

doi: 10.13241/j.cnki.pmb.2020.08.024

我院 2015-2018 年度抗菌药物的使用强度与鲍曼不动杆菌的耐药性的关系研究 *

张 慧¹ 孙盼盼² 纪润奇³ 胡杨杨⁴ 王 霞¹

(1 北京中医医院顺义医院检验科 北京 101300; 2 首都医科大学附属北京世纪坛医院检验科 北京 100038;

3 首都医科大学附属北京朝阳医院检验科 北京 100020; 4 首都医科大学附属北京同仁医院输血科 北京 100730)

摘要 目的:分析我院 2015-2018 年度抗菌药物的使用强度与鲍曼不动杆菌的耐药性的关系。**方法:**统计 2015 年 1 月~2018 年 12 月北京中医医院顺义医院抗菌药物的应用情况以及鲍曼不动杆菌的耐药性。鲍曼不动杆菌的耐药性资料来源于检验科临床送检的伤口分泌物、痰液、血液、尿液等病原学标本。**结果:**2015 年~2018 年,共分离到菌株 13246 株,其中分离到鲍曼不动杆菌株 1927 株,分离率为 14.55%。其中 2015 年的分离率为 3.11%,2016 年的分离率为 4.51%,2017 年的分离率为 5.15%,2018 年的分离率为 2.11%;鲍曼不动杆菌标本分离率最高的为痰液,占 78.83%,其次为伤口分泌物,占 12.51%,尿液标本占 5.81%,血液标本占 2.85%;鲍曼不动杆菌在我院所有致病菌中的排序均为第一位或者第二位;2015 年~2018 年抗菌药物的使用强度逐年升高,2018 年有所降低;2015 年~2018 年鲍曼不动杆菌对哌拉西林钠他唑巴坦钠、美洛培南以及亚胺培南的耐药率均逐年升高,2018 年有所降低;哌拉西林钠他唑巴坦钠、美洛培南以及亚胺培南的耐药性与抗菌药物使用强度之间具有明显的相关性($P<0.05$)。**结论:**哌拉西林钠他唑巴坦钠、美洛培南以及亚胺培南的使用,是造成鲍曼不动杆菌耐药的重要原因之一,临床应加以重视。

关键词: 抗菌药物;使用强度;鲍曼不动杆菌;耐药性

中图分类号:R969.3;R378 文献标识码:A 文章编号:1673-6273(2020)08-1511-04

Study on the Relationship between the Use Intensity of Antibiotics and the Resistance of *Acinetobacter Baumannii* in Our Hospital from 2015 to 2018*

ZHANG Hui¹, SUN Pan-pan², JI Run-qi³, HU Yang-yang⁴, WANG Xia¹

(1 Department of Laboratory, Shunyi Hospital, Beijing Chinese Medicine Hospital, Beijing, 101300, China;

2 Department of Laboratory, Beijing Shijitan Hospital Affiliated to Capital Medical University, Beijing, 100038, China;

3 Department of Laboratory, Beijing Chaoyang Hospital Affiliated to Capital Medical University, Beijing, 100038, China;

4 Department of Blood Transfusion, Beijing Tongren Hospital, Capital Medical University, Beijing, 100730, China)

ABSTRACT Objective: To study the relationship between the use intensity of antibiotics and the resistance of *Acinetobacter baumannii* in our hospital from 2015 to 2018. **Methods:** The application of antibiotics in our hospital from January 2015 to December 2018 and the resistance of *Acinetobacter baumannii* were analyzed. The drug resistance data of *Acinetobacter baumannii* come from the pathogenic samples such as wound secretion, sputum, blood, urine, etc. **Results:** From 2015 to 2018, a total of 13246 strains were isolated, of which 1927 strains were *Acinetobacter baumannii*, with the isolation rate of 14.55%. The separation rate was 3.11% in 2015, 4.51% in 2016, 5.15% in 2017 and 2.11% in 2018. The highest isolation rate of *Acinetobacter baumannii* was sputum (78.83%), followed by wound secretion (12.51%), urine (5.81%), blood (2.85%). *Acinetobacter baumannii* ranked first or second among all pathogenic bacteria in our hospital; the use intensity of antibiotics increased year by year from 2015 to 2018, and decreased in 2018. From 2015 to 2018, the drug resistance rate of *Acinetobacter baumannii* to piperacillin, tazobactam, meropenem and imipenem increased year by year, and decreased in 2018, there was a significant correlation between the drug resistance of piperacillin, tazobactam and imipenem and the intensity of antimicrobial use ($P<0.05$). **Conclusion:** The use of piperacillin sodium, tazobactam sodium, meropenem and imipenem is one of the important reasons for resistance of *Acinetobacter baumannii*. We should pay attention to it in clinical practice.

