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血液透析患者导管相关性血流感染的病原菌、耐药性以及影响因素分析*

吴素娟 郑淑英 周燕 申玲君 黄秋霞

(暨南大学附属第一医院血液透析中心 广东 广州 510630)

摘要 目的:研究血液透析患者导管相关性血流感染(CRBSI)的病原菌、耐药性以及影响因素。**方法:**将我院从2018年1月~2019年1月收治的100例CRBSI血液透析患者纳入研究,记作感染组。通过细菌培养分析病原菌分布情况,以药敏试验观察主要病原菌对常见抗菌药物的耐药性。另取同期于我院接受血液透析未发生CRBSI的患者100例作为无感染组,比较两组临床病理资料,并对血液透析患者CRBSI发生的影响因素进行多因素Logistic回归分析。**结果:**100例CRBSI患者共分离获取病原菌118株,按照占比从高到低的顺序依次是金黄色葡萄球菌、表皮葡萄球菌、大肠埃希菌、粪肠球菌、鲍氏不动杆菌、铜绿假单胞菌、肺炎克雷伯菌、其它病原菌,占比依次为25.42%、16.95%、15.25%、12.71%、9.32%、8.47%、7.63%、4.24%。金黄色葡萄球菌以及表皮葡萄球菌对万古霉素、替加环素的耐药率均为0.00%,且金黄色葡萄球菌对莫西沙星、庆大霉素的耐药率亦为0.00%。感染组合并基础疾病、导管留置时间 ≥ 2 周以及股静脉插管人数占比高于无感染组($P < 0.05$)。经多因素Logistic回归分析可得:合并基础疾病以及插管部位为股静脉均是血液透析患者CRBSI的独立危险因素($OR=2.006, 1.390, P < 0.05$)。**结论:**血液透析患者CRBSI病原菌主要为金黄色葡萄球菌、表皮葡萄球菌,上述两种病原菌对万古霉素、替加环素较为敏感,其中金黄色葡萄球菌对莫西沙星以及庆大霉素亦较为敏感。合并基础疾病,股静脉插管均会增加CRBSI发生的风险,值得临床重点关注。

关键词:血液透析;导管相关性血流感染;病原菌分布;耐药性

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Analysis of Pathogenic Bacteria, Drug Resistance and Influencing Factors of Catheter-related Bloodstream Infection in Hemodialysis Patients*

WU Su-juan, ZHENG Shu-ying, ZHOU Yan, SHEN Ling-jun, HUANG Qiu-xia

(Hemodialysis Center, The First Affiliated Hospital of Jinan University, Guangzhou, Guangdong, 510630, China)

ABSTRACT Objective: To study the pathogenic bacteria, drug resistance and influencing factors of catheter-related bloodstream infection (CRBSI) in hemodialysis patients. **Methods:** 100 patients with CRBSI hemodialysis who were admitted to our hospital from January 2018 to January 2019 were included in the study, which was referred to as the infection group. Bacterial culture was used to analyze the distribution of pathogenic bacteria, and drug sensitivity test was used to observe the resistance of main pathogenic bacteria to common antimicrobial drugs. In addition, 100 patients without CRBSI who received hemodialysis in our hospital during the same period were selected as the non-infection group. The clinical medical records of the two groups were compared, and the relationship between CRBSI occurrence and related factors in hemodialysis patients was analyzed by multivariate Logistic regression. **Results:** A total of 118 strains of pathogenic bacteria were isolated from 100 patients with CRBSI. In the order of proportion from high to low, *staphylococcus aureus*, *staphylococcus epidermidis*, *escherichia coli*, *enterococcus faecalis*, *acinetobacter baumannii*, *pseudomonas aeruginosa*, *klebsiella pneumoniae*, other pathogens, the proportions were 25.42%, 16.95%, 15.25%, 12.71%, 9.32%, 8.47%, 7.63% and 4.24% respectively. The drug resistance rate of *staphylococcus aureus* and *staphylococcus epidermidis* to vancomycin and tegacycline was 0.00%, and the drug resistance rate of *staphylococcus aureus* to moxifloxacin and gentamicin was also 0.00%. Infection group combination and basic diseases, catheter indwelling time ≥ 2 weeks, and the proportion of the number of patients intubated in femoral vein was higher than that in the non-infection group ($P < 0.05$). According to the multivariate Logistic regression analysis, the combination of basic diseases and femoral vein at the intubation site were independent risk factors for CRBSI in hemodialysis patients ($OR=2.006, 1.390; P < 0.05$). **Conclusion:** The main pathogens of CRBSI in hemodialysis patients are *staphylococcus aureus* and *staphylococcus epidermidis*, and the above two pathogens are more sensitive to vancomycin and tegacycline, *staphylococcus aureus* are also sensitive to moxifloxacin and gentamicin. In addition, combined with basic diseases, prolonged femoral venous intubation and catheter indwelling time all increase the risk of CRBSI, which are worthy of clinical attention.

