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分离自老年病房的鲍曼不动杆菌耐药机制初步研究*

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摘要 目的:检测老年住院患者分离的鲍曼不动杆菌的主要耐药基因,并研究不同耐药基因型与耐药表型之间的对应关系。**方法:**用PCR方法检测分离自老年住院患者的不同标本来源的170例非重复鲍曼不动杆菌的耐药基因。检测的耐药基因包括D类碳青霉烯酶:*bla*_{OXA-51}, *bla*_{OXA-23}, *bla*_{OXA-24}, *bla*_{OXA-58}, B类金属碳青霉烯酶:*bla*_{VIM}, *bla*_{IMP}, *bla*_{SIM}, *bla*_{GIM}, *bla*_{DIM}, *bla*_{NDM-1},以及A类超广谱β-内酰胺酶:*bla*_{KPC},共计11种。根据检测结果对菌株进行基因分型,并研究不同基因型与CRAB和CSAB这两种耐药表型之间的对应关系。**结果:**170株鲍曼不动杆菌的固有基因*bla*_{OXA-51}均为阳性,此外,主要检出基因为*bla*_{OXA-23},共124株。另外检测出*bla*_{KPC} 12株, *bla*_{OXA-58} 6株, *bla*_{NDM-1} 3株, *bla*_{SIM} 2株, *bla*_{OXA-24}, *bla*_{VIM}和*bla*_{DIM}各1株,IMP和GIM未检出。根据检出耐药基因的不同组合,分为*bla*_{OXA-51} + *bla*_{OXA-23} 阳性为基础的A型(124株)及*bla*_{OXA-23} 阴性为基础的B型(*bla*_{OXA-51}, 39株)、C型(*bla*_{OXA-51} + *bla*_{OXA-58}, 6株)、D型(*bla*_{OXA-51} + *bla*_{OXA-24}, 1株)共计四类基因型。从耐药表型来看,128株碳青霉烯耐药菌中有122株*bla*_{OXA-23}为阳性,在CRAB中占95.3%(122/128),42株碳青霉烯敏感株中,有40株*bla*_{OXA-23}为阴性,在CSAB中占95.2%(40/42)。**结论:**老年病房流行的耐碳青霉烯鲍曼不动杆菌的耐药基因型以*bla*_{OXA-23}阳性为主。其与鲍曼不动杆菌CRAB耐药表型、*bla*_{OXA-23}阴性与CSAB耐药表型之间有良好的对应关系。

关键词:鲍曼不动杆菌;老年患者;耐药基因**中图分类号:**R446.5 **文献标识码:**A **文章编号:**1673-6273(2019)01-99-05The Preliminary Research on Resistance Mechanism of *Acinetobacter baumannii* Prevalent in Geriatric Wards*ZHOU Yu, GONG Mei-liang, YAN Zhong-qiang, CONG Yu-long, DENG Xin-li[△]

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ABSTRACT Objective: To detect the major resistance genes of *A. baumannii* isolated from elderly hospitalized inpatients, and to research the relationship between the resistance genotype and the drug resistant phenotype. **Methods:** PCR was used to detect the resistance genes of 170 non repetitive AB isolated from different specimens of elderly inpatients, and the resistant genes included the class D carbapenem enzyme: *bla*_{OXA-51}, *bla*_{OXA-23}, *bla*_{OXA-24}, *bla*_{OXA-58}, class B carbapenem enzyme: *bla*_{VIM}, *bla*_{IMP}, *bla*_{SIM}, *bla*_{GIM}, *bla*_{DIM}, *bla*_{NDM-1}, and type A extended spectrum beta lactamases: *bla*_{KPC}. Genotyping was applied according to the test results, and the corresponding relationships between different genotypes and phenotypes (including CRAB and CSAB) were investigated. **Results:** *bla*_{OXA-51} was detected in all 170 isolates and *bla*_{OXA-23} was detected in 124 isolates. The other test results were as follows: *bla*_{KPC} (12 strains), *bla*_{OXA-58} (6 strains), *bla*_{NDM-1} (3 strains), *bla*_{SIM} (2 strains), *bla*_{OXA-24} (1 strains), *bla*_{VIM} (1 strains) and *bla*_{DIM} (1 strains), and *bla*_{IMP} and *bla*_{GIM} genes were not detected any more. According to the different combination of drug resistance genes, 170 strains were divided into four genotypes: type A was based on *bla*_{OXA-51} + *bla*_{OXA-23} (124 strains), and others were based on negative of *bla*_{OXA-23}: type B (*bla*_{OXA-51}, 39 strains), type C (*bla*_{OXA-51} + *bla*_{OXA-58}, 6 strains), type D (*bla*_{OXA-51} + *bla*_{OXA-24}, 1 strain). In the resistant phenotype, 122 of the 128 carbapenems resistant strains were positive for *bla*_{OXA-23}, *bla*_{OXA-23} positive strains in CRAB accounted for 95.3% (122/128), 40 of 42 carbapenems susceptible strains were negative for *bla*_{OXA-23}, *bla*_{OXA-23} negative strains in CSAB accounted for 95.2% (40/42). **Conclusion:** The resistant genotypes of carbapenem resistant AB prevalent in geriatric wards were mainly *bla*_{OXA-23} positive. There was a good correspondence between *bla*_{OXA-23} positive and CRAB phenotype, and correspondingly between *bla*_{OXA-23} negative and CSAB phenotype.

