

• 论著 •

2009 年中国 CHINET 铜绿假单胞菌细菌耐药性监测

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摘要: 目的 了解 2009 年我国不同地区铜绿假单胞菌临床分离株的耐药性和耐药特征, 指导临床合理使用抗菌药物。方法 对全国 14 所教学医院临床分离的 4 912 株铜绿假单胞菌采用纸片扩散法(K-B 法)进行药敏试验, 按 CLSI 2009 年标准判定药敏试验结果, 并用 WHONET 5.4 软件进行数据分析。结果 2009 年 14 所医院从临床标本中共分离出 4 912 株铜绿假单胞菌, 其中 91.9% 分离自住院患者, 73.6% 的菌株分离自呼吸道标本。铜绿假单胞菌对阿米卡星的耐药率最低, 为 14.8%, 对其他抗菌药物的耐药率均高于 18%。昆明医学院第一附属医院分离株对各抗菌药物的耐药率均高于 30%, 除对头孢哌酮-舒巴坦、哌拉西林-他唑巴坦和头孢哌酮外, 对其他 10 种抗菌药物的耐药率在 14 所医院中均为最高; 北京医院和安徽医科大学第一附属医院分离的菌株对大多数抗菌药物的耐药率在 35% 左右, 甘肃省人民医院分离株对抗菌药物(除庆大霉素和环丙沙星外)耐药率均低于 10%; 上海复旦大学附属儿科医院对各抗菌药物的耐药率均低于 10%。泛耐药铜绿假单胞菌的检出率为 1.7%。结论 我国铜绿假单胞菌的耐药性与 2007 年相比基本相仿, 略有减低, 但总体仍处于较高水平。不同医院抗菌药物的耐药性相差较大。ICU 仍是监控重点。我们应加强监测, 指导临床合理使用抗菌药物并控制院内耐药菌的流行。

关键词: 抗菌药物; 铜绿假单胞菌; 细菌耐药性监测

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CHINET 2009 surveillance of antimicrobial resistance in *Pseudomonas aeruginosa* in China

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Abstract: **Objective** To investigate the antimicrobial resistance of *P. aeruginosa* in China during 2009. **Methods** Clinical isolates of *P. aeruginosa* were collected from 14 teaching hospitals in China. Antimicrobial susceptibility was tested by Kirby-Bauer method. The data were analyzed by WHONET 5.4 software. **Results** Of the 4 912 clinical *P. aeruginosa* isolates, 91.9% strains were isolated from hospitalized patients, and 73.6% were isolated from respiratory tract. The isolates showed the lowest resistance rate (14.8%) to amikacin. The resistance rates to other antimicrobial agents

were above 18%. The resistance rates of the *P. aeruginosa* strains from Kunming Hospital were higher than 30% to most antibiotics, except cefoperazone-sulbactam, cefotaxime, cefoperazone and piperacillin-tazobactam. For the strains from Shanghai Pediatric Hospital, the resistance rate was less than 10% to each antimicrobial agent. The pan-resistant *P. aeruginosa* strains (only sensitive to colistin) accounted for 1.7%. **Conclusions** The antimicrobial resistance of *P. aeruginosa* is still a serious problem in China. The antimicrobial susceptibility pattern varied in different hospitals. ICU is still the focus of antibiotic resistance monitoring. The surveillance of antimicrobial resistance is very important for rational antimicrobial therapy.

Key words: antimicrobial agent; *Pseudomonas aeruginosa*; antimicrobial resistance

铜绿假单胞菌为医院感染中最常见的病原菌之一,极易在医院内各种潮湿的环境中生存。为进一步了解中国不同地区医院中分离的铜绿假单胞菌对抗菌药物的耐药性,本文继续报道 2009 年 CHINET 细菌耐药性监测网铜绿假单胞菌的监测结果。

材料与方法

一、细菌

收集 2009 年 1 月至 2009 年 12 月从中国不同地区 14 所教学医院临床分离的铜绿假单胞菌 4 912 株(剔除同一患者相同部位重复分离到的相同细菌),各医院按临床微生物实验室常规操作规程将菌株鉴定到种。以铜绿假单胞菌 ATCC27853 为药敏试验质控菌株。

二、抗菌药物纸片

阿米卡星、庆大霉素、哌拉西林、哌拉西林-他唑巴坦、头孢哌酮、头孢哌酮-舒巴坦、氨基曲南、头孢吡肟、头孢他啶、亚胺培南、美罗培南和环丙沙星等抗菌药物纸片购自 BBL 公司和 OXOID 公司。

