Xiaoming³

(1. Outpatient Department, 2. Supply Room, 3. Department of Gastroenterology, Qingdao Ninth People's Hospital, Qingdao 266002, China)

Abstract **Objective:** To investigate the ESBLs producing bacteria and their resistance in the elderly (>60 years old) with recurrent respiratory tract infection, and to provide clinical guidance for the prevention and treatment of recurrent respiratory tract infection in the elderly. **Methods:** From January 2018 to January 2019, the incidence of ESBLs bacterial infection in elderly patients with recurrent respiratory tract infection was analyzed. **Results:** A total of 124 strains of *Klebsiella pneumoniae* and 76 strains of *Escherichia coli* were isolated from 384 elderly patients with recurrent respiratory tract infection. The total detection rate of ESBLs was 40.50% (81/200), of which 48.39% (60/124) was from *Klebsiella pneumoniae* and 27.63% (21/76) was from *Escherichia coli*. The ESBLs strains from bacterial culture of elderly patients with recurrent respiratory tract infection were ampicillin, cefotaxime,

收稿日期 (Date of reception): 2020-03-18

通信作者 (Corresponding author): 李晓明, Email: yuqun91@163.com

ceftazidime, gentamicin, levofloxacin, ciprofloxacin, compound xinuoming and amikacin The resistance rate of ESBLs producing strains to ampicillin, cefotaxime, ceftazidime, cefepime, gentamycin, levofloxacin, ciprofloxacin, compound minophen and piperacillin was higher than that of non ESBLs producing strains ($P<0.05$). **Conclusion:** to understand the occurrence of ESBLs producing bacteria in elderly patients with recurrent respiratory tract infection and their drug resistance is helpful to guide the rational use of antibiotics and improve the therapeutic effect of elderly patients with recurrent respiratory tract infection.

Keywords elderly people; recurrent respiratory tract infection; ESBLs producing bacteria; drug resistance

反复呼吸道感染(recurrent respiratory tract infection, RRTI)系指每年呼吸道感染6次以上,或连续3次以上,每次间隔不超过1个月,为临床最为常见呼吸系统疾病。老年人群普遍通气功能及气道净化清除能力弱化、基础疾病众多,自身免疫力低下,易发生RRTI。研究^[1]显示:RRTI已成为老年人群尤其高龄老人的重要死因。细菌为RRTI发生的最常见病原体之一^[2],近年因抗生素的不合理应用,多重耐药菌株尤其产超广谱 β 内酰胺酶(ESBLs)菌株的出现,给临床治疗带来了极大的困难。本研究回顾性分析了2018年1月至2019年1月青岛市第九人民医院老年科200例RRTI患者ESBLs细菌感染发生情况及其耐药性分析,旨在为RRTI的防治提供临床指导。

1 对象与方法

1.1 对象

384例RRTI老年患者均来源于2018年1月至2019年1月青岛市第九人民医院呼吸内科门诊及住院患者,年龄60~93(72.6 \pm 4.8)岁,临床症状:头痛、畏寒、鼻塞、流涕、咽痛、咳嗽、少数低热,肺部干啰音。本研究经青岛市第九人民医院伦理会审核通过,研究对象享有知情权。

1.2 方法

1.2.1 细菌培养

遵照《全国临床检验操作规程》取老年呼吸道感染患者痰标本接种于血琼脂平板、巧克力平板,培养条件:35℃,5%CO₂培养24~48h,菌株鉴定采用梅里埃Vitek32(法国)细菌自动分析仪鉴定。质控菌株源于卫生部临床检验中心:肺炎克雷伯菌ATCC700603、大肠埃希菌ATCC25922。

1.2.2 药敏试验

采用纸片扩散法(Kirby-Bauer法)进行药敏试验,监测抗生素包括:氨苄西林、头孢噻肟、头孢西丁、头孢他啶、头孢吡肟、庆大霉

素、左氧氟沙星、环丙沙星、复方新诺明、亚胺培南、阿米卡星、哌拉西林、哌拉西林/他唑巴坦药敏纸片购自北京天坛药物生物技术开发公司。结果判读参照美国临床实验室标准化研究所CLSI2010标准^[3]。

