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血必净注射液联合比阿培南对重症肺炎患者肺功能的影响 *

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摘要 目的:研究血必净注射液联合比阿培南对重症肺炎患者肺功能的影响。**方法**:选择 2017 年 1 月～2019 年 12 月我院的 103 例重症肺炎患者,随机分为两组。对照组静脉滴注比阿培南 0.3 g ,每 8 h 给药 1 次;观察组联合静脉滴注血必净 50 mL,每天两次。检测两组的炎症因子:白介素 -1(Interleukin-1, IL-1)、肿瘤坏死因子 -α(Tumor necrosis factor-α, TNF-α)和 IL-6 水平,应激激素:皮质醇(Cortisol, Cor)、人血管紧张素Ⅰ(Human angiotensin I, AngⅠ)、去甲肾上腺素(Noradrenaline, NE)和人血管紧张素Ⅱ(Human angiotensinⅡ, AngⅡ)水平,肺功能:第一秒最大呼气量(Maximum expiratory volume in the first second, FEV_1)、FEV_1%pred、用力肺活量(Forced vital capacity, FVC)。**结果**:观察组的有效率明显高于对照组(P<0.05)。治疗后,两组的血清 IL-1、TNF-α、IL-6、Cor、AngⅠ、NE 和 AngⅡ水平水平均明显降低,FEV_1、FEV_1%pred 和 FEV_1/FVC 明显升高(P<0.05),且观察组的上述指标明显优于对照组(P<0.05)。**结论**:血必净注射液联合比阿培南对重症肺炎有显著的疗效,不但能明显改善肺功能,还能有效抑制患者的应激反应和炎症反应,值得推广。

关键词:血必净注射液;比阿培南;重症肺炎;炎症因子;应激激素;肺功能

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Effect of Xuebijing Injection Combined with Biapenem on Pulmonary Function in Patients with Severe Pneumonia*

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ABSTRACT Objective: To investigate the effect of Xuebijing injection combined with biapenem on pulmonary function in patients with severe pneumonia. **Methods:** Selected 103 cases of patients with severe pneumonia who were treated in our hospital from January 2017 to December 2019, divided into two groups randomly. The control group received 0.3 g of apenem once every 8 hours, while the observation group received 50 mL of Xuebijing twice a day. Detection of inflammatory factors in two groups: interleukin-1 (IL-1), tumor necrosis factor-α (TNF-α) and IL-6 levels, stress hormone: Cortisol (Cor), human angiotensin I (Ang I), norepinephrine (NE) and human angiotensin II (Ang II) levels, lung function: maximum expiratory volume in the first second (FEV_1), FEV_1%pred, Forced vital capacity (FVC). **Results:** The effective rate of the observation group was significantly higher than control group (P<0.05). After treatment, the levels of serum IL-1, TNF-α, IL-6, Cor, AngⅠ, NE and AngⅡ of the two groups were significantly reduced, and FEV_1, FEV_1%pred and FEV1/FVC were significantly increased (P<0.05), and the above indicators of the observation group were significantly better than the control group (P<0.05). **Conclusion:** Xuebijing injection combined with biapenem has a significant effect on severe pneumonia. It can not only improve the lung function, but also effectively inhibit the stress response and inflammatory response of patients. It is worth popularizing.

Key words: Xuebijing injection; Biapenem; Severe pneumonia; Inflammatory factor; Stress hormone; Lung function

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前言

重症肺炎一般是由于普通肺炎未及时得到有效控制发展而成,查体时大多可在患者的肺部听诊区闻及支气管呼吸音或湿罗音,主要症状表现为呼吸困难、发热、咯痰和咳嗽等,严重影响患者的身心健康[1,2]。重症肺炎多发于老年人,患者的病情重、预后差、进展快,部分患者甚至会并发多器官功能衰竭和消化道出血等,生存率较低[3,4]。随着免疫抑制宿主的不断增加、抗生素耐药率的升高等,重症肺炎的发生率逐年升高[5]。重症肺炎患者的并发症较多,病情进展迅速,文献报道重症肺炎的死亡率高达 15 %~30 %[6]。比阿培南不仅具有比较强的抗菌效果,同时具有比较广的抗菌谱, 对于革兰阴性杆菌的铜绿假单胞菌、肺炎克雷伯菌和鲍曼不动杆菌均有效较好的效果[7]。由于重症患者不但会表现出显著的呼吸系统症状,还会表现为全身炎症