Key words: Antibiotics; Use intensity; *Acinetobacter baumannii*; Drug resistance

Chinese Library Classification(CLC): R969.3; R378 **Document code:** A

Article ID: 1673-6273(2019)08-1511-04

前言

鲍曼不动杆菌是医院感染中一种极为重要的病原菌,广泛存在于人体表面、自然环境及人体上呼吸道内,而且该病原菌

是仅次于铜绿假单胞菌以及大肠杆菌的医源性感染病菌^[1,2]。鲍曼不动杆菌能引发医院获得性肺炎,特别是泌尿系感染、呼吸机相关性肺炎、伤口感染、继发性脑膜炎、血流感染、腹膜炎、骨髓炎、心内膜炎以及关节炎等^[3-5]。鲍曼不动杆菌由于具有比较

* 基金项目:国家自然科学基金项目(81371861)

作者简介:张慧(1989-),女,本科,检验师,研究方向:微生物,电话:13720033934, E-mail: z398560461@126.com

(收稿日期:2019-12-01 接受日期:2019-12-24)

强的获得性耐药性以及天然固有耐药性,导致治疗鲍曼不动杆菌感染的难度较高,严重影响机体的正常康复^[6,7]。从1940年青霉素开始应用于治疗临床疾病以来,抗菌药物迅速发展,无论从数量、品种,还是金额上,抗菌药物在医院总药品使用中均占有极为重要的地位^[8-10]。近年来,鲍曼不动杆菌的耐药率以及分离率呈逐年升高的趋势,为临床治疗造成较大的困难^[11]。监测细菌耐药性的变迁情况、分析影响耐药的相关因素对于控制感染以及合理用药具有重要的临床意义。本研究主要分析了我院2015-2018年度抗菌药物的应用强度与鲍曼不动杆菌的耐药性的关系,旨在为抗菌药物的合理使用提供依据。

1 资料与方法

1.1 一般资料

抗菌药物的应用情况资料调取自2015年1月~2018年12月北京中医医院顺义医院的HIS系统中。鲍曼不动杆菌的耐药性资料来源于2015年1月~2018年12月北京中医医院顺义医院检验科临床送检的伤口分泌物、痰液、血液、尿液等病原学标本,将同一患者的重复菌株进行剔除。

1.2 方法

统计鲍曼不动杆菌标本在2015年1月~2018年12月分布(伤口分泌物、痰液、血液、尿液)情况和构成比;统计2015年1月~2018年12月头孢哌酮钠舒巴坦钠、哌拉西林钠他唑巴

坦钠、美洛培南以及亚胺培南的使用强度;统计鲍曼不动杆菌对头孢哌酮钠舒巴坦钠、哌拉西林钠他唑巴坦钠、美洛培南以及亚胺培南的耐药率;采用Pearson相关性分析抗菌药物的使用强度与细菌耐药率之间的相关性, $r < 0.3$ 表明两者之间具有较弱的相关性, $r > 0.8$ 表明两组之间的相关性比较强^[9]。

1.3 统计学分析

采用SPSS 20.0,两组间计量资料对比用t检验,计数资料用 χ^2 检验,用Pearson相关性分析抗菌药物的使用强度与细菌耐药率之间的相关性, $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 鲍曼不动杆菌2015年~2018年的分离情况