三、药敏试验

各中心按统一方案采用纸片扩散法(K-B 法)进

行药敏试验,按 CLSI 2009 年标准^[1]判断结果,用 WHONET 5.4 软件进行数据分析。

结 果

一、菌种分布

2009 年 14 所医院从临床标本中分离出 4 912 株铜绿假单胞菌,见表 1,其中自门诊患者分离占 8.1%,自住院患者分离占 91.9%;住院患者中分离株的 16.6%来自 ICU。标本分布主要为上呼吸道和尿液,分别占 73.6%(3 616/4 912)和 6.7%(331/4 912),见表 2。

二、铜绿假单胞菌对抗菌药物的耐药性

4 912 株铜绿假单胞菌对各抗菌药物的敏感性,与 CHINET 2007 年^[2]结果相比,铜绿假单胞菌依然对阿米卡星的耐药率最低,为 14.8%,其余抗菌药物的耐药率均在 30.9%~18%,见表 3。耐药率自高至低依次为:哌拉西林>亚胺培南>氨基曲南>头孢哌酮>庆大霉素>美罗培南>哌拉西林-他唑巴坦>环丙沙星>头孢他啶>头孢吡肟>头孢哌酮-舒巴坦>阿米卡星。

表 1 4 912 株铜绿假单胞菌在 14 所医院的分布

Table 1. Distribution of 4 912 strains of *Pseudomonas aeruginosa* in different hospitals

| Hospital | No. of strains | % |
|--|----------------|------|
| Shanghai Huashan Hospital | 850 | 17.3 |
| The First Affiliated Hospital of Zhejiang University Medical College | 606 | 12.3 |
| Wuhan Tongji Hospital | 488 | 9.9 |
| Peking Union Hospital | 474 | 9.6 |
| Beijing Hospital | 467 | 9.5 |
| The First Affiliated Hospital of Kunming Medical College | 357 | 7.3 |
| Shanghai Ruijin Hospital | 331 | 6.7 |
| The First Affiliated Hospital of Guangzhou Medical College | 322 | 6.6 |
| The First Affiliated Hospital of Anhui Medical University | 308 | 6.3 |
| Shanghai Pediatric Hospital | 192 | 3.9 |
| The First Affiliated Hospital of Chongqing Medical University | 167 | 3.4 |
| The People's Hospital of Gansu Province | 131 | 2.7 |
| The First Affiliated Hospital of Xinjiang Medical University | 122 | 2.5 |
| Shanghai Children's Hospital | 97 | 2.0 |
| Total | 4 912 | 100 |

表 2 铜绿假单胞菌的标本分布
Table 2. Source of *Pseudomonas aeruginosa* isolates

| Specimen | No. of strains | % |
|---------------------|----------------|------|
| Respiratory tract | 3 696 | 75.2 |
| Urine | 369 | 7.5 |
| Wound | 237 | 4.8 |
| Blood | 140 | 2.9 |
| Aseptic fluid | 138 | 2.8 |
| Genital tract | 14 | 0.3 |
| Stool | 14 | 0.3 |
| Cerebrospinal fluid | 12 | 0.2 |
| Others | 292 | 5.9 |
| Total | 4 912 | 100 |

全国 14 所医院分离的铜绿假单胞菌对各种抗菌药物的耐药率和敏感率见表 4。其中昆明医学院附

属第一医院分离株对抗菌药物的耐药率较高,对各种抗菌药物的耐药率均高于 30%,除对头孢哌酮-舒巴坦、哌拉西林-他唑巴坦和头孢哌酮外,对其他 10 种抗菌药物的耐药率在 14 所医院中最高;北京医院和安徽医科大学附属第一医院分离的菌株对大多数抗菌药物的耐药率在 35%左右;复旦大学附属儿科医院对各抗菌药物的耐药率均低于 10%,除对头孢哌酮-舒巴坦的耐药率高于上海儿童医院外,对其余 13 种抗菌药物的耐药率在 14 所医院中均属最低;甘肃省人民医院对各种抗菌药物的耐药率均低于 14%;上海儿童医院中分离的菌株对各抗菌药物的耐药率均低于 30%;协和医院、广州医学院附属第一医院和浙江大学医学院附属第一医院除对头孢哌酮-舒巴坦以外的其他各抗菌药物耐药率均低于 30%。