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反应所引起的肝肾器官受累以及中毒等肺外症状，单用比阿培南的效果并不满意。近年来有研究发现，将抗生素与血必净联合使用能提高重症肺炎的疗效[8]。因此，本研究将血必净与比阿培南联用，分析其对重症肺炎患者肺功能、应激反应和炎症反应的影响。

1 资料与方法

1.1 一般资料

选择 2017 年 1 月～2019 年 12 月我院的 103 例重症肺炎患者，纳入标准：(1)符合重症肺炎的诊断标准[9]。(2)经血清学检查以及痰培养检查均证实为细菌感染，(3) 非过敏体质，(4)均知情同意。排除标准：(1)合并血液系统疾病(白血病、再生障碍性贫血或者血友病等)的患者；(2)合并急性肺栓塞的患者；(3)严重精神障碍的患者；(4)过敏体质患者；(5)有明显的肝肾功能异常者。用抽签法随机分为两组。观察组 51 例，男 26 例，女 25 例；年龄 43~79 岁，平均(62.34±13.79)岁；病程 3~12 d，平均(5.14±1.42)d；基础疾病：高血压 15 例、慢阻肺 7 例、冠心病 10 例、脑梗塞 4 例、糖尿病 2 例、重症胰腺炎 2 例、其他疾病 3 例。对照组 52 例，男 27 例，女 25 例；年龄 43~79 岁，平均(61.78±13.42)岁；病程 3~12 d，平均(5.09±1.36)d；基础疾病：高血压 16 例、慢阻肺 8 例、冠心病 10 例、脑梗塞 4 例、糖尿病 2 例、重症胰腺炎 2 例、其他疾病 4 例。两组的基线资料有可比性(P>0.05)。

1.2 方法

两组均接受化痰、营养支持、补液、退热和吸氧等常规治疗。对照组：静脉滴注比阿培南(辰欣药业，药准字 H20110035)0.3 g，每 8 h 给药 1 次；观察组：联合静脉滴注血必净注射液(天津红日药业，国药准字 Z20040033)50 mL，每天两次。均治疗 1 w。

1.3 观察指标

疗效标准[9]：(1)治愈：重症肺炎患者的血白细胞基本正常，体温明显降低，X 线胸片明显改善或正常，精神状态基本恢复，感染菌部分或完全清除，可以完全脱机。(2)显效：重症肺炎患者的血白细胞明显下降，体温有所降低，X 线胸片明显改善，精神状态基本恢复，感染菌部分得到清除，呼吸机参数明显降低或可以脱机。(3)有效：重症肺炎患者的血白细胞维持原水平或有所降低，体温维持原水平或有所降低，X 线胸片检查有所改善，精神状态有所改善，感染菌部分得到清除，呼吸机参数有所下降。(4)无效：重症肺炎患者的血白细胞继续升高或不变，发热升高或不退，X 线胸片出现恶化，精神状态恶化或不变，感染菌没有清除，呼吸机参数升高或不变。

治疗前后，均空腹采集 3 mL 上肢静脉血，用 ELISA 法检测 IL-1、TNF-α 和 IL-6 水平，并检测血清包括血清 Cor、Ang Ⅰ、NE 和 Ang Ⅱ等应激激素水平，均购自国药集团化学试剂公司；采取 FGY-200 肺功能检测仪（合肥健桥医疗公司生产）检测 FEV_1、FEV_1%pred、FVC 和 FEV_1/FVC。

1.4 统计学分析

采用 SPSS 21.0，计量资料用($\bar{x}\pm s$)示，行 t 检验，计数资料用%示，行 χ^2 检验，P<0.05 有统计学意义。

2 结果

2.1 疗效对比

观察组治疗的总有效率明为 94.12 %(48/51)，对照组治疗的总有效率为 71.15 %(37/52)，对比观察组治疗总有效率明显高于对照组(χ^2=9.415，P<0.05)，见表 1。

表 1 疗效比较[例(%)]

Table 1 Comparison of the clinical effect [n(%)]