2015年~2018年,共分离到菌株13246株,其中分离到鲍曼不动杆菌株1927株,分离率为14.55%。其中2015年的分离率为3.11%,2016年的分离率为4.51%,2017年的分离率为5.15%,2018年的分离率为2.11%。

2.2 鲍曼不动杆菌标本不同年度的分布情况

鲍曼不动杆菌标本分离率最高的为痰液,占78.83%,其次为伤口分泌物,占12.51%,尿液标本占5.81%,血液标本占2.85%。鲍曼不动杆菌在我院所有致病菌中的排序均为第一位或者第二位。见表1。

表1 鲍曼不动杆菌标本不同年度的分布情况[例(%)]

Table 1 Distribution of *Acinetobacter baumannii* in different years [n(%)]

Year	Wound Secretion	Sputum	Blood	Urine	Total	Sort
2015	53(12.83)	319(77.24)	11(2.66)	30(7.26)	413	1
2016	74(12.39)	477(79.90)	15(2.51)	31(5.19)	597	2
2017	82(12.02)	523(87.60)	23(3.37)	44(6.45)	682	1
2018	32(11.43)	200(71.43)	6(2.14)	7(2.50)	280	2
Total	241(12.51)	1519(78.83)	55(2.85)	112(5.81)	1927	

2.3 抗菌药物的使用强度

有所降低,见表2。

2015年~2018年抗菌药物的使用强度逐年升高,2018年

表2 我院抗菌药物的使用强度(%)

Table 2 The use intensity of antibiotics in our hospital (%)

Antibacterial drugs	Use intensity			
	2015	2016	2017	2018
Cefoperazone sodium sulbactam sodium	1.24	1.49	2.36	2.14
Piperacillin sodium tazobactam sodium	0.09	0.14	0.15	0.07
Meropenem	0.16	1.23	1.19	0.83
Imipenem	0.23	0.27	0.32	0.21

2.4 鲍曼不动杆菌的耐药性

2015年~2018年鲍曼不动杆菌对哌拉西林钠他唑巴坦钠、美洛培南以及亚胺培南的耐药率均逐年升高,2018年有所降低,见表3。

哌拉西林钠他唑巴坦钠、美洛培南以及亚胺培南的耐药性与抗菌药物使用强度之间具有明显的相关性($P < 0.05$),见表4。

3 讨论

细菌耐药是一个长期困扰国内外临床医师的重要难题,

2.5 抗菌药物的使用强度与鲍曼不动杆菌的耐药性的关系

表 3 我院鲍曼不动杆菌的耐药性(%)

Table 3 The drug resistance of *Acinetobacter baumannii* in our hospital (%)

Antibacterial drugs	Drug resistance			
	2015 Year	2016 Year	2017 Year	2018 Year
Cefoperazone sodium sulbactam sodium	0.00	0.00	0.00	0.00
Piperacillin sodium tazobactam sodium	51.39	64.27	73.56	52.48
Meropenem	41.32	53.78	56.29	43.51
Imipenem	34.57	49.82	53.74	30.26

表 4 抗菌药物的使用强度与鲍曼不动杆菌的耐药性的关系

Table 4 Relationship between the use intensity of antibiotics and the resistance of *Acinetobacter baumannii*

Antibacterial drugs	r	P
Cefoperazone sodium sulbactam sodium	0	0
Piperacillin sodium tazobactam sodium	1	0
Meropenem	0.873	0.03
Imipenem	0.892	0.02

细菌耐药不但会使住院时间大大延长,医疗费用明显增加,还会使感染性疾病的发病率及死亡率升高^[12,13]。目前几乎全部类别的抗菌药均出现了耐药细菌,甚至产生了泛耐药细菌以及耐药多药细菌,导致许多的基本抗菌药物丧失了作用^[14-16]。医院作为应用抗菌药物的重要场所,在医院中开展抗菌药物管理可以有效控制细菌耐药性问题。有研究表明,抗菌药物的使用剂量与细菌耐药性之间具有宏观的量化关系,细菌耐药性的产生不仅与药物以及细菌自身的特点有关,可能还与临床用药管理模式、抗菌药物的使用剂量和所在的地区有关^[17-19]。