Key words: *Acinetobacter baumannii*; Senile Patients; Resistance gene**Chinese Library Classification(CLC):** R446.5 **Document code:** A**Article ID:** 1673-6273(2019)01-99-05

前言

鲍曼不动杆菌(*Acinetobacter baumannii*, AB)广泛分布于自然界,在医院内环境、空气及皮肤表面均能发现^[1],是医院获得

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性感染的常见条件致病菌之一,常引起医院获得性肺炎、泌尿系统感染、血流感染等,尤其在免疫力低下的ICU患者中分离率较高^[2-5]。近年来AB耐药性呈大幅上升趋势,多重耐药AB的快速传播归因于其基因组在面对逆境和压力时可以迅速突变的能力^[6-8]。多重耐药AB感染患者由于治疗选择严重受限预后很差,国内研究显示ICU中多重耐药AB感染患者死亡率达47%,美国研究表明这一数据可高达52%-66%,而多重耐药AB引起的新生儿菌血症亦可导致58%的死亡率^[9-12]。AB耐药机制很复杂,主要分为生物学和物理学作用两大类,前者包括产耐药酶、对不同效应酶进行修饰或降解、青霉素结合蛋白改变等,后者包括膜孔蛋白缺失造成抗菌药物难以进入菌体、外排泵表达造成抗菌药物的加速外排等。诸多机制中, β -内酰胺类耐药基因尤其是碳青霉烯酶的产生在AB的多重耐药方面发挥重要作用^[13-15]。

现已报道的AB碳青霉烯酶,涉及到Ambler分类的A、B、D类酶。AB常见的是D类酶中 bla_{OXA-23} , bla_{OXA-24} , bla_{OXA-51} 和 bla_{OXA-58} 基因谱系编码的OXA类产物,这些基因可能位于质粒或者染色体,克拉维酸不能抑制酶的活性,在世界的很多地方都被发现^[16,17]。AB中普遍存在的 bla_{OXA-51} 基因使其成为AB鉴定的重要遗传标记,其编码产物可以水解青霉素类和碳青霉烯类,但作用非常弱,亦不能有效对抗广谱的头孢菌素类抗菌药物^[18]。 bla_{OXA-51} 对 β -内酰胺的耐药性需要基因上游插入序列ISAba1,后者作为一个强转录启动子而存在。此外,AB中还发现了B类金属碳青霉烯酶中的 bla_{VIM} , bla_{IMP} 和 bla_{SIM} 型,尤其在亚洲太平洋地区和拉丁美洲多见。这些酶使菌株对碳青霉烯类和除氨基糖苷之外的其他 β -内酰胺类抗生素高水平耐药,且发现与复杂的I类整合子有关^[19]。此外,大范围的A类超广谱 β -内酰胺酶,包括 bla_{CTX-M} , bla_{TEM} , bla_{SHV} , bla_{GES} , bla_{SCO} , bla_{PER} , bla_{KPC} 和 bla_{VEB} 家族,都在AB的研究中发现过^[20]。以上这些针对AB耐药基因的研究多集中在普通调研或ICU、新生儿等群体,老年患者由于免疫力低下和长期住院也是AB感染的易感人群,其研究资料却相对少见^[21]。