1.3 ESBLs 检测

ESBLs检测为双纸片协同试验,利用头孢噻肟(30 μ g/片)、头孢他啶(30 μ g/片)两种药物检测,当两种药物中任意一种加克拉维酸(10 μ g/片)与不加克拉维酸的抑菌圈直径大于5mm时,确认该菌株为产ESBLs菌株。

1.4 统计学处理

采用WHONET 5.6进行数据分析,统计产ESBLs菌株与非产ESBLs菌株耐药情况,耐药率比较采用卡方检验分析比较, $P<0.05$ 为差异有统计学意义。

2 结果

2.1 老年 RRTI 细菌培养产 ESBLs 检出率

384例RRTI老年患者共分离124株肺炎克雷伯菌及76株大肠埃希菌。产ESBLs总检出率为40.50%(81/200),其中肺炎克雷伯菌产ESBLs检出率48.39%(60/124),大肠埃希菌产ESBLs检出率27.63%(21/76)。

2.2 老年RRTI细菌培养产ESBLs菌株与非产ESBLs菌株耐药分析

老年RRTI细菌培养产ESBLs菌株对氨苄西林、头孢噻肟、头孢他啶、庆大霉素、左氧氟沙星、环丙沙星、复方新诺明、阿米卡星、哌拉西林耐药率均超过50%,非产ESBLs菌株耐药率均低于50%,产ESBLs菌株对氨苄西林、头孢噻肟、头孢他啶、头孢吡肟、庆大霉素、左氧氟沙星、环丙沙星、复方新诺明、哌拉西林耐药率均高于非产ESBLs菌株,差异有统计学意义($P<0.05$,表1)。

表1 老年反复呼吸道产ESBLs菌株与非产ESBLs菌株耐药分析

Table 1 Resistance analysis of ESBLs producing strains and non ESBLs producing strains in elderly recurrent respiratory tract

抗生素	产ESBLs (n=81)		非产ESBLs (n=119)		χ^2	P
	株数	耐药率/%	株数	耐药率/%		
氨苄西林	80	98.77	61	51.26	54.332	<0.001
头孢噻肟	57	70.37	45	37.82	21.654	<0.001
头孢西丁	24	29.63	23	19.33	3.430	0.064
头孢他啶	48	59.26	23	19.33	31.681	<0.001
头孢吡肟	32	39.51	16	13.45	16.462	<0.001
庆大霉素	59	72.84	34	28.57	36.025	<0.001
左氧氟沙星	48	59.26	37	31.09	14.443	<0.001
环丙沙星	52	64.20	35	29.41	22.222	<0.001
复方新诺明	62	76.54	56	47.06	16.042	<0.001
亚胺培南	0	0.00	0	0.00	—	—
阿米卡星	19	23.46	18	15.13	1.692	0.193
哌拉西林	69	85.19	16	13.45	98.093	<0.001
哌拉西林/他唑巴坦	23	28.40	19	15.97	3.751	0.053

3 讨论

老年人群为RRTI的高发人群,且随年龄增长RRTI发病率及病死率呈正比例增长。研究^[4]显示:肠杆菌科细菌为RRTI最重要的致病菌,约占检出革兰阴性菌70%以上,其最重要的耐药机制就是产ESBLs,以大肠埃希菌和肺炎克雷伯菌最为常见^[5]。本研究数据显示:在老年RRTI患者中产ESBLs总检出率为40.50%,其中肺炎克雷伯菌产ESBLs检出率为48.39%,大肠埃希菌产ESBLs检出率为27.63%。研究^[6-7]指出:产ESBLs检出率一直呈上升趋势,ESBLs主要为广谱头孢菌素尤其第三代头孢菌素和单环 β -内酰胺类抗生素不合理应用产生,能水解多数青霉素、头孢菌素及氨基糖苷类的 β -内酰胺酶,相关细菌耐药质粒可通过结合转移导致耐药基因在细菌间的传播,在部分住院患者中易引起爆发性流行从而给临床的感染控制带来极大的挑战。