Groups	n	Cure	Effective	Valid	Invalid	The total effect rate
Control group	52	12(23.08)	14(26.92)	11(21.15)	15(28.85)	37(71.15)
Observation group	51	17(33.33)	19(37.25)	12(23.53)	3(5.88)	48(94.12)*

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

2.2 两组血清 IL-1、TNF-α 和 IL-6 水平对比

治疗前，两组的血清 IL-1、TNF-α 和 IL-6 水平无明显差异(P>0.05)，治疗后，两组的上述指标均明显降低(P<0.05)，且观察组明显更低(P<0.05)，见表 2。

表 2 两组治疗前后的血清 IL-1、TNF-α 和 IL-6 水平对比($\bar{x}\pm s$)

Table 2 Comparison of serum levels of IL-1, TNF-α and IL-6 between the two groups before and after treatment ($\bar{x}\pm s$)

Groups	n		IL-1(pg/L)	TNF-α(mg/L)	IL-6(pg/L)
Control group	52	Before treatment	173.49±15.38	30.15±2.73	185.49±17.32
		After treatment	138.74±13.29#	21.39±1.48#	114.73±13.28#
Observation group	52	Before treatment	172.25±16.43	29.47±3.64	186.42±18.59
		After treatment	117.46±10.28*#	15.27±1.36*#	79.24±10.15*#

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

2.3 两组 FEV_1、FEV_1%pred 和 FEV_1/FVC 对比

治疗前，两组的 FEV_1、FEV_1%pred 和 FEV_1/FVC 无明显差异(P>0.05)，治疗后，两组的上述指标明显升高(P<0.05)，且观察组明显更高(P<0.05)，见表 3。

2.4 两组血清 Cor、Ang Ⅰ、NE 和 Ang Ⅱ水平对比

治疗前，两组的血清 Cor、Ang Ⅰ、NE 和 Ang Ⅱ水平无明显

差异（P>0.05），治疗后，两组的上述指标均明显降低（P<0.05），且观察组明显更低（P<0.05），见表 4。

表 3 两组治疗前后的 FEV_1、FEV_1%pred 和 FEV_1/FVC 对比（$\bar{x}\pm s$）

Table 3 Comparison of FEV_1, FEV_1% PRED and FEV_1 / FVC between the two groups before and after treatment ($\bar{x}\pm s$)

Groups	n		IL-1(pg/L)	TNF-α(mg/L)	IL-6(pg/L)
Control group	52	Before treatment	173.49±15.38	30.15±2.73	185.49±17.32
		After treatment	138.74±13.29#	21.39±1.48#	114.73±13.28#
Observation group	52	Before treatment	172.25±16.43	29.47±3.64	186.42±18.59
		After treatment	117.46±10.28*#	15.27±1.36*#	79.24±10.15*#

表 4 两组治疗前后的血清 Cor、Ang Ⅰ、NE 和 Ang Ⅱ水平对比（$\bar{x}\pm s$，pg /mL）

Table 4 Comparison of serum COR, ang Ⅰ, NE and ang Ⅱ levels between the two groups before and after treatment ($\bar{x}\pm s$, pg /mL)

Groups	n		Cor	Ang	NE	Ang
Control group	52	Before treatment	293.27±49.25	73412±12.37	60.32±15.17	48.65±12.17
		After treatment	172.39±24.84#	55.24±11.16#	44.54±14.39±	38.32±10.49#
Observation group	51	Before treatment	294.67±46.32	72.35±13.27	59.27±14.13	47.77±13.51
		After treatment	91.36±14.57*#	39.06±10.89*#	28.62±3.33*±	27.32±4.15*#

3 讨论

重症肺炎是常见的危重病症，病情进展快，病情危重，死亡率较高[10-12]，患者的治疗难度以及死亡率均明显高于普通肺炎，仅用抗生素无法取得满意的临床效果[13-16]。中医认为，重症肺炎患者大多具有比较明显的血脉不通和气虚痰瘀明显，肺部不耐外邪，邪淫太过，伤寒而病温，而致肺炎，而且风温之邪壅滞于机体肺卫之内，患者的抵抗力低下，邪气化热，痰热交阻，而引起肺炎的症状，因而中医认为对于重症肺炎的治疗应当注重对热毒内蕴、瘀热闭肺、正气亏虚和血瘀痰阻及等方面[17]。

