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替加环素对多重耐药鲍曼不动杆菌引起重症肺炎患者的临床疗效 *

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摘要 目的:探讨替加环素治疗多重耐药鲍曼不动杆菌引起的重症肺炎的临床疗效。**方法:**回顾性研究我院多重耐药鲍曼不动杆菌引起的重症肺炎60例,随机分为对照组和实验组,每组30例。对照组患者给予头孢哌酮舒巴坦治疗,实验组患者应用替加环素治疗。观察并比较两组患者治疗前后血清降钙素原(PCT)、C反应蛋白(CRP)及白细胞计数(WBC)的变化情况、不良反应情况、细菌清除情况及临床疗效。**结果:**与治疗前相比,两组患者血清PCT、CRP及WBC水平均降低(P<0.05);与对照组相比,实验组患者血清PCT、CRP及WBC水平较低(P<0.05);实验组不良反应发生率及再感染率低于对照组(P<0.05);实验组细菌清除率及临床总有效率高于对照组(P<0.05)。**结论:**对于由多重耐药鲍曼不动杆菌引起的重症肺炎,替加环素具有很好的临床疗效,值得在临床上推广使用。

关键词:替加环素;多重耐药鲍曼不动杆菌;重症肺炎

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Clinical Effect of Tigecycline in Treatment of Severe Pneumonia Infected by Multiple Drug Resistant of *Acinetobacter Bauman**

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ABSTRACT Objective: To investigate the clinical curative effect of tigecycline in the treatment of severe pneumonia infected bu the multiple drug resistant of *acinetobacter bauman*. **Methods:** 60 patients with severe pneumonia infected by the multiple drug resistant of acinetobacter bauman who were treated in our hospital were selected and randomly divided into the control group and the experiment group. The patients in the control group were treated with cefoperazone and sulbactam, while the patients in the experiment group were treated with tigecycline. Then the serum levels of procalcitonin (PCT) and C reactive protein (CRP), the white blood cell count (WBC), the adverse reactions, the bacterial clearance and clinical effect in the two groups were observed and compared before and after the treatment. **Results:** Compared with before treatment, the serum levels of PCT, CRP and WBC were lower in the two groups (P<0.05). Compared with the control group, the serum levels of PCT, CRP and WBC were lower in the experiment group after the treatment (P<0.05); Compared with the control group, the incidence of adverse reactions and the re-infection rate were lower in the experiment group, while the bacterial clearance rate and the clinical total effective rate were higher (P<0.05). **Conclusion:** Tigecycline has better clinical effect on the treatment of the severe pneumonia infected by the multi drug resistant of acinetobacter bauman, and it is worthy of clinical application.

Key words: Tigecycline; Multiple drug resistant *Acinetobacter Bauman*; Severe pneumonia

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前言

鲍曼不动杆菌(Ab)属于非发酵革兰阴性条件致病菌,在不动杆菌属中最为常见,其存在广泛,如生活中的水、土壤以及医院环境中,是院内感染的主要致病菌[1]。目前临床常用头孢哌酮舒巴坦进行治疗,随着抗生素的滥用,其临床治疗效果正在逐渐降低,因此,寻找一种能够提高其临床疗效的药物势在必行[2]。替加环素是第一类甘氨酰四环素类抗菌药物,是米诺环素的一种衍生物,具有广泛的抗菌谱,根据相关实验结果,其在绝大多数临床常见致病菌的试敏中都显示出了良好的抑菌效果,在多重耐药鲍曼不动杆菌(MDRAB)感染中具有不错的疗效[3,4],根据相关资料显示[5],替加环素治疗MDRAB成功率达

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76%。本实验通过对患者血清 PCT、CRP、WBC 水平与细菌清除率的检测，以及对不良反应与临床疗效的观察，来研究替加环素对多重耐药鲍曼不动杆菌引起重症肺炎的作用机制。

1 资料与方法

1.1 临床资料

选择于 2014 年 11 月～2016 年 8 月在海南省三亚市解放军第四二五医院就诊的由多重耐药鲍曼不动杆菌引起的重症肺炎患者 60 例，男性 36 例，女性 24 例，年龄 42～74 岁，平均年龄(52.55± 6.15)岁，APACHE-II 评分为(26.55± 3.42)。纳入标准：(1) 符合由中国卫生部制定的关于多重耐药鲍曼不动杆菌重症肺炎的诊断标准，并通过痰培养进行确诊；(2)对于研究中使用的药物无过敏反应史；(3) 本次治疗前一个月内未使用过抗生素类药品；(4)患者年龄在 30 岁以上。排除标准：(1)不符合多重耐药鲍曼不动杆菌重症肺炎的诊断标准；(2) 合并严重肝肾功能不全或心脑血管疾病患者；(3) 对研究中使用的药物有过敏反应史；(4)妊娠期、哺乳期及备孕妇女；(5)患者不能严格按照医嘱进行服药，不能积极配合治疗者。随机数字表法分为实验组和对照组，其中实验组患者 30 例，男性 18 例，女性 12 例，年龄 42～73 岁，平均年龄(52.45± 6.02)岁；对照组患者 30 例，男性 18 例，女性 12 例，年龄 43～74 岁，平均年龄(53.02± 6.38)岁。两组患者均未有脱落，且两组间平均年龄、性别组成、病情发展状况、APACHE-II 评分及基础疾病等基本资料选择无偏倚性(P＞0.05)。本次研究获得批准，并在我市伦理委员会的追踪监督下完成。