表 3 2009 年和 2007 年铜绿假单胞菌对各种抗菌药物的敏感率和耐药率(%)
Table 3. Resistance and susceptibility rates of *Pseudomonas aeruginosa* to antimicrobial agents compared between 2009 and 2007 (%)

| Antimicrobial agent | Susceptibility rate | | Resistance rate | |
|-------------------------|---------------------|------|-----------------|------|
| | 2009 | 2007 | 2009 | 2007 |
| Amikacin | 80.2 | 73.9 | 14.8 | 18.7 |
| Piperacillin-tazobactam | 75.8 | 67.2 | 24.1 | 32.8 |
| Ceftazidime | 73.7 | 65.2 | 20.3 | 29.3 |
| Cefepime | 71.0 | 63.2 | 19.7 | 26.0 |
| Meropenem | 70.0 | 66.6 | 25.2 | 28.5 |
| Piperacillin | 68.9 | 59.9 | 30.9 | 40.1 |
| Gentamicin | 68.2 | 56.2 | 26.9 | 39.2 |
| Ciprofloxacin | 66.3 | 61.2 | 23.9 | 29.8 |
| Imipenem | 66.2 | 61.4 | 30.5 | 35.8 |
| Cefoperazone-sulbactam | 62.5 | 54.8 | 18.2 | 22.8 |
| Cefoperazone | 53.9 | 45.4 | 29.1 | 40.3 |
| Aztreonam | 49.6 | 48.4 | 29.9 | 31.2 |

表 4 2007 年和 2009 年各医院铜绿假单胞菌对各种抗菌药物的耐药率(%)

Table 4. The resistance rates compared between 2007 and 2009 by hospital (%)

| Antibiotic | HSH | | RJH | | ZJH | | PUH | | BJH | | TJH | | GZH | |
|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | 2007 | 2009 | 2007 | 2009 | 2007 | 2009 | 2007 | 2009 | 2007 | 2009 | 2007 | 2009 | 2007 | 2009 |
| Piperacillin | 57.4 | 36.8 | 28.0 | 18.7 | 30.7 | 28.8 | 37.7 | 24.3 | 55.0 | 44.1 | 35.4 | 28.7 | 34.6 | 23.6 |
| Ceftazidime | 39.7 | 21.3 | 22.2 | 19.3 | 25.5 | 14.7 | 27.7 | 14.6 | 43.0 | 32.8 | 16.7 | 12.2 | 33.1 | 17.6 |
| Cefoperazone | 59.4 | 36.5 | 24.7 | 18.1 | 33.5 | 20.2 | 38.3 | 20.6 | 51.3 | 41.3 | 37.1 | 25.5 | 37.3 | 25.0 |
| Cefepime | 33.0 | 17.1 | 14.3 | 14.2 | 24.1 | 11.6 | 18.9 | 15.0 | 42.6 | 32.8 | 22.7 | 17.6 | 33.7 | 19.0 |
| Aztreonam | 43.7 | 33.0 | 31.4 | 21.8 | 33.3 | 21.7 | 28.1 | 22.2 | 43.1 | 47.5 | 22.4 | 18.3 | 21.0 | 26.6 |
| Cefoperazone-sulbactam | 26.4 | 26.8 | 18.6 | 15.5 | 16.0 | 16.9 | 22.3 | 12.7 | 39.7 | 31.5 | 19.6 | 11.5 | 23.5 | 16.0 |
| Piperacillin-tazobactam | 45.8 | 31.4 | 22.9 | 16.7 | 26.9 | 19.2 | 33.7 | 20.1 | 47.9 | 36.2 | 27.3 | 24.1 | 27.4 | 19.5 |
| Imipenem | 47.8 | 42.4 | 23.7 | 21.9 | 39.1 | 29.6 | 34.1 | 23.9 | 50.6 | 49.5 | 22.5 | 20.7 | 36.5 | 21.6 |
| Meropenem | 34.8 | 31.1 | 17.3 | 18.5 | 33.0 | 25.2 | 24.6 | 16.1 | 43.3 | 43.7 | 19.5 | 11.7 | 30.6 | 16.3 |
| Amikacin | 30.6 | 11.6 | 16.1 | 16.9 | 19.6 | 11.5 | 17.4 | 8.9 | 15.7 | 15.6 | 22.4 | 17.5 | 13.1 | 9.1 |
| Gentamicin | 57.0 | 30.0 | 25.6 | 22.6 | 35.2 | 16.9 | 31.7 | 19.1 | 46.0 | 35.5 | 45.0 | 25.9 | 37.7 | 12.2 |
| Ciprofloxacin | 50.4 | 30.1 | 24.4 | 22.1 | 28.2 | 19.3 | 25.4 | 15.8 | 27.8 | 28.1 | 25.9 | 15.2 | 35.4 | 19.1 |