本研究以分离自老年住院患者的AB为实验对象,检测以下耐药基因:D类碳青霉烯酶 bla_{OXA-51} 、 bla_{OXA-23} 、 bla_{OXA-24} 、 bla_{OXA-58} (其中 bla_{OXA-51} 为AB固有基因);B类金属碳青霉烯酶中的 bla_{VIM} , bla_{IMP} , bla_{SIM} , bla_{GIM} , bla_{DIM} , bla_{NDM-1} ;A类超广谱 β -内酰胺酶 bla_{KPC} ,分析老年病房AB耐药基因的分子分型。以期明确老年住院患者多重耐药AB的分子耐药机制,及耐药基因与耐药表型之间的关系,为进一步的诊疗防治提供理论基础和依据。

1 材料与方法

1.1 菌株来源

从2014到2015年共收集到170例非重复AB菌株,源自170位住院超过48小时的有感染指征的老年患者,年龄61-99岁,平均86.8岁。90%菌株分离自呼吸道标本,其余来源于尿,导管,胆汁和胸腹水。其中包括作为试验组的128株多重耐药的碳青霉烯耐药株(CRAB)及作为对照组的42株对各类抗菌药物较敏感的碳青霉烯敏感菌株(CSAB)。

1.2 主要试剂与仪器

MH琼脂平板(OXOID);VITEK2全自动鉴定和药敏分析

仪(法国生物梅里埃);PCR仪(PE公司);稳压稳流电泳仪(北京六一仪器厂);数码凝胶图像处理系统(上海小源科技有限公司);PCR反应试剂盒(Invitrogen);GeneRuler 100 bp Ladder (Fermentas公司);K10CD干式恒温器(杭州蓝焰科技公司)。

1.3 方法

1.3.1 引物设计和合成 引物序列参考文献^[22-25],具体见表1,均由上海生工生物公司合成。

1.3.2 模板制备 采用煮沸法,将MH平板上过夜培养的新鲜菌落均匀溶于2 mL灭菌纯水中,调成1麦氏浓度,取1-1.5 mL于灭菌EP管中,置于K10CD干式恒温器10 min后,高速(13000 r/min)离心10 min,分离出的上清液作为模板备用。

1.3.3 PCR反应体系和反应条件 反应总体积25 μ L,包括Taq酶1 μ L,10 $\times$ buffer 2.5 μ L,模板1 μ L(10 μ M),引物各1 μ L,纯水补足至25 μ L(需18.5 μ L)。反应条件:94 $^{\circ}$ C预变性4 min后,进行30个扩增过程的循环(变性、退火、延伸):94 $^{\circ}$ C 30 s,52-56 $^{\circ}$ C 60 s,72 $^{\circ}$ C 70 s。最终72 $^{\circ}$ C 5 min。反应产物置于4 $^{\circ}$ C备用。

1.3.4 电泳 用TAE缓冲液配置1.5%的琼脂糖凝胶,加热融化后加入3 μ L的EB,倒入电泳槽凝固。拔出梳子,每孔加入与Loading buffer充分混匀后的PCR产物10 μ L,Marker加5 μ L。电压120 V,电泳40 min,在凝胶成像仪上打开紫外灯进行观察,记录结果。

1.3.5 扩增产物的验证 将每种产物的阳性结果随机挑选一个送上海生工测序,其结果在网上进行Blast比对分析,以确定是否为目的基因。

1.4 统计分析

应用SPSS19.0统计软件对实验结果进行数据分析,采用卡方检验进行两组率的比较, $P<0.05$ 为差异有统计学意义。

2 结果

2.1 耐药基因扩增结果

170株菌共扩增出 bla_{OXA-51} 170株, bla_{OXA-23} 124株, bla_{OXA-58} 6株, bla_{OXA-24} 1株, bla_{IMP} 0株, bla_{GIM} 0株, bla_{VIM} 和 bla_{DIM} 各1株, bla_{SIM} 2株, bla_{NDM-1} 3株, bla_{KPC} 12株(阳性结果见图1)。

2.2 AB耐药基因的分子分型

根据检测结果中的优势耐药基因存在与否,将170株AB人为分成四类基因型的组合,分别是以 bla_{OXA-51} + bla_{OXA-23} 阳性为基础的A型(124株)及 bla_{OXA-51} 阳性, bla_{OXA-23} 阴性为基础的B型(bla_{OXA-51} ,39株)、C型(bla_{OXA-51} + bla_{OXA-58} ,6株)、D型(bla_{OXA-51} + bla_{OXA-24} ,1株)。其中A型在 bla_{OXA-51} + bla_{OXA-23} 基础上,与其它碳青霉烯酶基因有不同组合,故又分为A1~A8八种亚型:A1是单纯 bla_{OXA-51} + bla_{OXA-23} 的组合,A2~A8是以 bla_{OXA-51} + bla_{OXA-23} 为基础,与其他不同酶的组合(详见表2)。

