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细菌耐药监测
Bacterial Resistance Surveillance

2017－2024 年北京市某三甲医院鲍曼不动杆菌复合群的检出情况和耐药分布

Detection and antimicrobial resistance distribution of *Acinetobacter baumannii* complex in a grade A tertiary hospital in Beijing (2017－2024)

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摘要:目的 分析 2017－2024 年北京市某三甲医院鲍曼不动杆菌复合群(*Acinetobacter baumannii* complex, ABC)的菌种分布特征及耐药性差异,为临床微生物精准鉴定和抗菌药物合理使用提供科学依据。**方法** 基于本院细菌耐药监测网数据,收集 ABC 复合群菌株的耐药监测资料。用质谱仪对菌种进行精确鉴定,用 WHONET 5.6 软件分析菌种的药敏结果,组间耐药率比较用 SPSS 26.0 进行卡方检验。**结果** 共纳入首次分离的 ABC 菌株 2 752 株,其中鲍曼不动杆菌(ABA)占 91.75%,皮特不动杆菌(APT)占 6.90%,医院不动杆菌(ANO)占 1.31%,另检出醋酸钙不动杆菌 1 株。痰液和尿液为最主要的标本来源,ABA 和 APT 所致血流感染亦较常见。药敏结果显示:各菌种对 12 种常用抗菌药物的耐药率差异均具有统计学意义(均 $P<0.05$)。ABA 耐药率最高,ANO 次之,APT 敏感性最佳。ABA 对 β－内酰胺类抗菌药物,如哌拉西林/他唑巴坦、头孢他啶、亚胺培南和美罗培南的耐药率均超过 80%;而 ANO 对上述药物的耐药率为 30%～50%,APT 仅为 10%～30%。ABA 与 ANO 对复方新诺明和米诺环素的耐药率比较,在统计学上差异均无统计学意义(均 $P>0.05$)。醋酸钙不动杆菌仅对多西环素和复方新诺明耐药,而对 β－内酰胺类和氟喹诺酮类均敏感。**结论** ABC 不同菌种在标本分布、分离科室及耐药谱方面存在显著异质性,建议微生物实验室加强菌种精准鉴定与耐药性动态监测,为临床抗感染治疗提供精准指导。

关键词:鲍曼不动杆菌;皮特不动杆菌;医院不动杆菌;准确鉴定;基质辅助激光解吸电离飞行时间质谱;耐药率

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Abstract: Objective To analyze the species distribution and antimicrobial resistance profiles of *Acinetobacter baumannii* complex (ABC) isolates from a Grade A tertiary hospital in Beijing (2017－2024), providing evidence for clinical microbiological identification and antimicrobial therapy. **Methods** ABC isolates were collected from the hospital's antimicrobial resistance surveillance network. Species identification was performed by mass sectrometry and susceptibility testing was analyzed using WHONET 5.6. Statistical comparisons of resistance rates were performed with SPSS 26.0 (chi－square test). **Results** Among 2 752 non－repetitive ABC isolates, *Acinetobacter baumannii* (ABA) accounted for 91.75%, followed by *Acinetobacter pittii* (APT, 6.90%) and *Acinetobacter nosocomialis*

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(ANO, 1.31%). Sputum and urine were the predominant specimen types, with ABA and APT frequently isolated from bloodstream infections. The resistance profile varied statistically significantly defferences across the bacterial species for all 12 common antimicrobials (all $P<0.05$). Among these, ABA demonstrated the highest resistance rates, ANO showed an intermediate profile, and APT was the most susceptible. Specifically, ABA exhibited resistance rates exceeding 80% to β-lactam antibiotics, including piperacillin/tazobactam, ceftazidime, imipenem and meropenem. In contrast, ANO showed resistance rates of 30%-50%, and APT only 10%-30% to the same agents. Resistance profiles between ABA and ANO differed statistically significantly except for trimethoprim-sulfamethoxazole and minocycline (all $P>0.05$). The single *Acinetobacter calcoaceticus* isolate was only resistant to doxycycline and trimethoprim-sulfamethoxazole, while remaining susceptible to all other β-lactam and fluoroquinolone agents tested. **Conclusion** ABC species exhibit distinct clinical distributions and resistance patterns, emphasizing the need for accurate species identification and ongoing resistance surveillance to guide appropriate empirical therapy.