血必净注射液为当归、红花、赤芍、丹参和川芎等多种中药材的提取物，该药的活性成分有阿魏酸、丹参素、川芎嗪、芍药苷和红花黄色素 A 等[18]。血必净注射液中，赤芍可以行血中之滞，当归可以化痰润肺，丹参以及川芎可以活血化瘀，红花可以化毒和消痰，诸药共奏通络止痛、溃散毒邪以及活血祛瘀之功效。药理研究发现，赤芍可以对血小板聚集进行抑制，改善机体肺部的循环；当归可以明显减轻心肌缺血，改善机体外周的循环，减轻缺氧反应和炎症反应；红花能有效改善血管内液体的渗出[19,20]。重症肺炎能造成毛细血管内皮细胞以及肺泡上皮细胞受到损伤，明显减少肺实变、肺水肿和肺泡表面活性物质，降低肺顺应性、通气与血流比例失调、增大呼吸功耗，造成肺换气功能障碍，二氧化碳分压降低[21-23]。晚期肺纤维化，肺通气功能也会受到损伤，二氧化碳分压降低伴动脉血二氧化碳分压明显升高[24,25]。观察组的 FEV_1、FEV_1%pred 和 FEV_1/FVC 高于对照组，与张华[26]的研究类似，观察血必净注射液联合利奈唑胺治疗重症肺炎的效果及对肺功能指标影响，结果显示血必净注射液 + 利奈唑胺治疗联合治疗组的临床症状和肺功能指标，不良反应发生率以及疗效总有效率均显著优于单独利奈唑胺治疗，表明血必净注射液能明显改善重症肺炎患者的肺功能。分析其原因为必净注射液能够疏通脉络、活血化瘀，防止微循环障碍，从而改善患者的肺功能指标。

研究发现，重症肺炎可以诱发机体内皮细胞、中性粒细胞、NK 细胞和巨噬细胞等释放出大量的炎症介质，如 C 反应蛋白、IL-1、TNF-α 和 IL-6 等，对机体细胞造成严重的损害，引起 " 瀑布样炎症反应 " 的发生，使得 " 促炎 - 抑炎 " 细胞因子严重失去平衡[27-30]。本研究发现，观察组的血清 IL-1、TNF-α 和 IL-6 水平明显低于对照组，与陈彬[31]等学者的研究类似，探讨血必净注射液对慢性阻塞性肺疾病急性加重期患者血清炎性因子水平的影响，结果显示治疗后，两组血清 IL-8、CRP 均较治疗前明显改善，治疗组治疗后 IL- 8、CRP 的变化程度较对照组更明显，同时该学者也发现血清 IL-8 和 CRP 水平与肺功能 FEV_1/Pred 及 FEV_1/FVC 均呈负相关。蔡福良[32]等学者的研究也发现两组治疗后血清 IL-6、TNF-α 水平均较治疗前明显下降，血必净组 IL-6、TNF-α 水平下降较对照组更加显著。表明血必净注射液联合比阿培南对重症肺炎病人机体内的炎症指标进行有效的控制，抑制全身性炎症综合征的发展。病原菌导致的全身炎症反应可以引起应激反应，能通过抑制免疫功能以及加速蛋白质分解而使病情加重。研究发现，在重症肺炎患者的应激激素水平会发生明显的改变，其增减的幅度与重症肺炎的病情程度改变具有较高的一致性[33]。观察组的血清 Cor、Ang Ⅰ、NE 和 Ang Ⅱ水平明显低于对照组，车晓宇[34]等学者的研究与本研究相似，该学者研究结果显示必净联合抗菌药物治疗 7 d 后，ICU 重症肺炎患者血清应激激素指标 Cor、Ang Ⅰ、Ang Ⅱ水平均低于抗菌药物治疗组。表明血必净注射液联合比阿培南能对重症肺炎患者的全身应激反应发挥抑制作用。其机制可能与血必净注射液具有减少炎性渗出、改善微循环、降低血小板的聚集性以及黏附性、增强细胞免疫和非特异性免疫、使炎症局限化、抑制炎症因子分泌等多种药理效果相关。

综上所述，血必净注射液联合比阿培南对重症肺炎有显著的疗效，不但能明显改善肺功能，还能有效抑制患者的应激反应和炎症反应，值得推广。

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