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重症监护病房呼吸机相关肺炎的病原菌分布及耐药性分析 *

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摘要 目的：研究重症监护病房（ICU）呼吸机相关肺炎的病原菌分布及耐药性情况。**方法：**采集2016年4月-2017年8月于我院ICU住院治疗的58例呼吸机相关肺炎患者痰样本进行病原菌培养，观察病原菌分布情况。同时对主要病原菌进行药敏试验，分析病原菌对头孢他啶、头孢曲松、环丙沙星、奈替米星、妥布霉素、氨曲南、亚胺培南、阿米卡星八种常见抗生素的耐药性情况。**结果：**58例呼吸机相关肺炎患者共培养204株病原菌，204株病原菌中根据占比分别为革兰氏阴性菌69.61%（142/204）、真菌15.20%（31/204）以及革兰氏阳性菌15.20%（31/204），且革兰氏阴性菌占比均明显高于真菌以及革兰氏阳性菌（P<0.05），其中革兰氏阴性菌中肺炎克雷伯菌占比21.08%（43/204）、铜绿假单胞菌占比18.14%（37/204）、鲍氏不动杆菌占比10.78%（22/204）、产气肠杆菌占比9.31%（19/204）。呼吸机相关肺炎患者病原菌中肺炎克雷伯菌、产气肠杆菌、金黄色葡萄球菌对亚胺培南的耐药性均低于其他七种抗生素，差异有统计学意义（P<0.05），铜绿假单胞菌对奈替米星的耐药性均低于其他七种抗生素，差异有统计学意义（P<0.05），鲍氏不动杆菌耐药性均较高。**结论：**ICU中呼吸机相关肺炎主要是由革兰氏阴性菌引发，且耐药情况不容乐观，其中革兰氏阴性菌对亚胺培南最为敏感，值得临床重点关注。

关键词：呼吸机相关肺炎；重症监护病房；耐药性；病原菌

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Analysis of Distribution and Drug Resistance of Pathogenic Bacteria of Ventilator-Associated Pneumonia in Intensive Care Unit*

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ABSTRACT Objective: To study the distribution and drug resistance of pathogenic bacteria of ventilator-associated pneumonia in intensive care unit (ICU). **Methods:** Sputum samples were collected from 58 patients with ventilator associated pneumonia who were treated in ICU of our hospital from April 2016 to August 2017 for pathogenic bacteria culture, and the distribution of pathogenic bacteria was observed. At the same time, the main pathogenic bacteria were tested for drug sensitivity, and analyzed the resistance of pathogenic bacteria to eight common antibiotics, including ceftazidime, ceftriaxone, ciprofloxacin, netilmicin and tobramycin, aztreonam, imipenem, amikacin. **Results:** A total of 204 strains of pathogenic bacteria were isolated from 58 patients with ventilator-associated pneumonia, the proportion in 204 strains of pathogenic bacteria was gram negative bacteria with 69.61% (142/204), fungi with 15.20% (31/204), gram positive bacteria with 15.20% (31/204), respectively, the proportion of gram negative bacteria was significantly higher than that of fungi and gram positive bacteria (P<0.05), among the gram negative bacteria, *Klebsiella pneumoniae* was accounted for 21.08% (43/204), Pseudomonas aeruginosa was accounted for 18.14% (37/204), *Acinetobacter baumannii* was accounted for 10.78% (22/204), *Enterobacter* was accounted for 9.31% (19/204). The drug resistance of *Klebsiella pneumoniae*, *Enterobacter cloacae* and *Staphylococcus aureus* to imipenem in the pathogens of patients with ventilator-associated pneumonia were lower than those of the other seven antibiotics, the difference was statistically significant (P<0.05), the drug resistance of *Pseudomonas aeruginosa* to netilmicin was lower than that of the other seven antibiotics, and the difference was statistically significant (P<0.05), the drug resistance of *Acinetobacter baumannii* was higher. **Conclusion:** Ventilator-associated pneumonia in ICU is mainly caused by Gram negative bacteria, and the drug resistance is not optimistic. Among them, gram negative bacteria are most sensitive to imipenem, which is worthy of clinical attention.