2.3 AB耐药基因型与耐药表型的关系

将170株菌按照对碳青霉烯类药物敏感性不同分为耐药的CRAB组和敏感的CSAB组,分别统计耐药基因型在各组的比例,发现CRAB组以耐药基因A型为主,为122株(95.3%),即以 bla_{OXA-23} 为主;CSAB组以B型为主,即95.2%的菌株除固有基因外,不含其他碳青霉烯酶基因(详见表3)。CRAB和CSAB两组间 bla_{OXA-23} 阳性率的差异有统计学意义($P<0.01$)。

表 1 耐药基因的引物序列
Table 1 Primer sequence of drug-resistant genes

Primers	Sequence	Target gene
OXA-23F	5'-GATCGGATTGGAGAACCAGA-3'	<i>bla</i> _{OXA-23}
OXA -23R	5'- ATTTCTGACCGCATTTCCAT -3'	
OXA -24F	5'- GGTTAGTTGGCCCCCTTAAA -3'	<i>bla</i> _{OXA-24}
OXA -24R	5'-AGTTGAGCGAAAAGGGGATT-3'	
OXA -51F	5'- TAATGCTTTGATCGGCCTTG-3'	<i>bla</i> _{OXA-51}
OXA -51R	5'- TGGATTGCACTTCATCTTGG-3'	
OXA -58F	5'- AAGTATTGGGGCTTGTGCTG -3'	<i>bla</i> _{OXA-58}
OXA -58R	5'- CCCCTCTGCGCTCTACATAC -3'	
VIM-F	5'- GATGGTGTGTTGGTCGCATA -3'	<i>bla</i> _{VIM}
VIM-R	5'- CGAATGCGCAGCACCAG -3'	
IMP-F5	5'- GGAATAGAGTGGCTTAAATCTC -3'	<i>bla</i> _{IMP}
IMP-R	5'- GGTTTAAAYAAAACAACCACC -3'	
SIM-F	5'- TACAAGGGATTTCGGCATCG-3'	<i>bla</i> _{SIM}
SIM-R	5'- TAA TGG CCT GTT CCC ATG TG-3'	
GIM-F	5'- TCGACACACCTTGGTCTGAA -3'	<i>bla</i> _{GIM}
GIM-R	5'- AACTTCCAACCTTGCCATGC -3'	
NDM-F	5'-GGTTTGCGCATCTGGTTTTC -3'	<i>bla</i> _{NDM}
NDM-R	5'-CGGAATGGCTCATCACGATC -3'	
DIM-F	5'-GCTTGTCTTCGCTTGCTAACG -3'	<i>bla</i> _{DIM}
DIM-R	5'- CGTTCGGCTGGATTGATTTG-3'	
KPC-F	5'- CATTCAAGGGCTTTCTTGCTGC -3'	<i>bla</i> _{KPC}
KPC-R	5'- ACGACGGCATAGTCATTTGC -3'	

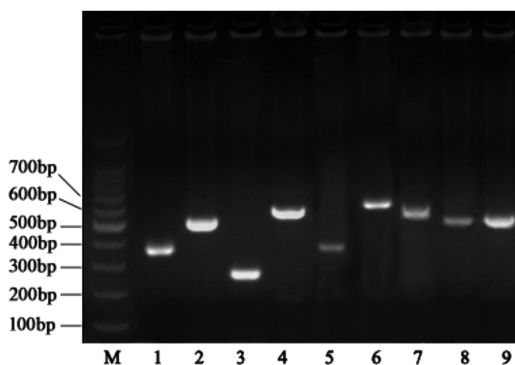


图 1 鲍曼不动杆菌耐药基因扩增电泳图

Fig.1 Electrophoretogram of resistance gene of *A. baumannii*

From left to right: Marker, *bla*_{OXA-51}(353bp), *bla*_{OXA-23}(501bp), *bla*_{OXA-24}(246bp), *bla*_{OXA-58}(599bp), *bla*_{VIM}(390bp), *bla*_{DIM}(699bp), *bla*_{NDM-1}(621bp), *bla*_{SIM}(570bp), *bla*_{KPC}(538bp).