续表 4 2007 年和 2009 年各医院铜绿假单胞菌对各种抗菌药物的耐药率(%)
Table 4. The resistance rates compared between 2007 and 2009 by hospital (%)

| Antibiotic | CQH | | GSH | | XJH | | PED | | SCH | | AHH | | KMH | |
|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | 2007 | 2009 | 2007 | 2009 | 2007 | 2009 | 2007 | 2009 | 2007 | 2009 | 2007 | 2009 | 2007 | 2009 |
| Piperacillin | 44.5 | 31.1 | 9.1 | 9.2 | - | 38.3 | 8.5 | 6.3 | 28.5 | 14.4 | - | 39.3 | - | 60.4 |
| Ceftazidime | 31.5 | 25.7 | 4.7 | 4.6 | 13.3 | 32.8 | 5.5 | 3.7 | 29.9 | 14.4 | - | 22.6 | - | 40.3 |
| Cefoperazone | 39.5 | 73.5 | 5.1 | 13.2 | - | - | 6.7 | 6.3 | 28.1 | 16.7 | - | 41.1 | - | - |
| Cefepime | 29.5 | 21.0 | 7.6 | 6.1 | 13.3 | 28.0 | 1.2 | 1.6 | 4.4 | 8.2 | - | 23.4 | - | 48.3 |
| Aztreonam | 22.1 | 32.9 | 9.2 | 13.0 | - | 100 | 1.2 | 7.3 | 23.5 | 20.8 | - | 42.6 | - | 58.9 |
| Cefoperazone-sulbactam | 21.9 | 10.8 | 3.0 | 1.5 | 20.0 | 19.8 | 1.8 | 2.6 | 8.0 | 10.3 | - | 24.3 | - | - |
| Piperacillin-tazobactam | 32.9 | 14.4 | 6.5 | 6.7 | 25.0 | 24.6 | 1.8 | 3.7 | 21.9 | 12.1 | - | 37.2 | - | 31.5 |
| Imipenem | 39.0 | 13.8 | 3.2 | 8.4 | 25.8 | 25.8 | 7.3 | 6.8 | 27.7 | 18.6 | - | 30.1 | - | 61.3 |
| Meropenem | 35.2 | 12.0 | 1.9 | 7.6 | - | 26.7 | 3.6 | 6.8 | 19.1 | 17.7 | - | 42.3 | - | 56.7 |
| Amikacin | 22.6 | 19.2 | 3.0 | 2.3 | 4.0 | 12.4 | 1.2 | 0.0 | 4.4 | 6.2 | - | 25.6 | - | 39.2 |
| Gentamicin | 54.8 | 34.7 | 18.2 | 16.0 | 36.7 | 34.5 | 2.4 | 3.1 | 5.8 | 6.2 | - | 35.7 | - | 62.5 |
| Ciprofloxacin | 36.6 | 30.1 | 15.4 | 7.6 | 5.8 | 14.9 | 1.2 | 1.1 | 2.2 | 4.1 | - | 33.8 | - | 53.1 |

HSJ: Shanghai Huashan Hospital; RJH: Shanghai Ruijin Hospital; ZJH: The First Affiliated Hospital of Zhejiang University Medical College; PUH: Peking Union Hospital; BJH: Beijing Hospital; TJH: Wuhan Tongji Hospital;GZH: The First Affiliated Hospital of Guangzhou Medical College; CQH: The First Affiliated Hospital of Chongqing Medical University; GSH: The People's Hospital of Gansu Province; XJH: The First Affiliated Hospital of Xinjiang Medical University; PED:Shanghai Pediatric Hospital;SCH: Shanghai Children's Hospital; AHH: The First Affiliated Hospital of Anhui Medical University; KMH: The First Affiliated Hospital of Kunming Medical College.