产ESBLs菌株多呈多重耐药属性^[8]。本研究药敏实验数据显示:RRTI老年患者产ESBLs菌株对多种抗生素耐药率均超过50%,亚胺培南比较敏感,与非产ESBLs菌株耐药性比较,产ESBLs菌株对氨苄西林、头孢噻肟、头孢他啶、头孢吡肟、庆大霉素、左氧氟沙星、环丙沙星、复方新诺明、哌

拉西林耐药率均高于非产ESBLs菌株,差异具有统计学意义。研究^[9-10]报道:碳氢酶烯类仍是产ESBLs菌株首选的药物;但临床研究^[11]指出:少部分菌株可产生KPC酶导致肺炎克雷伯等肠杆菌科对碳氢酶烯类耐药,尤其值得引起临床工作者的重视。内酰胺酶抑制剂合剂如哌拉西林/他唑巴坦、头霉素类头孢西丁以及氨基糖苷类如阿米卡星均有一定的敏感性,本研究上述药物的耐药率均低于30%,临床可根据药敏试验选择两种敏感抗生素联合治疗。产ESBLs菌株在老年患者中检出较为多见^[12],基础疾病长期用药对药物的耐药性造成了老年患者对感染性疾病的耐受力下降,产ESBLs菌株普遍对头孢菌素及单环酰胺类抗生素高度耐药,患者病情往往进展迅猛,甚至危及生命。因质粒介导的 β -内酰胺酶可分解单酰胺类和青霉素类抗菌药物及第3代头孢菌素,所以药敏结果即使敏感临床也不主张应用此类药物。ESBLs耐药基因编码位点多与其他耐药基因相连或连接导致菌株对氨基糖苷类、磺胺类及喹诺酮类药物耐药^[13]。

肠杆菌科细菌的多重耐药性已成为治疗过程中所面临的棘手难题, β -内酰胺酶也是肠杆菌科细菌耐药的主要耐药机制,以产ESBLs细菌感染老年RRTI病情尤为严重,预后较差。菌株的耐药情况多具有地区差异性,这与当地的临床用药

