

doi: 10.13241/j.cnki.pmb.2017.17.040

替加环素对重症呼吸机相关性肺炎患者呼吸力学与血清炎症因子的影响*

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摘要 目的:研究替加环素治疗重症呼吸机相关性肺炎的疗效及对患者呼吸力学及血清炎症因子水平的影响。**方法:**选取 2014 年 9 月至 2016 年 8 月本院收治的 88 例重症呼吸机相关性肺炎患者,根据投硬币法分为观察组和对照组,44 例每组。对照组采用常规治疗方案,观察组在常规治疗基础上采用替加环素治疗。观察并比较两组患者治疗前后呼吸力学、血清炎症因子指标及临床疗效。**结果:**治疗后,观察组临床总有效率高于对照组($P<0.05$)。观察组肺部感染控制时间、治愈时间均短于对照组($P<0.05$)。观察组呼吸做功、气道峰压、气道阻力均低于对照组,动态顺应性高于对照组($P<0.05$)。观察组 IL-6、IL-8、TNF- α 水平低于对照组($P<0.05$)。**结论:**重症呼吸机相关性肺炎患者经替加环素治疗后,能有效改善患者呼吸力学与血清炎症因子水平,临床疗效良好。

关键词:替加环素;呼吸机相关性肺炎;呼吸力学;炎症因子

中图分类号:R563.1 **文献标识码:**A **文章编号:**1673-6273(2017)17-3359-04

The Application of Tigecycline in the Treatment of Severe Ventilator-associated Pneumonia and its Influence on Respiratory Mechanics and Serum Inflammatory Factors*

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ABSTRACT Objective: To study the clinical efficacy of tigecycline on the treatment of severe ventilator-associated pneumonia and its influence on the respiratory mechanics and serum inflammatory factors levels of patients. **Methods:** 88 patients with severe ventilator-associated pneumonia admitted in our hospital from September 2014 to August 2016 were selected and randomly divided into the observation group and the control group, with 44 cases in each group. The patients in the control group were treated with conventional method, while the patients in the observation group were treated with tigecycline on the basis of the control group. Then the clinical curative effect and indexes of respiratory mechanics and serum inflammatory factors were observed and compared between the two groups before and after the treatment. **Results:** After treatment, the total clinical efficacy of the observation group was significantly higher than that of the control group ($P<0.05$). The time of pulmonary infection control and cure in the observation group were significantly shorter than those of the control group ($P<0.05$). The respiratory work, peak airway pressure and respiratory resistance in the observation group were significantly lower than those of the control group, while the dynamic compliance was significantly higher ($P<0.05$). The serum levels of IL-6, IL-8 and TNF- α in the observation group were significantly lower than those of the control group ($P<0.05$). **Conclusion:** Tigecycline can improve the respiratory mechanics and serum inflammatory factors in patients with severe ventilator-associated pneumonia, with better clinical curative effect.

Key words: Tigecycline; Ventilator associated pneumonia; Respiratory mechanics; Inflammatory factors

Chinese Library Classification(CLC): R563.1 **Document code:** A

Article ID: 1673-6273(2017)17-3359-04

前言

重症呼吸机相关性肺炎是临床中较为常见的一种并发症,主要发生在机械通气后,此病有着较高的发病率、死亡率,常常会引起败血症、炎症性反应以及多器官衰竭,甚至会给患者生命安全带来严重威胁^[1]。在治疗重症呼吸机相关性肺炎中最为重要的原则是控制与缓解肺部发生的感染,进而改善患者呼吸

功能^[2]。当前在治疗重症呼吸机相关性肺炎中最为常见的方式包括常规灌洗吸痰、抗感染等治疗方式,然而相关研究者提出常规治疗方式难以彻底清除气道中的堵塞物,也难以有效的改善肺功能,会导致感染继续,治疗效果不甚理想^[3]。对于重症呼吸机相关性肺炎抗生素的使用原则包括足量、恰当、尽早,并且需避免抗生素的过度使用。替加环素的生物特性和药理性支持耐药菌导致的且治疗方案有限的其他感染,相关研究者提出替