在所有 4 912 株铜绿假单胞菌中,泛耐药菌株 3.9%(13/331,12/308),其次重庆医科大学附属第一医院为 3.6%(6/167),而上海复旦大学附属儿科医院、甘肃省人民医院、广州医学院附属第一医院和新疆医科大学附属第一医院在所分离的铜绿假单胞菌中均未检出泛耐药菌株,见表 5。

表 5 各医院泛耐药铜绿假单胞菌的分布情况

Table 5. Prevalence of pan-drug resistant *P. aeruginosa* in different hospitals

| Hospital | No. of strains | % |
|--|----------------|------|
| Shanghai Huashan Hospital | 9 | 10.6 |
| The First Affiliated Hospital of Zhejiang University Medical College | 12 | 14.1 |
| Beijing Hospital | 14 | 16.5 |
| Peking Union Hospital | 4 | 4.7 |
| Shanghai Ruijin Hospital | 13 | 15.3 |
| The First Affiliated Hospital of Guangzhou Medical College | 0 | 0 |
| Wuhan Tongji Hospital | 7 | 8.2 |
| Shanghai Children's Hospital | 1 | 1.2 |
| The First Affiliated Hospital of Chongqing Medical University | 6 | 7.1 |
| The First Affiliated Hospital of Anhui Medical University | 12 | 14.1 |
| The People's Hospital of Gansu Province | 0 | 0 |
| The First Affiliated Hospital of Xinjiang Medical University | 0 | 0 |
| Shanghai Pediatric Hospital | 0 | 0 |
| The First Affiliated Hospital of Kunming Medical College | 7 | 8.2 |
| Total | 85 | 100 |

讨 论

铜绿假单胞菌天然对多种抗菌药物耐药,而且具有极强的环境适应能力,是医院感染常见的条件

致病菌^[3],主要导致呼吸道、泌尿道和血流感染^[4-5]。本次监测较 2008 年 CHINET^[6]增加 2 所医院,各监测点的分离菌总数增加 782 株^[2]。铜绿假单胞菌主要分离自住院患者(91.9%),以呼吸道标本中分

离株最多见(75.2%),其次是尿液(7.5%)。临床科室以 ICU 最常见(16.7%),与加拿大和美国报道相似^[7]。ICU 患者常作气管插管或气管切开,加上机械通气、人工吸痰等操作,使感染的机会大大增加^[8]。

CHINET2009 年监测数据与 2007 年相比,铜绿假单胞菌对抗菌药物的耐药率基本相仿,并略有下降。上海华山医院、北京协和医院、北京医院和广州医学院附属第一医院分离株的耐药率下降明显,尤其对头孢吡肟、头孢他啶、头孢哌酮、哌拉西林的耐药率。但铜绿假单胞菌的总体耐药率仍处于较高水平,该菌对抗菌药物敏感率最高的是阿米卡星,为 80.2%,对其他抗菌药物的敏感率均低于 76%。本次调查还发现不同医院分离的铜绿假单胞菌耐药性差别较大,如对庆大霉素的耐药率,昆明医学院附属第一医院分离出菌株的耐药率为 62.5%,而甘肃省人民医院仅为 16.0%。其次,成人与儿童医院分离的铜绿假单胞菌的耐药率也明显不同,上海儿科医院的菌株对各抗菌药物的耐药率均低于 10%,对全部 13 种抗菌药物的耐药率是 14 所医院中最低者;上海儿童医院中分离的菌株对各种抗菌药物的耐药率均低于 30%。推测这可能与儿童患者中极少应用氟喹诺酮类和氨基糖苷类药物有关。不同地区分离菌株的耐药率也不同,甘肃省人民医院的菌株除对庆大霉素、头孢哌酮、氨曲南和环丙沙星外,对其他各种抗菌药物的耐药率均低于 10%,耐药率明显低于其他医院。北京医院检出的菌株对亚胺培南的耐药率高达 50.6%,而昆明医学院附属第一医院更高达 61.3%,这可能与不同医院的科室设置、收治对象、病种及用药习惯等有关,同时也提示各医院在进行抗感染治疗时应根据当地的监测结果及药敏试验结果合理选用抗菌药物^[2]。

泛耐药铜绿假单胞菌的出现是抗感染治疗面临的一个非常棘手的问题。本次监测 14 所医院中 10 所均检出泛耐药株,总检出率为 1.7%(85/4 912),比 2008 年的 2.1%有所下降,但上海瑞金医院、重庆医科大学第一附属医院分离的泛耐药株有较大的

增加(2.3%和 4.5%,2.3%和 4.2%)^[6]。该菌大多分离自 ICU,且多为克隆传播^[8],易引医院感染暴发流行,因此加强消毒隔离等医院感染的控制措施极为重要。

铜绿假单胞菌对抗菌药物的高耐药性仍是我国临床医学面临的严峻问题,应加强细菌耐药性监测,关注我国细菌耐药的发展趋势,加强抗菌药物的管理和合理用药,加强医院感染控制措施,防止多重耐药和泛耐药细菌在医院内的播散。同时为卫生行政部门制定合理使用抗菌药物、控制细菌耐药性发展的政策提供信息。

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