Key words: *Acinetobacter baumannii*; *Acinetobacter pittii*; *Acinetobacter nosocomialis*; accurate identification; matrix-assisted laser desorption ionization time of flight mass spectrometry; resistance rate

鲍曼不动杆菌复合群(*Acinetobacter baumannii* complex, ABC)因其高感染率及多重耐药性,已成为全球范围内导致感染发病率和病死率上升的重要病原体之一[1]。ABC是一组在表型上难以区分的病原菌,目前已明确包括6种菌种。其中,鲍曼不动杆菌(*Acinetobacter baumannii*, ABA)是人类主要的致病菌,常引起高病死率的医院感染[2]。医院不动杆菌(*Acinetobacter nosocomialis*, ANO)和皮特不动杆菌(*Acinetobacter pittii*, APT)也与医院获得性感染及社区获得性感染密切相关[3]。近年来,从人类临床样本中和环境中陆续分离出新菌种,如赛氏不动杆菌(*Acinetobacter seifertii*, ASE)、乳酸不动杆菌(*Acinetobacter lactucae*, ALA)[4]和醋酸钙不动杆菌(*Acinetobacter calcoaceticus*, ACA)[5]。目前,常规用于微生物鉴定的商业系统仍难以准确区分ABC复合群内的不同菌种[6]。部分原因是数据库菌种有限,另一个原因是用于鉴定细菌种类的底物不是专门为鉴定不动杆菌而定制的。因此,现有的大规模流行病学研究往往未能对由ABA与其他非ABA菌种引起的感染进行明确区分。随着检测技术的进步和数据库的不断完善,基质辅助激光解吸电离飞行时间质谱(matrix-assisted laser desorption ionization time of flight mass spectrometry, MALDI-TOF MS)已能够实现对ABC内各菌种的快速、准确鉴定[7]。本研究旨在明确北京市某三级甲等医院中ABC各菌种在不同临床科室的分布特征、样本来源及其耐药性差异,从而为临床经验性抗感染治疗提供科学依据。

资料与方法

1 材料

菌株 2017年1月至2024年12月以本院向全国细菌耐药监测网报送的ABC 6类菌株入选为研究对象。本研究经北京大学第一医院生物医学研究伦理委员会审批(伦理批号:2021-191)。为避免重复分析,剔除同一患者同一部位重复分离的相同菌种菌株。菌株的收集与处理均按照相应年度北京市细菌耐药监测网的监测方案执行。

试剂 血平板培养基,郑州安图绿科生物工程有限公司生产;中国兰培养基,郑州安图绿科生物工程有限公司生产;α-氰基-4-羟基肉桂酸,纯度:99%,批号:39468,无水乙腈,纯度:99.9%,批号:AX0152、三氟乙酸,纯度:99%,批号:302031,均由德国默克生命科学生产;革兰阴性细菌药敏卡AST-N335,批号:418985,法国生物梅里埃公司生产。

仪器 MALDI Biotyper微生物快速鉴定系统,德国Bruker公司产品;VITEK-2-COMPACT药敏分析系统,法国生物梅里埃公司产品。

2 研究方法

2.1 细菌培养

所有样本均接种在血平板和中国兰平板上,放入5% CO_2环境,孵育24~48 h。

2.2 细菌物种鉴定

将纯培养的细菌菌落均匀涂布于不锈钢靶板上,室温下干燥10 min。随后,在样品表面滴加基质溶液1 μL(由α-氰基-4-羟基肉桂酸、无水乙腈和三氟乙酸组成),室温下共结晶10 min。样品制备完成后,用质谱仪进行检测。将获得的质谱图与Bruker公司默认数据库进行比对,选取匹配评分≥2.0的结果作为最终鉴定结果,确保鉴定至种水平。

2.3 抗菌药物敏感性试验

用 Vitek 2 全自动药敏系统进行抗菌药物敏感性试验。质控菌株包括大肠埃希菌 ATCC 25922、大肠埃希菌 ATCC 35218 及铜绿假单胞菌 ATCC 27853 等。药敏结果依照美国临床实验室标准化协会(Clinical and Laboratory Standards Institute, CLSI)推荐的 CLSI M100 第 35 版标准进行判读[8],其中头孢哌酮/舒巴坦参照头孢哌酮的折点标准判读。所有质控菌株的药敏结果均在预期范围内,确保实验数据的可靠性。

3 统计学处理

所有菌株的鉴定与药敏结果均用 WHONET 5.6 软件进行整理与分析。用 SPSS 26.0 软件进行统计分析。不同菌种对各类抗菌药物的耐药率比较用 R×C 列联表行 χ^2 检验(R×C χ^2 test)。对于具有统计学意义的比较,进一步用 2×2 χ^2 检验进行两两比较,并结合 *Bonferroni* 校正法控制多重比较带来的Ⅰ类错误风险。