习惯关系密切, 监测本地区的感染菌株分布及耐药规律, 对提高临床治疗的有效率有重要的临床意义。

参考文献

1. Mansouri S, Kalantar Neyestanaki D, Shokoohi M, et al. Characterization of AmpC, CTX-M and MBLs types of β -lactamases in clinical isolates of *Klebsiella pneumoniae* and *Escherichia coli* producing extended spectrum β -lactamases in Kerman, Iran[J]. *Jundishapur J Microbiol*, 2014, 7(2):e8756.
2. Rosello A, Hayward AC, Hopkins S, et al. Impact of long-term care facility residence on the antibiotic resistance of urinary tract *Escherichia coli* and *Klebsiella*[J]. *J Antimicrob Chemother*, 2017, 72(4): 1184-1192.
3. 周丽燕, 洪滢, 蒋晓梅. 产超广谱 β -内酰胺酶肺炎克雷伯菌耐药性分析[J]. *临床合理用药杂志*, 2014, 22(13): 80-81. ZHOU Liyan, HONG Yan, JIANG Xiaomei. Analysis of production of extended spectrum beta lactamases of antibiotic resistance of *Klebsiella pneumoniae*[J]. *Chin J Clin Rat Drug Use*, 2014, 7(13): 80-81.
4. Abodakpi H, Chang KT, Sánchez Díaz AM, et al. Prevalence of extended-spectrum beta-lactamase and carbapenemase-producing bloodstream isolates of *Klebsiella pneumoniae* in a tertiary care hospital[J]. *J Chemother*, 2018, 30(2): 115-119.
5. 陈越, 孙景勇, 倪语星, 等. 2012年中国CHINET铜绿假单胞菌耐药性监测[J]. *中国感染与化疗杂志*, 2015, 15(3): 199-203. CHEN Yue, SUN Jingyong, NI Yuxing, et al. 2012 CHINET surveillance of antimicrobial resistance in *Pseudomonas aeruginosa* in China[J]. *Chinese Journal of Infection and Chemotherapy*, 2015, 15(3): 199-203.
6. 龚光明, 李桃, 张晓芳, 等. 产超广谱 β -内酰胺酶肠杆菌科细菌的临床分布与耐药性分析[J]. *中华医院感染学杂志*, 2016, 26(1):13-15. GONG Guangming, LI Tao, ZHANG Xiaofang, et al. Clinical distribution and drug resistance of extended-spectrum β -lactamase-producing *Enterobacteriaceae*[J]. *Chinese Journal of Nosocomiology*, 2016, 26(1): 13-15.
7. Park YS, Bae IK, Kim J, et al. Risk factors and molecular epidemiology of community-onset extended-spectrum β -lactamase-producing *Escherichia coli* bacteremia[J]. *Yonsei Med J*, 2014, 55(2): 467-475.
8. Ghafourian S, Sadeghifard N, Soheili S, et al. Extended Spectrum Beta-lactamases: Definition, Classification and Epidemiology[J]. *Curr Issues Mol Biol*, 2015, 17: 11-21.
9. 冯慧芬, 赵秋民, 段广才, 等. 产超广谱 β -内酰胺酶大肠埃希菌和肺炎克雷伯菌的耐药性及其危险因素分析[J]. *现代预防医学*, 2015, 42(7): 1325-1327, 1341. FENG Huifen, ZHAO Qiumin, DUAN Guangcai, et al. Drug resistance and risk factors of extended spectrum- β lactamases producing *Escherichia coli* and *Klebsiella pneumoniae*[J]. *Modern Preventive Medicine*, 2015, 42(7): 1325-1327.
10. Shakib P, Ramazanzadeh R, Taherikalani M, et al. Detection of extended-spectrum beta-lactamases (ESBLs) and antibiotic susceptibility patterns in *Klebsiella pneumoniae* in Western, Iran[J]. *Infect Disord Drug Targets*, 2018, 18(2): 156-163.
11. Wei DD, Wan LG, Yu Y, et al. Characterization of extended-spectrum beta-lactamase, carbapenemase, and plasmid quinolone determinants in *Klebsiella pneumoniae* isolates carrying distinct types of 16S rRNA methylase genes, and their association with mobile genetic elements[J]. *Microb Drug Resist*, 2015, 21(2): 186-193.
12. Elsharif RH, Ismail DK, El-Kholy YS, et al. Integron-mediated multidrug resistance in extended-spectrum β -lactamase-producing *Escherichia coli* and *Klebsiella pneumoniae* isolated from fecal specimens in Egypt[J]. *J Egypt Public Health Assoc*, 2016, 91(2): 73-79.
13. 孙利伟, 杜克凝, 田玉玲, 等. 新生儿产超广谱 β -内酰胺酶菌感染临床及耐药性分析[J]. *临床儿科杂志*, 2013, 31(3): 209-212. SUN Liwei, DU Kening, TIAN Yuling, et al. Analysis of clinical manifestations and drug resistance of extended-spectrum beta-lactamase producing bacteria infection in neonates[J]. *Journal of Clinical Pediatrics*, 2013, 31(3): 209-212.

本文引用: 于群, 黄伟英, 李晓明. 老年反复呼吸道感染产ESBLs细菌调查及耐药性分析[J]. *临床与病理杂志*, 2020, 40(8): 2076-2079. doi: 10.3978/j.issn.2095-6959.2020.08.023

Cite this article as: YU Qun, HUANG Weiyang, LI Xiaoming. Investigation on the ESBLs bacteria and analysis of drug resistance in elderly patients with recurrent respiratory tract infection[J]. *Journal of Clinical and Pathological Research*, 2020, 40(8): 2076-2079. doi: 10.3978/j.issn.2095-6959.2020.08.023