鲍曼不动杆菌主要存在于人体表面、自然环境以及机体的上呼吸道中,是仅次于铜绿假单胞菌以及大肠杆菌的一种医源性感染病菌^[20,21]。鲍曼不动杆菌是引起创口感染、呼吸道感染、脑膜炎感染、菌血症感染和泌尿道感染的重要诱因,具有较强的耐药性,而且具有较强的获得性耐药性,使临床治疗鲍曼不动杆菌感染的难度大大增加,不利于患者的正常康复^[22-24]。2015年~2018年,我院共分离到菌株13246株,其中分离到鲍曼不动杆菌株1927株,分离率为14.55%。鲍曼不动杆菌在我院所有致病菌中的排序均为第一位或者第二位。表明鲍曼不动杆菌是造成我院医源性感染的一种重要病原菌,我院面临着比较严重的鲍曼不动杆菌感染防控形势。我院鲍曼不动杆菌标本分离率最高的为痰液,占78.83%。由于呼吸系统是诱发鲍曼不动杆菌感染的主要途径之一。有研究发现,鲍曼不动杆菌感染中大约有55%通过呼吸系统进行^[25],这也是造成我院鲍曼不动杆菌标本主要来源于痰液的根本原因。

本研究发现,2015年~2018年鲍曼不动杆菌对哌拉西林钠他唑巴坦钠、美洛培南以及亚胺培南的耐药率均逐年升高。哌拉西林钠他唑巴坦钠、美洛培南以及亚胺培南的耐药性与抗菌药物使用强度之间具有明显的相关性。表明鲍曼不动杆菌对哌拉西林钠他唑巴坦钠、美洛培南以及亚胺培南耐药基因的产生,与这些抗菌药物大量、广泛以及不规范应用具有一定的关

系,应当有计划地控制抗菌药物的使用时间和使用剂量。美罗培南以及亚胺培南均属于碳青霉烯类抗菌药物。赵欣等^[26]研究表明,产生碳青霉烯类抗菌药物耐药性的鲍曼不动杆菌会丢失外膜蛋白,而且C类头孢菌素酶的表达水平较高,表明鲍曼不动杆菌耐药性的产生可能与头孢菌素酶的生成和外膜蛋白的丢失相关。合理控制哌拉西林钠他唑巴坦钠、美洛培南以及亚胺培南的使用强度有助于使鲍曼不动杆菌的耐药率下降。影响细菌耐药性发生的因素多种多样,包括药物本身的抗菌活性、动力学特征以及作用机制等^[27-29]。本研究发现,抗菌药物的使用强度也会影响鲍曼不动杆菌的耐药。临床上需要严格掌握抗菌药物的使用适应症,合理选择抗菌药物的配伍以及品种,正确掌握疗程、剂量以及给药方法^[30,31]。

综上所述,哌拉西林钠他唑巴坦钠、美洛培南以及亚胺培南的使用,是造成鲍曼不动杆菌耐药的重要原因之一,临床应加以重视。

参考文献(References)

- [1] San-Jun C, Shan R, Yong-En X. Preparation of ompk/omp22 fusion protein of *acinetobacter baumannii* and determination of induced antibody response in mice[J]. Chinese Journal of Biologicals, 2018, 31(11): 1188-1191
- [2] Huang PY, Shie SS, Ye JJ. Acquisition and clearance of multidrug resistant *Acinetobacter baumannii* on healthy young adults concurrently burned in a dust explosion in Taiwan the implication for antimicrobial stewardship[J]. Bmc Infectious Diseases, 2017, 17(1): 598-616
- [3] Bobenchik AM, Deak E, Hindler JA, et al. Performance of Vitek 2 for Antimicrobial Susceptibility Testing of *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Stenotrophomonas maltophilia* with Vitek 2 (2009 FDA) and CLSI M100S 26th Edition Breakpoints[J]. J Clin Microbiol, 2017, 1(3): 450-456
- [4] Blanco N, Harris AD, Rock C, et al. Risk factors and outcomes