结　果

1 菌株种类

经 WHONET 系统自动审核及人工复核后,2017 年1 月 1 日至 2024 年 12 月 31 日,共纳入 2 752 株从患者首次分离的鲍曼不动杆菌复合群菌株。其中,鲍曼不动杆菌占 91.75%(2 525 株/2 752 株);皮特不动杆菌占 6.90%(190 株/2 752 株);医院不动杆菌占 1.31%(36 株/2752 株);醋酸钙不动杆菌仅 1 株,其他类别菌种未检出,见表 1。

2 各菌种的科室分布

不同菌种的科室来源存在一定差异。鲍曼不动杆菌主要来源于急诊科(32.55%)和呼吸内科(20.47%),其次为重症监护病房(6.02%)和妇科(5.19%)。皮特不动杆菌主要分离自呼吸内科(14.21%)、泌尿外科(14.21%)、心外科(10.52%)及急诊科(7.89%)。医院不动杆菌则主要来自呼吸内科(22.22%)和急诊科(22.22%),泌尿外科(11.11%)和儿童内科(11.11%)亦有一定比例。唯一 1 株醋酸钙不动杆菌分离自泌尿外科。结果见表 2。

表 1 2017 – 2024 年鲍曼不动杆菌复合群各类菌种检出量(株)及检出率(%)

Table 1 Detection quantities (n) and rates (%) of various *Acinetobacter baumannii* complex bacterial species from 2017 to 2024

Year	Acinetobacter species			
	Acinetobacter baumannii (n, %)	*Acinetobacter pittii* (n, %)	*Acinetobacter nosocomialis* (n, %)	*Acinetobacter calcoaceticus* (n, %)
2017	353(99.16)	3(0.84)	–	–
2018	337(93.87)	20(5.57)	2(0.56)	–
2019	274(91.03)	23(7.64)	4(1.33)	–
2020	240(87.59)	24(8.76)	10(3.65)	–
2021	293(91.28)	24(7.48)	4(1.25)	–
2022	273(89.51)	25(8.20)	7(2.30)	–
2023	395(91.01)	36(8.29)	3(0.69)	–
2024	360(89.55)	35(8.71)	6(1.49)	1(0.25)
Total(%)	2 525(91.75)	190(6.90)	36(1.30)	1(0.04)

–: Not detected.

表 2 鲍曼不动杆菌复合群各类菌种科室分布

Table 2 Department distribution of various *Acinetobacter baumannii* complex bacterial species

Acinetobacter baumannii (n=2 525)		*Acinetobacter pittii* (n=190)		*Acinetobacter nosocomialis* (n=36)	
Department	Number of isolates (n, %)	Department	Number of isolates (n, %)	Department	Number of isolates (n, %)
Emergency department	822(32.55)	Respiratory medicine	27(14.21)	Respiratory medicine	8(22.22)
despiratory medicine	517(20.47)	Urology	27(14.21)	Emergency mepartment	8(22.22)
Intensive care unit	152(6.02)	Cardiac surgery	20(10.52)	Urology	4(11.11)
Gynecology	131(5.19)	Emergency department	15(7.89)	Pediatrics	4(11.11)
Neurology	107(4.24)	Geriatric medicine	12(6.32)	Nephrology	3(8.33)
Cardiac surgery	96(3.80)	Intensive care unit	10(5.26)	Cardiac surgery	2(5.56)
Geriatric medicine	79(3.13)	Pediatrics	8(4.21)	Neurology	2(5.56)
Urology	57(2.26)	Gynecology	5(2.63)	Cardiology	2(5.56)
Nephrology	50(1.98)	Infectious diseases	5(2.63)	Otology	1(2.78)
Cardiac care unit	41(1.62)	Pediatric surgery	4(2.11)	Geriatric medicine	1(2.78)
Pediatric surgery	25(0.99)	Dermatology	4(2.11)	Hematology	1(2.78)
Others	448(17.74)	Others	53(27.89)	Others	–

–: Not detected.