* 基金项目:陕西省科技攻关项目(2010K13-02-33)

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(收稿日期:2016-12-12 接受日期:2016-12-30)

加环素可应用于多重耐药鲍曼不动杆菌所导致的重症呼吸机相关性肺炎^[4]。为给临床在治疗重症呼吸机相关性肺炎提供更多可借鉴之处,本文就替加环素在重症呼吸机相关性肺炎治疗中的应用及对呼吸力学与血清炎症因子的影响进行探讨。

1 资料与方法

1.1 临床资料

选取 2014 年 9 月至 2016 年 8 月期间本院收治的 88 例重症呼吸机相关性肺炎患者,纳入标准:① 患者临床诊断均和呼吸机相关性肺炎诊断中的标准相符^[5];② 本次研究对象均无严重器官功能障碍;③ 辅助通气治疗时间在 3 d 及其以上,随之出现重症呼吸机相关性肺炎的症状和体征;④ 患者均自愿配合本次研究,依从性较好。排除标准:① 对本次研究中所使用的药物存在过敏史;② 经替加环素治疗 3 d 内被诊断出属于耐药菌株定植者;③ 合并精神疾病者、意识不清晰者;④ 患有其它可能会对本次研究结果造成影响的疾病,如肺结核、肺部肿瘤等。整个研究均在患者及其家属的知情同意下完成,同时取得了本院伦理委员会的批准和实施。根据投硬币法将本次研究对象分为观察组和对照组两组,44 例每组。其中观察组中男性 28 例,女性 16 例;年龄 58~79 岁,平均(67.43±1.26)岁。对照组中男性 31 例,女性 13 例;年龄为 59~78 岁,平均(66.09±1.31)岁。两组患者性别、年龄等临床资料比较差异性不明显($P>0.05$),可比性较强。

1.2 方法

对照组采用常规治疗方案,使用吸痰管对患者气管导管深部的痰液进行收集,随之对标本予以常规的细菌培养,开展药敏试验和细菌性检查,根据所检查出的结果予以具有针对性的抗身素、呼吸锻炼、体位引流等治疗。观察组在常规治疗基础上

加以替加环素(生产厂家:浙江海正药业股份有限公司,规格:50 mg,生产批号:20140211)进行治疗,剂量为 100 mg 的替加环素采取持续静脉滴注的方式给药,2 次/天,所有患者均连续治疗 14 d。

1.3 观察指标

评判两组患者治疗后的临床疗效^[6],标准如下:实验室和影像学检查提示为正常,体征或临床症状消失则为治愈;实验室和影像学检查提示为基本正常,体征或临床症状显著改善则为显效;实验室和影像学检查提示伴有感染,体征或临床症状有所缓解则为有效;上述标准未达到者则为无效。

比较两组患者肺部感染控制时间、呼吸衰竭重症病房停留时间、治愈时间。分析两组患者治疗前后呼吸力学指标,包括呼吸做功、气道峰压、气道阻力、动态顺应性。比较两组患者治疗前后血清炎症因子指标变化情况,分别在治疗前后抽取两组患者 5 mL 的空腹静脉血,使用乙二胺四乙酸二钠进行抗凝处理,此安全美联免疫吸附法检测白介素 -4、白介素 -8、肿瘤坏死因子 - α ,由上海生工生物技术有限公司提供试剂盒,均依据说明书完成本次操作。

1.4 统计学处理

本次实验数据处理选择 SPSS11.5 软件包进行,计量资料用($\bar{x} \pm s$)来表示,采用 t 检验,计数资料用[n(%)]来表示,采取 χ^2 检验,等级资料采取[n(%)]来表示,并进行秩和检验,其 $P<0.05$ 表明差异具有统计学意义。

2 结果

2.1 两组患者治疗的临床疗效比较分析

治疗后,观察组总的临床疗效率显著比对照组高($P<0.05$),见表 1。

表 1 两组患者治疗的临床疗效比较分析[n(%)]

Table 1 Comparison of clinical efficacy between two groups[n(%)]