- associated with multidrug-resistant *Acinetobacter baumannii* upon intensive care unit admission[J]. Antimicrob Agents Chemother, 2018, 62(1): e01631-17
- [5] Xie R, Zhang XD, Zhao Q, et al. Analysis of global prevalence of antibiotic resistance in *Acinetobacter baumannii* infections disclosed a faster increase in OECD countries [J]. Emerging Microbes and Infections, 2018, 7(1): 31-48
 - [6] Russo A, Giuliano S, Ceccarelli G, et al. Comparison of Septic Shock Due to Multidrug-Resistant *Acinetobacter baumannii* or *Klebsiella pneumoniae* Carbapenemase-Producing *K. pneumoniae* in Intensive Care Unit Patients[J]. Antimicrob Agents Chemother, 2018, 62(6): e02562-17
 - [7] Wintachai P, Naknaen A, Pomwiset R, et al. Isolation and characterization of Siphoviridae phage infecting extensively drug-resistant *Acinetobacter baumannii* and evaluation of therapeutic efficacy in vitro and in vivo[J]. J Med Microbiol, 2019, 68(7): 1096-1108
 - [8] Campanini-Salinas J, Andrades-Lagos J, Mella-Raipan J, et al. Novel Classes of Antibacterial Drugs in Clinical Development, a Hope in a Post-antibiotic Era[J]. Curr Top Med Chem, 2018, 18(14): 1188-1202
 - [9] Jones A, Mandal A, Sharma S. Antibacterial and Drug Elution Performance of Thermoplastic Blends[J]. J Polymers and the Environment, 2017, 26(8): 1-13
 - [10] Azarudeen RS, Thirumarimurugan M, Athmiya KP, et al. Antibacterial chitosan-copolymer membranes for drug delivery: synthesis, characterization, drug release profile and kinetics [J]. J Chem Technol Biotechnol, 2017, 92(7): 1659-1666
 - [11] Gemma Jiménez-Guerra, Victor Heras-Cañas, Miguel Gutiérrez-Soto, et al. Urinary tract infection by *Acinetobacter baumannii* and *Pseudomonas aeruginosa*: evolution of antimicrobial resistance and therapeutic alternatives[J]. J Med Microbiol, 2018, 67(6): 34-39
 - [12] Empaire GD, Guzman Siritt ME, Rosenthal VD, et al. Multicenter prospective study on device-associated infection rates and bacterial resistance in intensive care units of Venezuela: International Nosocomial Infection Control Consortium (INICC) findings [J]. Int Health, 2017, 9(1): 44-49
 - [13] Kim B, Hwang IS, Lee HJ, et al. Identification of a molecular marker tightly linked to bacterial wilt resistance in tomato by genome-wide SNP analysis[J]. Theor Appl Genet, 2018, 131(5): 1017-1030
 - [14] Tanja Ilić, Sanda Gračan, Adela Arapović, et al. Changes in bacterial resistance patterns in children with urinary tract infections on antimicrobial prophylaxis at University Hospital in Split[J]. Med Sci Monit, 2011, 17(7): CR355-61
 - [15] İbrahim Gökçe, Neslihan Çiçek, Serçin Güven, et al. Changes in Bacterial Resistance Patterns of Pediatric Urinary Tract Infections and Rationale for Empirical Antibiotic Therapy[J]. Balkan Med J, 2017, 34(5): 432-435
 - [16] Duan K, Kumar A. Understanding Bacterial Antibiotic Resistance and Pathogenicity Through Investigating Bacterial Membrane Proteins[J]. J Membrane Biology, 2018, 251(7): 1-3
 - [17] Mario Sánchez Sánchez, Cruzpulido WL, Eduardo Bladinieres Cámara. Bacterial Prevalence and Antibiotic Resistance in Clinical Isolates of Diabetic Foot Ulcers in the Northeast of Tamaulipas, Mexico[J]. Int J Low Extrem Wounds, 2017, 16(2): 129-134