3 讨论

CRAB 的研究以往多集中在 ICU 或新生儿,但针对老年病房 CRAB 的感染特点、耐药性和耐药机制的研究资料相对较少。老年患者作为特殊群体,由于免疫力低、基础疾病多、住院

时间长、病情较危重等特点,也应该作为多重耐药 AB 感染和爆发的重点监测对象。本研究针对分离自老年患者的 CRAB 和 CSAB, 选择具有代表性的 D 类碳青霉烯酶:*bla*_{OXA-51},*bla*_{OXA-23},*bla*_{OXA-24},*bla*_{OXA-58}, B 类金属碳青霉烯酶 *bla*_{VIM},*bla*_{IMP},*bla*_{SIM},*bla*_{GIM},*bla*_{DIM},*bla*_{NDM-1}, 以及 A 类超广谱 β- 内酰胺酶 *bla*_{KPC} 的耐药基因进行检测。根据检测结果中优势耐药基因存在与否,将菌株分为以优势基因 *bla*_{OXA-23} 阳性为基础的 A 型及 *bla*_{OXA-23} 阴性为基础的 B、C、D 基因型。在十一种常见碳青霉烯酶基因中,所有菌株都能检出 AB 固有基因 *bla*_{OXA-51},与以往报道一致。

碳青霉烯耐药的 CRAB 中,*bla*_{OXA-23} 的检出率最高,阳性率达 95.3%,这与既往报道中亚洲地区多重耐药 AB 以 *bla*_{OXA-23} 流行株为主是一致的。多项分子流行病学调查研究显示,亚洲地区 CRAB 以产 *bla*_{OXA-23} 碳青霉烯酶为主,中国、韩国、日本及一些东南亚国家均报道过携带 *bla*_{OXA-23} 的多重耐药 AB 的爆发流行^[26-28],欧洲地区也偶有 *bla*_{OXA-23} AB 流行株的报道^[29]。本研究证实了在老年患者这个特殊群体中,CRAB 分子流行特点仍以 *bla*_{OXA-23} 为主,与亚洲地区整体流行趋势一致。另外,*bla*_{OXA-23} 的突变体 *bla*_{OXA-239} 已被发现于临床分离株,其在水解头孢菌素和氨曲南方面具有更高的效率^[30]。但本研究中的 *bla*_{OXA-23} 经过测序,未发现 *bla*_{OXA-239} 突变体。此外,CRAB 中同一耐药基因检出

表 2 170 株 AB 碳青霉烯酶耐药基因型的不同组合

Table 2 Different combinations of carbapenem resistant genotypes of 170 *A. baumannii*

<i>bla</i> _{OXA-51}	<i>bla</i> _{OXA-23}	<i>bla</i> _{OXA-24}	<i>bla</i> _{OXA-58}	<i>bla</i> _{VIM}	<i>bla</i> _{SIM}	<i>bla</i> _{DIM}	<i>bla</i> _{NDM-1}	<i>bla</i> _{KPC}	Drug-resistant genotypes	Quantity of strains
+	+	-	-	-	-	-	-	-	A1	108
+	+	-	-	-	-	-	-	+	A2	10
+	+	-	-	-	-	+	-	-	A3	1
+	+	-	-	-	-	-	+	+	A4	1
+	+	-	-	+	-	-	+	-	A5	1
+	+	-	-	-	-	+	-	-	A6	1
+	+	-	-	-	+	-	-	-	A7	1
+	+	-	-	-	+	-	-	+	A8	1
+	-	-	-	-	-	-	-	-	B	39
+	-	-	+	-	-	-	-	-	C	6
+	-	+	-	-	-	-	-	-	D	1

表 3 170 株 AB 碳青霉烯酶耐药基因型的不同组合与耐药表型的关系

Table 3 The relationship between different combinations of carbapenem resistant genotypes and drug resistant phenotype of 170 *A. baumannii*