Key words: Hemodialysis; Catheter related bloodstream infection; Distribution of pathogenic bacteria; Drug resistance

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作者简介:吴素娟(1984-),女,本科,主治医师,研究方向:血液净化,E-mail:wsj8421@163.com

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前言

血液透析往往需要通过深静脉置管完成血液净化治疗,然而,由于各种原因引起的导管感染发病率正呈逐年升高趋势^[1-3]。国外疾病预测控制中心相关研究指出,美国平均导管感染率约为 5.3/千个导管的留置,感染患者的病死率高达 25.0%^[4]。其中导管相关性血流感染(Catheter related blood stream infection, CRBSI)是临床上最为常见的深静脉导管相关感染之一^[5,6],一旦发生将会增加患者的痛苦,增加临床治疗难度,不利于患者的病情康复,且会在一定程度上增加患者家庭的经济负担^[7-9]。鉴于此,本研究通过分析血液透析患者 CRBSI 的病原菌、耐药性以及影响因素,旨在为血液透析患者 CRBSI 的防治提供参考依据,现作以下报道。

1 对象与方法

1.1 一般资料

将我院从 2018 年 1 月~2019 年 1 月收治的 100 例 CRBSI 血液透析患者纳入研究,记作感染组。纳入标准:(1)所有患者均接受规律性血液透析治疗;(2)血液透析时间已超过 3 个月;(3)无严重营养不良者;(4)无临床病理资料缺失。排除标准:(1)入院前即已存在血液感染或(和)免疫性疾病者;(2)合并恶性肿瘤者;(3)意识障碍或无法正常交流沟通者;(4)心、肺、肾等重要脏器发生严重病变者;(5)正参与其他研究者。男女人数分别为 51 例,49 例,年龄 51~78 岁,平均年龄(61.39±4.95)岁;插管次数 1~5 次,平均插管次数(3.03±0.34)次。另取同期于我院接受血液透析未发生 CRBSI 的患者 100 例作为无感染组。男女人数分别为 53 例,47 例,年龄 52~77 岁,平均年龄(61.04±5.02)岁;插管次数 1~6 次,平均插管次数(3.05±0.32)次。两组一般资料对比无显著差异($P>0.05$),均衡可比。所有患者均在知情同意书上签字,本研究获批于医院伦理委员会。

1.2 研究方法

(1)细菌培养及药敏试验:获取所有感染组患者的中心静脉或外周静脉血样,采用生物梅里埃 VITEK2 Compact 型全自动细菌鉴定(药敏)仪以及相关配套试剂外加分析软件完成病原菌的鉴定,严格遵循临床检验规程操作。其中药敏试验结果主要是参照 2017 年 CLSI 标准完成判定^[10],以金黄色葡萄球菌 ATCC29213,铜绿假单胞菌 ATCC27853 以及大肠埃希菌 ATCC25922 作为质控菌株。(2)临床病理资料采集:通过我院自制的临床病理资料调查问卷完成,主要包括以下几点:①年龄;②性别;③是否合并基础疾病;④插管次数;⑤导管留置时间;⑥插管部位。

1.3 评价标准

CRBSI 判定标准如下^[10]:(1)出现发热或(和)寒颤等全身中毒症状,且有菌血症,血培养分离获取病原微生物,至少有 1 次检测结果显示为阳性;(2)与中华医学会重症学专业委员会制定的《血管内导管相关感染的预防与治疗指南》^[10]中相关标准相符。

1.4 统计学处理

上述数据应用 SPSS 22.0 软件分析,计数资料以[n(%)]表示,实施 χ^2 检验,计量资料以($\bar{x}\pm s$)表示,实施 t 检验,血液透析患者 CRBSI 发生的影响因素采用多因素 Logistic 回归分析,将 $P<0.05$ 记作差异有统计学意义。

2 结果

2.1 100 例 CRBSI 患者病原菌分布情况分析

100 例 CRBSI 患者共分离获取病原菌 118 株,按照占比从高到低的顺序依次是金黄色葡萄球菌、表皮葡萄球菌、大肠埃希菌、粪肠球菌、鲍氏不动杆菌、铜绿假单胞菌、肺炎克雷伯菌、其它病原菌,占比依次为 25.42%、16.95%、15.25%、12.71%、9.32%、8.47%、7.63%、4.24%。见表 1。