3 各菌种的标本来源

各菌种的主要标本来源以呼吸道和尿液为主,但具体分布存在一定差异。鲍曼不动杆菌主要分离自痰液(72.59%)、尿液(7.37%)、支气管分泌物(4.08%)和全血(3.00%)。皮特不动杆菌则主要来源于痰液(35.26%)、尿液(31.05%)、支气管分泌物(8.42%)和全血(4.74%)。医院不动杆菌主要分离自痰液(52.77%)、尿液(30.56%)、肺泡灌洗液(8.33%)和支气管分泌物(5.56%)。醋酸钙不动杆菌仅1株,分离自尿液样本。结果见表3。

4 各菌种对抗菌药物的耐药情况

经χ^2检验分析,ABC复合群中不同菌种对各类抗菌药物的耐药率在统计学上差异均有统计学意义(均$P<0.001$)。总体而言,鲍曼不动杆菌的耐药率最高,其次为医院不动杆菌,而皮特不动杆菌的抗菌药物敏感性相对较高。鲍曼不动杆菌对β-内酰胺类抗菌药物,如哌拉西林/他唑巴坦、头孢他啶、亚胺培南和美罗培南的耐药率均超过80%。相比之下,皮特不动杆菌对上述药物的耐药率仅为10%~30%。两两比较显示,ABA与ANO在复方新诺明和米诺环素的耐药率之间在统计学上差异均无统计学意义(均$P>0.05$),其余抗菌药物的耐药率在统计学上差异均有统计学意义(均$P<0.05$)。醋酸钙不动杆菌仅对多西环素和复方新诺明耐药,对其余抗菌药物均表现为敏感。结果见表4。

表3 鲍曼不动杆菌复合群各类菌种标本类型分布

Table 3 Source distribution of various *Acinetobacter baumannii* complex bacterial species

Acinetobacter baumannii ($n=2\,525$)		*Acinetobacter pittii* ($n=190$)		*Acinetobacter nosocomialis* ($n=36$)	
Specimens	Number of isolates (%)	Specimens	Number of isolates (%)	Specimens	Number of isolates (%)
Sputum	1 833 (72.59%)	Sputum	67 (35.26%)	Sputum	19 (52.77%)
Urine	186 (7.37%)	Urine	59 (31.05%)	Urine	11 (30.56%)
Bronchial secretions	103 (4.08%)	Bronchial secretions	16 (8.42%)	BALF	3 (8.33%)
Blood	76 (3.00%)	Blood	9 (4.74%)	Bronchial secretions	2 (5.56%)
Pharyngeal swab	45 (1.78%)	Wound secretion	5 (2.63%)	Blood	1 (2.78%)
BALF	40 (1.58%)	Pharyngeal swab	4 (2.11%)	–	–
Wound secretion	39 (1.54%)	BALF	3 (1.58%)	–	–
Others	203 (8.04%)	Others	27 (14.21%)	Others	–

BALF: Bronchoalveolar lavage fluid; –: Not detected.

表4 鲍曼不动杆菌复合群各菌种对抗菌药物的耐药分布

Table 4 Resistance rate of various *Acinetobacter baumannii* complex bacterial species to antimicrobial angents

Antimicrobial angents	*Acinetobacter baumannii* (ABA)		*Acinetobacter pittii* (APT)		*Acinetobacter nosocomialis* (ANO)		chi-square test (*P* value)			
	Total	Resistance rate (%)	Total	Resistance rate (%)	Total	Resistance rate (%)	Total	ABA versus APT	ABA versus ANO	APT versus ANO
Cefoperazone/sulbactam	2347	57.39	142	4.93	28	32.14	<0.001	<0.001	0.007	<0.001
Piperacillin/tazobactam	2313	82.79	174	26.44	33	51.52	<0.001	<0.001	<0.001	0.004
Ceftazidime	2429	80.20	187	10.16	36	38.89	<0.001	<0.001	<0.001	<0.001
Cefepime	2414	68.39	183	13.66	35	34.29	<0.001	<0.001	<0.001	0.003
Imipenem	2343	80.58	185	11.35	33	45.45	<0.001	<0.001	<0.001	<0.001
Meropenem	2362	81.41	170	12.35	33	48.48	<0.001	<0.001	<0.001	<0.001
Tobramycin	2307	67.40	184	5.43	36	33.33	<0.001	<0.001	<0.001	<0.001
Ciprofloxacin	2344	80.29	186	17.20	36	38.89	<0.001	<0.001	<0.001	0.003
Levofloxacin	2343	75.42	188	13.30	36	38.89	<0.001	<0.001	<0.001	<0.001
Trimethoprim/sulfamethoxazole	2233	50.38	179	15.64	34	47.06	<0.001	<0.001	0.701	<0.001
Doxycycline	2160	80.19	128	1.56	27	40.74	<0.001	<0.001	<0.001	<0.001
Minocycline	2262	15.30	158	1.90	33	9.09	<0.001	<0.001	0.324	0.031