Key words: Ventilator associated pneumonia; Intensive care unit; Drug resistance; Pathogenic bacteria

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前言

重症监护病房（Intensive care unit, ICU）患者普遍存在一种或多种基础疾病，免疫功能相对较差，加之频繁接受有创治疗以及广泛应用抗生素，进一步增加了细菌感染发生的风险[1]。其中呼吸机相关肺炎感染是患者院内感染的主要形式，是机械通

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气治疗 ICU 患者最为常见的严重并发症，亦是导致 ICU 患者死亡的主要原因[2-4]。其病原菌普遍特点是较难医治，且对临床抗菌药物具有极高的耐药性，从而导致患者迁延不愈，临床治疗效果不理想[5-7]。因此，明确 ICU 呼吸机相关肺炎的病原菌感染情况，并指导临床抗生素的合理应用，对提高临床治疗效果，改善患者预后具有极其重要的意义[8,9]。鉴于此，本文通过研究 ICU 呼吸机相关肺炎的病原菌分布情况并分析其对临床常用抗生素的耐药性，旨在为临床有效防治 ICU 呼吸机相关肺炎感染提供参考依据，现作如下报道。

1 资料与方法

1.1 一般资料

选择 2016 年 4 月 -2017 年 8 月于我院 ICU 住院治疗的呼吸机相关肺炎患者 58 例作为研究对象。纳入标准[10]：(1)所有病例均符合 2001 年卫生部颁发的《医院感染诊断标准》中有关呼吸机相关肺炎感染的诊断标准；(2) 接受呼吸机治疗时间超过 48 h 发生的肺部炎症；(3)体温超过 37.5℃，且呼吸道存在脓性分泌物，可闻分布湿性啰音；(4)经胸部 X 线检查发现肺部存在浸润性阴影；(5)所有患者均签署了知情同意书。排除标准：(1)分离支气管分泌物后未得病原菌；(2)合并严重心、肝、肾功能缺陷者；(3)恶性肿瘤者；(4)精神失常者。其中男 32 例，女 26 例，年龄 33～82 岁，平均年龄(61.31± 10.46)岁；气管切开 41 例，经口气管插管 17 例；原发基础疾病：慢性肺部疾病 19 例，脑血管疾病 17 例，心肺复苏 10 例，其他病因 12 例。我院伦理委员会已批准本次研究。

1.2 研究方法

使用带标本收集瓶的一次性无菌吸痰管，经气管插管或气管切开完成分泌物标本的采集。采用 ATB 全自动细菌鉴定以及药敏测试仪(购自法国梅里埃公司)完成细菌培养鉴定以及相关药敏试验，药敏试验采用 K-B 纸片扩散法。统计过程中注意若相同菌种标本采集时间≤ 7d，则视为同一菌株，不予以重复统计。

1.3 观察指标

观察呼吸机相关肺炎患者分泌物标本中的病原菌分布情况，并分析相关病原菌对头孢他啶、头孢曲松、环丙沙星、奈替米星、妥布霉素、氨曲南、亚胺培南、阿米卡星八种抗生素的耐药性情况。

1.4 统计学方法

本研究数据均采用 SPSS20.0 软件进行检测分析，计数资料以率(%)表示，采用 χ^2 检验，计量资料用均数± 标准差($\bar{x}\pm s$)表示，实施 t 检验，P<0.05 表示差异具有统计学意义。

2 结果

2.1 ICU 呼吸机相关肺炎患者分泌物标本中 204 株病原菌分布情况分析

58 例呼吸机相关肺炎患者共培养 204 株病原菌，分别为革兰氏阴性菌 69.61%(142/204)、真菌 15.20%(31/204)以及革兰氏阳性菌 15.20%(31/204)，且革兰氏阴性菌占比均明显高于真菌以及革兰氏阳性菌，差异有统计学意义(P<0.05)。其中革兰氏阴性菌中肺炎克雷伯菌占比 21.08%(43/204)、铜绿假单胞菌占比 18.14%(37/204)、鲍氏不动杆菌占比 10.78%(22/204)、产气肠杆菌 9.31%(19/204)。见下表 1。

2.2 主要革兰氏阴性、阳性菌对临床常用的八种抗生素耐药性分析

呼吸机相关肺炎患者病原菌中肺炎克雷伯菌、产气肠杆菌、金黄色葡萄球菌对亚胺培南的耐药性均低于其他七种抗生素，差异有统计学意义(P<0.05)，铜绿假单胞菌对奈替米星的耐药性均低于其他七种抗生素，差异有统计学意义(P<0.05)，鲍氏不动杆菌耐药性均较高。见表 2。

表 1 ICU 呼吸机相关肺炎患者分泌物标本中 204 株病原菌分布情况分析

Table 1 Analysis of the distribution of 204 pathogenic bacteria in the specimen of the secretions of ICU patients with ventilator-associated pneumonia

Types of pathogenic bacteria	n(%)
Gram negative bacteria	142(69.61)
Klebsiella pneumoniae	43(21.08)
Pseudomonas aeruginosa	37(18.14)
Acinetobacter baumannii	22(10.78)
Enterobacter	19(9.31)
Others	21(10.29)
Gram positive bacteria	31(15.20)
Staphylococcus aureus	20(9.80)
Others	11(5.39)
Fungi	31(15.20)
Candida albicans	16(7.84)
Candida Kurus	14(6.86)
Others	1(0.49)