Groups	Cure	Markedly	Valid	Invalid	Total efficacy
Observation group(n=44)	25(56.82)	9(20.45)	6(13.64)	4(9.09)	40(90.91)*
Control group(n=44)	14(31.82)	3(6.82)	14(31.82)	13(29.55)	31(70.45)

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

2.2 两组患者临床指标分析

观察组的肺部感染控制时间、呼吸衰竭重症病房停留时

间、治愈时间显著短于对照组,差异具有统计学意义($P<0.05$),见表 2。

表 2 两组患者临床指标分析($\bar{x} \pm s$)

Table 2 Analysis of clinical indicators between two groups($\bar{x} \pm s$)

Groups	Pulmonary infection control time (d)	Respiratory failure intensive care unit length of stay(d)	Cure time(d)
Observation group(n=44)	7.43±0.76*	9.87±1.21*	8.95±0.91*
Control group(n=44)	10.87±1.43	13.85±1.54	12.43±1.53

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

2.3 两组患者呼吸力学指标分析

治疗前,两组患者的呼吸做功、气道峰压、气道阻力、动态顺应性比较无显著性差异($P>0.05$),治疗后,两组患者的呼吸做功、气道峰压、气道阻力呼吸力学指标较治疗前显著降低($P<0.05$),动态顺应性较治疗前显著升高($P<0.05$),其中观察

组的呼吸做功、气道峰压、气道阻力呼吸力学指标显著低于对照组($P<0.05$),动态顺应性显著高于对照组($P<0.05$),见表 3。

2.4 两组患者血清炎症因子水平比较

治疗前,两组患者的 IL-6、IL-8、TNF- α 血清炎症因子水平比较无显著性差异($P>0.05$),治疗后,两组患者的 IL-6、IL-8、

TNF- α 血清炎症因子水平较治疗前显著降低($P<0.05$),其中观察组(P<0.05),见表4。
观察组的 IL-6、IL-8、TNF- α 血清炎症因子水平显著低于对照组

表3 两组患者呼吸力学指标分析($\bar{x} \pm s$)Table 3 Analysis of Respiratory mechanics indicators between two groups($\bar{x} \pm s$)

Items	Time	Observation group(n=44)	Control group(n=44)
WOB(J/L)	Before treatment	0.86 $\pm$ 0.08	0.87 $\pm$ 0.06
	After treatment	0.36 $\pm$ 0.02 ^{*#}	0.57 $\pm$ 0.05 [*]
PIP(cmH ₂ O)	Before treatment	33.03 $\pm$ 3.11	33.08 $\pm$ 3.15
	After treatment	17.43 $\pm$ 1.54 ^{*#}	25.03 $\pm$ 2.21 [*]
Raw(cmH ₂ O $\cdot$ L ⁻¹ $\cdot$ s ⁻¹)	Before treatment	16.04 $\pm$ 1.43	16.08 $\pm$ 1.46
	After treatment	9.43 $\pm$ 0.96 ^{*#}	12.46 $\pm$ 1.21 [*]
Cdyn(ml/mmH ₂ O)	Before treatment	19.45 $\pm$ 1.76	19.48 $\pm$ 1.79
	After treatment	33.65 $\pm$ 3.12 ^{*#}	24.65 $\pm$ 2.14 [*]

Note: compared with before treatment, ^{*}P<0.05; compared with control group after treatment, [#]P<0.05.

表4 两组患者血清炎症因子水平比较($\bar{x} \pm s$)Table 4 Comparison of serum inflammatory factors between two groups($\bar{x} \pm s$)

Items	Time	Observation group(n=44)	Control group(n=44)
IL-6(ng/L)	Before treatment	0.51 $\pm$ 0.08	0.52 $\pm$ 0.09
	After treatment	0.31 $\pm$ 0.04 ^{*#}	0.45 $\pm$ 0.06 [*]
IL-8(ng/L)	Before treatment	2.35 $\pm$ 0.24	2.38 $\pm$ 0.25
	After treatment	0.91 $\pm$ 0.03 ^{*#}	1.52 $\pm$ 0.15 [*]
TNF- α (ng/L)	Before treatment	32.04 $\pm$ 3.11	32.12 $\pm$ 3.09
	After treatment	19.87 $\pm$ 1.42 ^{*#}	24.65 $\pm$ 2.12 [*]

Note: compared with before treatment, ^{*}P<0.05; compared with control group after treatment, [#]P<0.05.