表 1 100 例 CRBSI 患者病原菌分布情况分析(n=118)

Table 1 Analysis of pathogen distribution in 100 patients with CRBSI(n=118)

| Pathogenic bacteria | Number of plants (plants) | Proportion(%) |
|-----------------------------------|---------------------------|---------------|
| <i>Staphylococcus aureus</i> | 30 | 25.42 |
| <i>Staphylococcus epidermidis</i> | 20 | 16.95 |
| <i>Escherichia coli</i> | 18 | 15.25 |
| <i>Acinetobacter baumannii</i> | 11 | 9.32 |
| <i>Enterococcus faecalis</i> | 15 | 12.71 |
| <i>Pseudomonas aeruginosa</i> | 10 | 8.47 |
| <i>Klebsiella pneumoniae</i> | 9 | 7.63 |
| Others | 5 | 4.24 |

2.2 CRBSI 主要病原菌对常见抗菌药物的耐药性分析

金黄色葡萄球菌以及表皮葡萄球菌对万古霉素、替加环素

的耐药率均为 0.00%,且金黄色葡萄球菌对莫西沙星、庆大霉素的耐药率亦为 0.00%。见表 2。

表 2 CRBSI 主要病原菌对常见抗菌药物的耐药性分析【株(%)】

Table 2 Resistance analysis strains of main pathogenic bacteria of CRBSI to common antimicrobial agents plants (%)

| Antibacterials | <i>Staphylococcus aureus</i> (n=30) | <i>Staphylococcus epidermidis</i> (n=20) |
|--------------------|-------------------------------------|--|
| Gbenzyl penicillin | 25(83.33) | 20(100.00) |
| Ciprofloxacin | 7(23.33) | 10(50.00) |
| Levofloxacin | 5(16.67) | 5(25.00) |
| Moxifloxacin | 0(0.00) | 6(30.00) |
| Gentamicin | 0(0.00) | 4(20.00) |
| Erythromycin | 20(66.67) | 14(70.00) |
| Clindamycin | 18(60.00) | 11(55.00) |
| Vancomycin | 0(0.00) | 0(0.00) |
| Tegacycline | 0(0.00) | 0(0.00) |
| Achromycin | 5(16.67) | 5(25.00) |

2.3 两组患者的临床病理资料对比

感染组合并基础疾病、导管留置时间 ≥ 2 周以及股静脉插

管人数占比高于无感染组($P<0.05$);而两组不同年龄、性别以及插管次数人数占比对比均不明显($P>0.05$)。见表 3。

表 3 两组患者的临床病理资料对比【例(%)】

Table 3 Comparison of clinicopathological data between the two groups[n(%)]

| Clinicopathological data | | Infection group(n=100) | Non-infection group(n=100) | χ^2 | P |
|---------------------------------|--------------|------------------------|----------------------------|----------|-------|
| Age {years} | <60 | 46(46.00) | 48(48.00) | 0.080 | 0.777 |
| | ≥ 60 | 54(54.00) | 52(52.00) | | |
| Gender | Male | 51(51.00) | 53(53.00) | 0.080 | 0.777 |
| | Female | 49(49.00) | 47(47.00) | | |
| Cannula(Times) | <3 | 41(41.00) | 45(45.00) | 0.326 | 0.568 |
| | ≥ 3 | 59(59.00) | 55(55.00) | | |
| Catheter indwelling time(weeks) | <2 | 27(27.00) | 65(65.00) | 29.066 | 0.000 |
| | ≥ 2 | 73(73.00) | 35(35.00) | | |
| Combination of basic diseases | Yes | 53(53.00) | 36(36.00) | 5.851 | 0.016 |
| | No | 47(47.00) | 64(64.00) | | |
| Intubation site | Jugular vein | 37(37.00) | 53(53.00) | 5.172 | 0.023 |
| | Femoral vein | 63(63.00) | 47(47.00) | | |

2.4 血液透析患者 CRBSI 影响因素的多因素 Logistic 回归分析

以血液透析患者是否发生 CRBSI 为因变量 (是=1, 否=0), 以导管留置时间、是否合并基础疾病及插管部位为自变量, 其中自变量赋值如下: 导管留置时间<2周=0, ≥ 2 周=1;