3 讨论

呼吸机相关肺炎主要是指患者原本并未发生肺部感染，但在接受有创机械通气治疗 48 h 后所出现肺部感染的情况，或是原本已发生肺部感染，接受有创机械通气治疗 48 h 后病情发生恶化[11,12]。国内外已有研究报道表明[13,14]，在 1996 年 -1999 年 ICU 中接受呼吸机治疗的患者发生呼吸机相关肺炎的概率为 23.1%，且相比未发生呼吸机相关肺炎的患者，住院治疗时间明显延长，病死率显著升高。对于呼吸机相关肺炎患者，应及时予以抗生素药物治疗，以降低病死率，缩短机械通气治疗时间以及住院时间[15-17]。然而，随着抗菌药物在临床上的广泛应用，其耐药性也呈逐渐上升趋势。因此，明确呼吸机相关肺炎的病原菌分布情况及其耐药性显得尤为重要，可为抗菌药物的应用提供指导作用[18-21]。

本研究结果显示：204 株病原菌中革兰氏阴性菌占比均明显高于真菌以及革兰氏阳性菌(P<0.05)，其中革兰氏阴性菌中肺炎克雷伯菌占比 21.08%(43/204)、铜绿假单胞菌占比 18.14%(37/204)、鲍氏不动杆菌占比 10.78%(22/204)、产气肠杆菌 9.31%(19/204)。这与危群华等人的研究报道类似[22,23]，说明了 ICU 呼吸机相关肺炎感染中多见于革兰氏阴性菌，且其中以肺炎克雷伯菌、铜绿假单胞菌、鲍氏不动杆菌和产气肠杆菌

表 2 主要革兰氏阴性、阳性菌对临床常用的八中种抗生素耐药性分析[n(%)]

Table 2 Analysis of drug resistance of gram positive and gram negative bacteria to eight kinds of antibiotics commonly used in clinic[n(%)]

Antibiotics	*Klebsiella pneumoniae* (n=43)	*Pseudomonas aeruginosa* (n=37)	*Acinetobacter baumannii* (n=22)	*Enterobacter* (n=19)	*Staphylococcus aureus* (n=20)
Ceftazidime	43(100.00)*	31(83.78)#	15(68.18)	19(100.00)*	16(80.00)*
Cefatriaxone	43(100.00)*	37(100.00)#	22(100.00)	19(100.00)*	20(100.00)*
Ciprofloxacin	43(100.00)*	35(94.59)#	16(72.73)	19(100.00)*	18(90.00)*
Netilmicin	43(100.00)*	2(5.41)	16(72.73)	19(100.00)*	12(60.00)*
Tobramycin	43(100.00)*	30(81.08)#	12(54.55)	19(100.00)*	10(50.00)*
Aztreonam	43(100.00)*	37(100.00)#	16(72.73)	19(100.00)*	18(90.00)*
Imipenem	2(4.65)	9(24.32)#	13(59.09)	0(0.00)	0(0.00)
Amikacin	43(100.00)*	30(81.08)#	12(54.55)	19(100.00)*	10(50.00)*

Note: Compared with imipenem,*P<0.05; compared with netilmicin, #P<0.05.

为主。分析原因,作者认为肺炎克雷伯菌通常存在于人体上呼吸道以及肠道内,当机体抵抗力下降时,便会经由呼吸道进入肺内,从而导致大叶与小叶融合性实变,进一步促使肺部炎症的发生。铜绿假单胞菌在自然界分布较为广泛,可在潮湿环境中生存,且能定植在正常人的咽部,当气管切开予以机械通气时,可能导致其位置发生变化,进一步导致肺部感染。鲍氏不动杆菌在自然界内同样广泛分布存在,在潮湿环境中的生存能力极强,且具有较强的粘附力,经常粘附于各种医疗器械上,当患者接受侵入性操作时便有可能引发感染[24,25]。此外,肺炎克雷伯菌、产气肠杆菌、金黄色葡萄球菌对亚胺培南的耐药性均低于其他七种抗生素(P<0.05),这提示了我们在临床治疗中,对于肺炎克雷伯菌、产气肠杆菌、金黄色葡萄球菌引发的呼吸机相关肺炎,应尽量采用亚胺培南进行治疗,以提高临床效果。与此同时,铜绿假单胞菌对奈替米星的耐药性均低于其他七种抗生素(P<0.05),说明采用奈替米星治疗由铜绿假单胞菌引发的呼吸机相关肺炎效果最佳,应尽量避免采用其余七种抗生素进行治疗。另外, 鲍氏不动杆菌对八种抗生素的耐药性均已超过50%,表明了采用上述抗生素治疗铜绿假单胞菌引发的呼吸机相关肺炎的效果均不太理想,应予以其他种类抗生素进行治疗。

综上所述,ICU 中呼吸机相关肺炎主要是由革兰氏阴性菌引发,且耐药性均较高,临床上采用亚胺培南进行治疗可取得较为理想的效果。

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（上接第 2913 页）

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