3 讨论

重症呼吸机相关性肺炎是医院中较为常见的一种感染性疾病,主要和患者使用呼吸机有关,此病的病死率较高,是危重患者致死的主要因素之一。在治疗重症呼吸机相关性肺炎中选取抗菌药物应以安全可靠、效果确切为主,主要是因为能有效、快速控制炎症感染^[7,8]。重症呼吸机相关性肺炎患者病情变化快且重,肺部通气换气功能呈下降趋势,伴有较为严重的感染,若不能采取及时有效的措施予以治疗,极有可能导致全身炎症反应,严重者可能会发生多器官功能衰竭^[9,10]。

替加环素在抗生素药物中有着最为广泛的抗菌谱,对革兰阳性菌、厌氧菌、部分分枝杆菌、革兰阴性菌有着较佳的抗菌活性^[11,12]。替加环素能相结合于细菌核糖体 30S 亚基,对细菌蛋白质的合成具有抑制作用,有较大侧链的空间位阻效应,在四环素耐药的细菌中能发挥良好的抗菌作用^[13,14]。本次研究结果表明,经替加环素治疗的重症呼吸机相关性肺炎患者,其临床疗效显著优于单纯常规治疗,提示替加环素对患者临床症状发挥着明显改善作用。本次研究中还发现经替加环素治疗的重症呼吸机相关性肺炎患者,其肺部感染控制时间、呼吸衰竭重症病房停留时间、治愈时间显著比常规治疗的重症呼吸机相关性肺炎患者时间短,提示替加环素能加快患者机体恢复的速度。

替加环素能有效清除病灶中所累积的分泌物,有利于患者通气换气等肺功能的恢复,再加之痰菌培养使用敏感抗身素,能尽可能控制炎症反应进一步发展,促进疾病尽早康复。替加

环素不但能有效控制全身及肺部感染症状,还能有效改善患者呼吸力学有关指标^[15,16]。在临床中监测机械通气时较为常用的指标包括呼吸做功、阻力、顺应性、压力等,上述指标的波动能有效评估病情变化^[17]。本次研究结果显示,分别对重症呼吸机相关性肺炎患者予以替加环素联合常规治疗以及常规治疗,发现两种治疗方案均能有效改善患者呼吸功能,主要表现为呼吸做功、气道峰压、气道阻力呼吸力学指标较治疗前显著降低,动态顺应性较治疗前显著升高。然而加以替加环素进行治疗对患者,其各项呼吸力学指标的改善效果明显优于单纯常规治疗。提示替加环素更能有效改善呼吸功能,究其原因主要是因为替加环素能充分清除气道深处分泌物,进而加强机械通气效果。

重症呼吸机相关性肺炎患者的炎症因子在血清中的含量呈现出升高的趋势,表现为炎症反应亢进,TNF- α 主要是由活化单核巨噬细胞所产生的炎症因子,当感染病灶出现后,在局部病灶中是最早募集的一种内源性炎症因子,对肺泡上皮细胞炎症性损伤发挥着介导性作用^[18,19]。IL-6、IL-8 具有确切功能的内源性趋化因子,IL-6、IL-8 炎症因子的大量合成能对中性粒细胞、单核巨噬细胞等炎症细胞起到募集作用,在炎症反应中发挥着极其重要的级联放大效应^[20]。本次研究结果显示,重症呼吸机相关性肺炎患者经替加环素治疗后,IL-6、IL-8、TNF- α 血清炎症因子水平得到显著性降低,其降低的效果显著优于单纯的常规治疗。提示替加环素辅助治疗能有效缓解炎症反应,清除病灶。

总之,重症呼吸机相关性肺炎患者经替加环素治疗后,能

有效改善患者呼吸力学与血清炎症因子水平,临床疗效良好。

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