合并基础疾病=1, 无基础疾病=0; 插管部位为颈内静脉=0, 插管部位为股静脉=1。经多因素 Logistic 回归分析可得: 合并基础疾病以及插管部位为股静脉均是血液透析患者 CRBSI 的独立危险因素($P<0.05$)。见表 4。

表 4 血液透析患者 CRBSI 影响因素的多因素 Logistic 回归分析

Table 4 Multivariate Logistic regression analysis of influencing factors of CRBSI in hemodialysis patients

| Variable | β | SE | Wald χ^2 | P | OR | 95%CI |
|-------------------------------------|---------|-------|---------------|-------|-------|-------------|
| Catheter indwelling time | 0.331 | 0.374 | 1.385 | 0.256 | 0.145 | 0.081~1.007 |
| Combination of basic diseases | 2.117 | 1.258 | 10.884 | 0.001 | 2.006 | 1.345~3.683 |
| Femoral vein at the intubation site | 3.083 | 2.305 | 8.204 | 0.005 | 1.390 | 1.048~2.385 |

3 讨论

血液透析是临床上用以治疗肾功能衰竭患者的重要维持性治疗方式, 其中 CRBSI 属于血液透析患者较为常见的严重

并发症之一,对患者的病情恶化具有促进作用,如不予以及时有效的干预,甚至会引起患者死亡^[11,12]。由此可见,寻求有效降低血液透析患者 CRBSI 发生风险以及治疗 CRBSI 的方式具有极其重要的意义^[13,14]。抗菌药物是目前临床上用以治疗 CRBSI 的主要方式之一,然而,由于近年来国内抗菌药物的滥用情况日益加剧,导致了大量耐药菌株的滋生以及传播,增加了抗感染治疗的难度^[15-17]。如何选择合理有效的抗菌药物成为临床医师共同关注的热点之一。

本研究发现,100 例血液透析 CRBSI 患者共分离获取病原菌 118 株,且以金黄色葡萄球菌、表皮葡萄球菌为主。这在李翠等人的研究结果中得到了佐证^[18]:血液透析患者 CRBSI 的主要病原菌为革兰阳性菌,且以金黄色葡萄球菌多见。分析原因,金黄色葡萄球菌和人体皮肤的常驻菌种一致,因此可能通过患者亦或是医护人员的手部接触导致感染的发生^[19-21]。因此,在临床实际工作中应注重无菌操作。另外,本研究发现血液透析 CRBSI 患者分离获取的菌株中存在部分条件致病菌,导致该结果的主要原因可能是患者免疫功能低下以及营养状况较差,值得临床重点关注^[22-24]。此外,金黄色葡萄球菌以及表皮葡萄球菌对万古霉素、替加环素的耐药率均为 0.00%,且金黄色葡萄球菌对莫西沙星、庆大霉素的耐药率亦为 0.00%。这一点在既往研究中也得到了证实^[25,26],说明了在针对血液透析 CRBSI 患者的抗感染治疗过程中,应严格根据药敏试验结果选用合理有效的抗菌药物,从而达到理想的抗感染效果。另外,感染组合并基础疾病、导管留置时间 ≥ 2 周以及股静脉插管人数占比高于无感染组。经多因素 Logistic 回归分析可得:合并基础疾病以及插管部位为股静脉均是血液透析患者 CRBSI 的独立危险因素。这在赵丽平等人的研究报告中得以证实^[27]:导管留置时间、插管部位以及基础疾病均是血液透析患者 CRBSI 的影响因素。究其原因,随着导管留置时间的不断延长,会于其表面形成疏松的纤维蛋白鞘层,从而有助于皮肤穿刺部位的细菌定植于导管上,并于导管表面进行繁殖、迁移,最终进入血液,引发感染;股静脉与肛门和尿道相邻,处于腹股沟区,极易受到尿液以及粪便的污染,加之股静脉血流较为缓慢,血栓形成风险较大,为细菌的侵入后生长提供了有利条件,从而增加了 CRBSI 发生风险;而合并基础疾病患者普遍存在不同程度的机体免疫功能下降,从而导致机体对细菌的杀伤能力降低,增加了 CRBSI 的几率^[28-30]。

综上所述,金黄色葡萄球菌、表皮葡萄球菌是引起血液透析患者 CRBSI 的主要病原菌,两种病原菌均对万古霉素、替加环素十分敏感,且金黄色葡萄球菌对莫西沙星、庆大霉素亦十分敏感,可能作为临床抗菌药物的选择的参考。此外,合并基础疾病,股静脉插管均会增加 CRBSI 发生的风险,应予以重视。

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