1.2 治疗方法

对照组：头孢哌酮钠舒巴坦钠(辉瑞制药有限公司，国药准字 H20057403)，用法用量：取 3 g 本品，用适量的 5 %葡萄糖溶液或 0.9%注射用氯化钠溶液进行溶解后静脉注射，静脉滴注时间应至少为 15-60 min；实验组：替加环素(江苏豪森药业股份有限公司，国药准字 H20123394)，用法用量：首次用量 100 mg，后改为 50 mg，应用适量 0.9%氯化钠注射液或 5%葡萄糖注射液溶解后静脉注射。

1.3 观察指标

在治疗前及治疗结束后的一天抽取患者肘部静脉血 5 mL，送至我院检验科进行检验。观察并记录治疗前后两组患者 PCT、CRP 及 WBC 水平变化情况；观察治疗期间两组患者出现的不良反应并计算不良反应发生率；并对两组患者的细菌清除情况进行观察，计算细菌清除率。

1.4 疗效判断

痊愈：临床症状及体征完全消失，实验室及影像学检测所有指标均恢复正常；显效：患者咳嗽、咯痰等症状明显改善，实验室及影像学检测基本恢复正常；有效：患者咳嗽、咯痰等临床症状有所改善，血象及肺部影像等指标对比治疗前有所好转，但为达到显效标准；无效：未达到以上标准者。总有效率＝(痊愈＋显效＋有效)/ 总例数× 100%。

1.5 统计学分析

所有计量数据录入 SPSS19.0 软件进行统计学分析，不良反应发生率、细菌清除率及临床总有效率采用卡方检验，血清 PCT、CRP 及 WBC 水平采用 t 检验，若检验后 P＜0.05，则认为有统计学意义。

2 结果

2.1 治疗前后两组患者血清 PCT、CRP 及 WBC 水平比较

与治疗前相比，两组患者血清 PCT、CRP 及 WBC 均降低(P<0.05)；与对照组比较，实验组患者血清 PCT、CRP 及 WBC 水平明显较低，差异具有统计学意义(P<0.05)，见表 1。

表 1 治疗前后两组患者血清 PCT、CRP 及 WBC 水平比较($\bar{x}\pm s$)

Table 1 Comparison of the serum levels of PCT, CRP and WBC between the two groups before and after treatment ($\bar{x}\pm s$)

Groups		PCT(mg/mL)	CRP(mg/L)	WBC(*10⁹)
Experiment group (n=30)	Before treatment	8.25± 1.13	62.15± 8.85	21.52± 3.01
	After treatment	1.13± 0.12*#	3.54± 0.42*#	6.25± 0.65*#
Control group (n=30)	Before treatment	8.22± 1.08	62.33± 8.92	21.65± 3.03
	After treatment	3.58± 0.48*	15.35± 3.51*	11.25± 1.45*

Note: compared with before treatment, *P＜0.05; compared with the control group after treatment, #P＜0.05.

2.2 两组患者不良反应发生情况比较

实验组患者不良反应发生率明显低于对照组，差异具有统计学意义(P<0.05)。见表 2。

2.3 两组患者细菌清除率比较

治疗后与对照组相比，实验组患者细菌清除率及再感染率明显较低，差异有统计学意义(P＜0.05)。见表 3。

表 2 两组患者不良反应比较[例(%)]

Table 2 Comparison of the adverse reaction between the two groups[n(%)]

Groups	Nausea and vomiting	Nausea and vomiting	Oliguria	Incidence of adverse reactions
Experiment group(n=30)	5(16.67)	3(10.00)	2(6.67)	10(33.33)
Control group(n=30)	8(26.67)	6(20.00)	5(16.67)	19(63.33)*

Note: compared with before treatment, *P＜0.05; compared with the control group after treatment, #P＜0.05.