讨　论

不动杆菌属是一类需氧、不发酵乳糖的革兰氏阴性球杆菌,广泛分布于自然和医院环境中。该属经历了显著的分类学修订,目前已确认包含 87 个有效发表名称的菌种(https://lpsn.dsmz.de/genus/acinetobacter,访问日期:2025 年 8 月 21 日)。其中, ABC 因其在临床中的重要性而备受关注[9]。除鲍曼不动杆菌外,复合群中其他菌种如皮特不动杆和医院不动杆菌也逐渐被证实与医院感染密切相关[10]。然而,由于该复合群内各菌种在表型和基因型上高度相似,传统的鉴定方法难以实现准确的菌种水平识别。目前国内大部分实验室仍采用传统的生化鉴定系统[11],给临床诊断和流行病学监测带来了挑战。因此,加强对非鲍曼不动杆菌的识别与耐药性监测,对于指导临床精准抗感染治疗和制定防控策略具有重要意义。

本研究在用 MALDI-TOF 准确鉴别菌种的基础上,系统分析了近 8 年北京市某三甲医院 ABC 各菌种的临床分布特征及耐药情况。结果显示, ABA 仍为最主要的分离菌种,占比高达 91.75%,明显高于国际报道的约 80% 的流行水平[12-13]。但低于国内四川地区报道的 98.6%[14]。与此同时, APT 和 ANO 的检出率亦高于该地区,提示本院在菌种分布上具有一定的地域和临床特征差异。尽管 ABA 仍占绝对优势,但非鲍曼不动杆菌的检出比例相对较高,尤其是 APT 的年度构成比从 2017 年的 0.84% 上升至 8.71%,这一趋势可能与院内感控措施的选择性压力和易感宿主比例增加等原因有关。因此,临床应更加重视对 ABC 不同菌种的准确鉴别,以提高病原诊断的精准性,为个体化抗感染治疗和医院感染防控提供可靠依据。

研究显示,ABA 对碳青霉烯类抗生素的耐药率超过 80%,显著高于皮特不动杆菌和医院不动杆菌。据全球流行病学报道,96% 耐碳青霉烯类 ABA 菌株的耐药性是由获得性 OXA 型碳青霉烯酶基因介导的,其中 $bla_{\mathrm{OXA-23}}$ 和 $bla_{\mathrm{OXA-40}}$ 基因占主导地位[2]。ABA 仍是当前临床抗感染治疗面临的最大挑战,尤其是在重症监护、呼吸科等高危科室中,应加强耐药菌的监测与防控。

APT 主要分离自呼吸内科、泌尿外科和心外科的痰和尿液样本,与其他报道相似[15-16]。APT 与多种院内感染相关联,如呼吸机相关性肺炎和伤口感染,血流感染也较为常见(约占 5%)。法国一家医院还曾发现,APT 在血培养样本中的分离率高于 ABA[17]。3 种常见菌种中,APT 的耐药率最低,对碳青霉烯类抗生素耐药率约为 10%。国内曾发现过 1 株从严重肺炎患者中分离出的泛耐药的 APT 菌株[18]。*tet*(X2)是导致 APT 对替加环素产生临床耐药性的一个决定因素[19]。此外,其碳青霉烯类耐药性则与携带 *NDM-1*、$bla_{\mathrm{OXA-58}}$、$bla_{\mathrm{GIM-1}}$、bla_{TEM} 及 $bla_{\mathrm{VIM-2}}$ 等耐药基因相关[20-22]。

ANO 的检出率远低于 APT,但对碳青霉烯类抗生素的耐药率超过以往报道,高达 50%[23]。ANO 的耐药性可能与 AdeABC 外排泵的过度表达相关[24]。LIU 等[25]曾在报道 APT 较 ANO 导致的菌血症死亡率较高,但 2 者之间在统计学上差异无统计学意义,不过该研究结论是基于 2 种菌株的耐药性无显著差异的情况下。

本研究从 1 名泌尿外科的患者尿液中分离到 1 株 ACA,并表现出对抗生素的高度敏感性。虽然 ACA 的低致病性很少引人关注,但它是一个重要的潜在抗生素耐药性基因库[26],可将其转移到其他 ABC 菌种中。另外 ACA 能够很好地适应肠胃系统,影响肠道上皮细胞[27]。

本研究提示:ABC 不同菌种在标本分布、分离科室及耐药谱方面存在显著异质性,建议微生物实验室加强菌种精准鉴定与耐药性动态监测,为临床抗感染治疗提供精准指导。

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