Drug-resistant phenotype(n)	Drug-resistant genotypes	Different combinations of drug-resistant genes	Quantity of strains(n, %)
CRAB (128)	A1	<i>bla</i> _{OXA-51} + <i>bla</i> _{OXA-23}	106(82.8%)
	A2	<i>bla</i> _{OXA-51} + <i>bla</i> _{OXA-23} + <i>bla</i> _{KPC}	10(7.8%)
	A3	<i>bla</i> _{OXA-51} + <i>bla</i> _{OXA-23} + <i>bla</i> _{DIM}	1(0.8%)
	A4	<i>bla</i> _{OXA-51} + <i>bla</i> _{OXA-23} + <i>bla</i> _{KPC} + <i>bla</i> _{NDM-1}	1(0.8%)
	A5	<i>bla</i> _{OXA-51} + <i>bla</i> _{OXA-23} + <i>bla</i> _{NDM-1} + <i>bla</i> _{VIM}	1(0.8%)
	A6	<i>bla</i> _{OXA-51} + <i>bla</i> _{OXA-23} + <i>bla</i> _{NDM-1}	1(0.8%)
	A7	<i>bla</i> _{OXA-51} + <i>bla</i> _{OXA-23} + <i>bla</i> _{SIM}	1(0.8%)
	A8	<i>bla</i> _{OXA-51} + <i>bla</i> _{OXA-23} + <i>bla</i> _{KPC} + <i>bla</i> _{SIM}	1(0.8%)
	B	<i>bla</i> _{OXA-51}	3(2.3%)
	C	<i>bla</i> _{OXA-51} + <i>bla</i> _{OXA-58}	2(1.6%)
	D	<i>bla</i> _{OXA-51} + <i>bla</i> _{OXA-24}	1(0.8%)
CSAB (42)	B	<i>bla</i> _{OXA-51}	36(85.7%)
	C	<i>bla</i> _{OXA-51} + <i>bla</i> _{OXA-58}	4(9.5%)
	A1	<i>bla</i> _{OXA-51} + <i>bla</i> _{OXA-23}	2(4.8%)

率超过 95%,提示病房内发生了克隆传播的可能性,这一点可通过 PFGE 实验加以证实。

在 CSAB 敏感株中,*bla*_{OXA-23} 的阳性率只有 4.8%,也即是阴性率为 95.2%。这个结果难以与其他研究进行比较,因为既往研究多集中在检测耐药 AB 的耐药基因,较少关于 AB 耐药株和敏感株之间耐药基因的比对,也缺少耐药基因与耐药表型之间对应关系和对应程度的资料。本研究证实了在 CSAB 中同样有 *bla*_{OXA-23} 的存在,但比例极低,敏感株中偶发耐药株的优势基因,进一步说明了 AB 耐药机制的复杂性,在表达调控及一些协同或制约作用的影响下,耐药基因与耐药表型并不能绝对对应,但对大多数菌株来说具有一定代表性。

在所有检测的碳青霉烯酶基因中,*bla*_{OXA-23} 的阳性率和阴性率与 CRAB 及 CSAB 的对应程度是最高的,具有统计学意义,提示了利用此基因从分子水平对 CRAB 进行快速检测和筛查的可能性。虽然在 CRAB 中也有其他几种耐药基因的检出;*bla*_{KPC}、*bla*_{OXA-58}、*bla*_{NDM-1}、*bla*_{SIM}、*bla*_{OXA-24}、*bla*_{VIM} 和 *bla*_{DIM},但这几种耐药基因在 CRAB 中的百分比都比较低(0.8~7.8%),可除外对 CRAB 的代表性。对照耐药表型后可发现,这些菌株在 *bla*_{OXA-23} 的基础上,即使多了其他金属酶或超广谱 β- 内酰胺酶,在对各类药物的耐药程度上跟只有 *bla*_{OXA-23} 阳性的菌株相比并没有明显区别,说明在 *bla*_{OXA-23} 的基础上,其余金属酶或超广谱 β- 内酰胺酶对菌株耐药表型的改变作用不大,*bla*_{OXA-23} 的存在

与否才是决定 AB 对碳青霉烯类抗菌药物是否耐药的关键因素。分析结果显示有几株菌的耐药基因型与耐药表型之间的对应关系比较少见,提示除了耐药基因的存在与否外,耐药基因本身的表达调控及与其他耐药机制之间的协作或制约作用也对耐药表型的改变至关重要。

4 结论

本研究通过对分离自老年患者的 AB 十一种耐药基因的检测及对 AB 碳青霉烯敏感株和耐药株之间耐药基因的比对,明确了其中一种碳青霉烯酶基因 *bla_{OXA-23}* 与碳青霉烯耐药表型的良好对应关系,并通过本次分离菌株中 *bla_{OXA-23}* 对 CRAB 高达 95% 的阳性预测值和对 CSAB 的 95% 阴性预测值,提示了利用 *bla_{OXA-51}* + *bla_{OXA-23}* 的组合形式对 CRAB 进行快速分子诊断和筛查的可能性。对 AB 耐药基因型的分析及其与耐药表型之间对应关系的研究,有利于加深对 AB 产生多重耐药性的分子机制的了解,通过明确耐药基因对耐药表型的作用,为抗生素新药的作用靶点和研发提供新策略,并为建立耐药 AB 的分子水平的快速诊断提供理论基础和依据。

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