表 3 两组患者细菌清除率及再感染率比较[例(%)]

Table 3 Comparison of the bacterial clearance rate and the reinfection rate between the two groups [n(%)]

Groups	Clearance rate	No clearance rate	Reinfection rate
Experiment group(n=30)	24(80.00)	6(20.00)	2(6.67)
Control group(n=30)	18(60.00)	12(40.00)	7(23.33)*

Note: Compared with the control group, *P<0.05.

2.4 两组患者的临床疗效比较

与对照组相比,实验组临床总有效率较高,差异有统计学意义(P<0.05)。见表 4。

表 4 两组患者疗效比较[例(%)]

Table 4 Comparison of the curative effect between the two groups [n(%)]

Groups	Cure	Excellent	Effective	Invalid	Total effective rate
Experiment group (n=30)	10(33.33)	12(40.00)	5(16.67)	3(10.00)	27(90.00)*
Control group(n=30)	6(20.00)	7(23.33)	7(23.33)	10(33.33)	20(66.67)

Note: compared with the control group, *P<0.05.

3 讨论

鲍曼不动杆菌能够使人体的任何部位与组织发生感染,泌尿系统、神经系统、呼吸系统、创伤处以及腹腔为主要感染部位,其中一半以上的感染为呼吸系统感染,占 54.2%。肺部感染既存在内源感染又存在外源感染,其中致病菌从口咽部吸入,是内源性感染的最有可能的发病机制[6,7];肺部感染的主要表现有咳嗽、血性痰、气急、发热、胸痛等,肺部听诊可存在细湿罗音,影像学常显示支气管肺炎的特征,也会有片状或大叶性浸润阴影,渗出性胸膜炎及肺脓肿表现不常见[8]。受到感染者多为抵抗力弱的患者、危重疾病患者、老年患者,以及广谱抗生素长期应用的患者与侵入性操作应用患者[9]。相关研究表明,其耐药性呈快速获得与传播的特点,对于化学消毒剂与紫外线的抵抗力较强,常规的消毒方法只能对其生长进行抑制而不能灭菌,广泛耐药、全耐药、多重耐药的鲍曼不动杆菌已在世界范围内开始流行,是抗感染领域的一大难题,也是我国目前最主要的超级细菌,其对于临床上常用抗生素的耐药率存在持续上升情况[10]。鲍曼不动杆菌具有十分复杂的耐药机制,主要包括产生如 β 内酰胺酶、氨基糖苷类修饰酶等抗菌药物灭活酶;菌体相关靶位置基因突变、结构改变等导致药物的作用靶位发生变化;外排汞的表达过度与外膜孔蛋白的通透性降低,引起作用靶位上药物的量降低[11,12]。这些复杂的耐药机制,导致鲍曼不动杆菌引起重症肺炎的治疗在临床上成为一道难题。

降钙素原(PCT)在血清中是一种降钙素前肽物质,并无激素活性[13]。当人体出现严重的寄生虫、真菌、细菌的感染,以及多脏器功能衰竭与脓毒血症时,血清中的 PCT 含量就会升高,而人体发生自身免疫性疾病与病毒感染或过敏反应时则不会出现升高现象,因此具有较高的灵敏性与准确性,也常用于病毒与细菌感染的鉴别[14]。降钙素原作为全身细菌感染一种的标记物,已在下呼吸道感染中被广泛应用,可以对疾病的疗效与进程进行提示。C 反应蛋白(CRP),是一种人体受到病原微生物入侵、组织损伤等炎症的刺激,进而使肝细胞合成的急性蛋白[15]。CRP 能够使白细胞的吞噬作用增强,对单核 / 巨噬细胞功能进行调节,使入侵人体的病原体,坏死、损伤、凋亡的组织细胞得以清除。CRP 在正常人的血清中的含量很低,而细菌感染或组织损伤等刺激炎性系统使其激活,CRP 的含量升高十分明显,其与炎症的严重程度呈正相关[16]。白细胞(WBC)具有防御疾病、吞噬细菌的主要作用,其在血清中的含量升高,通常提示人体存在急、慢性感染等各种细菌感染性疾病[17-19]。与对照组比较,实验组患者血清 PCT、CRP 及 WBC 水平明显较低(P<0.05),说明替加环素能有效改善患者的炎症反应。此外实验组患者不良反应发生率明显低于对照组(P<0.05),说明替加环素能有效降低不良反应发生率。我们还发现,治疗后与对照组相比,实验组患者细菌清除率及再感染率明显较低(P<0.05),说明替加环素能够有效控制感染,清除致病菌。本研究结果还显示,治疗后与对照组相比,实验组临床总有效率较高(P<0.05),说明替加环素能有效提高临床疗效。

综上所述,替加环素能有效改善患者的炎症反应、降低不良反应发生率,控制感染,清除致病菌,提高临床疗效。

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