 - [18] Schmidt K, Mwaigwisya S, Crossman LC, et al. Identification of bacterial pathogens and antimicrobial resistance directly from clinical urines by nanopore-based metagenomic sequencing[J]. J Antimicrob Chemother, 2017, 72(1): 104-114
 - [19] Ghassabi F, Hashempour T, Moghadami M, et al. Bacterial etiology and antibiotic resistance pattern of septicemia in HIV and non-HIV patients admitted to tertiary care hospitals, Shiraz, South of Iran[J]. Cell Mol Biol (Noisy-le-grand), 2017, 63(9): 115-121
 - [20] Makris D, Petinaki E, Tsolaki V, et al. Colistin versus Colistin Combined with Ampicillin-Sulbactam for Multiresistant *Acinetobacter baumannii* Ventilator-associated Pneumonia Treatment: An Open-label Prospective Study[J]. Indian J Crit Care Med, 2018, 22(2): 67-77
 - [21] Jayasimha Rao, Dwi Susanti, Johnathon C. Childress, et al. Tn 2008-Driven Carbapenem-Resistance in *Acinetobacter baumannii* Isolates from a Period of Increased Incidence of Infections in a Southwest Virginia Hospital[J]. J Glob Antimicrob Resist, 2018, 12(13): 79-87
 - [22] Nasser K, Mustafa AS, Khan MW, et al. Draft Genome Sequences of Six Multidrug-Resistant Clinical Strains of *Acinetobacter baumannii*, Isolated at Two Major Hospitals in Kuwait[J]. Genome Announcements, 2018, 6(16): e00264-18
 - [23] Lari AR, Ardebili A, Hashemi A. AdeR-AdeS mutations & overexpression of the AdeABC efflux system in ciprofloxacin-resistant *Acinetobacter baumannii* clinical isolates [J]. The Indian Journal of Medical Research, 2018, 147(4): 413-421
 - [24] Nahaichuk VI, Nazarchuk OA, Osadchuk NI, et al. The analytical prognosis of the susceptibility to aminoglycosides and doxycycline in *Acinetobacter baumannii* isolated from burns of intensive care unit patients[J]. Wiad Lek, 2018, 71(3 pt 2): 705-709
 - [25] Kenyon JJ, Kasimova AA, Shashkov AS, et al. *Acinetobacter baumannii* isolate BAL_212 from Vietnam produces the K57 capsular polysaccharide containing a rarely occurring amino sugar N-acetylviosamine[J]. Microbiology, 2018, 164(2): 217-220
 - [26] 赵忱, 刘长庭. 鲍曼不动杆菌的耐药机制研究进展[J]. 解放军医学院学报, 2017, 38(5): 490-492
 - [27] Avinash P, Umesha S, Marahel S. Role of hydrogen peroxide and ascorbate-glutathione pathway in host resistance to bacterial wilt of eggplant[J]. Russian J Plant Phy, 2017, 64(3): 375-385
 - [28] Guzek A, Rybicki Z, Tomaszewski D. Changes in bacterial flora and antibiotic resistance in clinical samples isolated from patients hospitalized in the Military Institute of Medicine in Warsaw, Poland, between 2005-2012[J]. Przegl Epidemiol, 2017, 71(2): 165-176
 - [29] Upadhyay S, Khyriem AB, Bhattacharya P, et al. High-level aminoglycoside resistance in *Acinetobacter baumannii* recovered from Intensive Care Unit patients in Northeastern India[J]. Indian J Med Microbiol, 2018, 36(1): 43-48
 - [30] Khillan V, Kale P, Pamecha V, et al. Infections in live donor liver transplant recipients: A study of timeline, aetiology and antimicrobial resistance of bacterial and fungal infections from the developing world[J]. Indian J Med Microbiol, 2017, 35(4): 604-606
 - [31] Zhang F, Zhao X, Li Q, et al. Bacterial community structure and abundances of antibiotic resistance genes in heavy metals contaminated agricultural soil[J]. Environ Sci Pollut Res Int, 2018, 25(1): 9547-9555