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血必净注射液联合替加环素治疗脓毒症休克患者的临床疗效观察 *

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摘要 目的:研究血必净注射液联合替加环素治疗脓毒症休克患者的临床疗效。**方法:**选取 2015 年 9 月至 2016 年 8 月我院收治的 86 例脓毒症休克患者,根据患者入院顺序分为观察组和对照组,42 例每组。对照组使用血必净注射液完成治疗,观察组在此基础上加以替加环素。比较两组患者治疗前后 APACHEII 评分、尿量、血清 LAC、血尿素氮(BUN)、肌酐(SCr)、炎症因子及心肌酶水平的变化。**结果:**治疗后,两组患者 APACHEII 评分均较治疗前显著降低($P<0.05$),尿量均较治疗前显著增加($P<0.05$),和对照组相比,观察组的 APACHEII 评分较低($P<0.05$),尿量较多($P<0.05$);两组患者血清 LAC、BUN、SCr、IL-6、CRP、TNF- α 、CK-MB、cTnI、LDH 水平较治疗前显著降低($P<0.05$),且观察组的以上指标水平较对照组显著降低($P<0.05$)。**结论:**血必净注射液联合替加环素治疗脓毒症休克患者能有效改善患者病情严重程度,提高患者心肾功能并抑制炎症反应,临床疗效较单用血必净注射液更好。

关键词:血必净注射液;替加环素;脓毒症休克;乳酸;肾功能

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Observation on the Curative Effect of Xuebijing Injection Combined with Tigecycline on the Patients with Septic Shock*

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ABSTRACT Objective: To study the clinical efficacy of Xuebijing injection combined with tigecycline in the treatment of septic shock patients. **Methods:** From September 2015 to August 2016, 86 cases of patients with septic shock were enrolled in our hospital. According to the order of admission, the patients were divided into the observation group and the control group. The control group was treated with Xuebijing injection, and the observation group was treated with tigecycline on the basis of control group. The changes of APACHEII score, urine volume, serum LAC, blood urea nitrogen (BUN), creatinine (SCr), inflammatory factors and myocardial enzyme levels were compared between the two groups before and after treatment. **Results:** After treatment, the APACHEII scores of both groups were significantly lower than those before treatment ($P<0.05$), and the urine output were significantly higher than those before treatment ($P<0.05$). Compared with the control group, the APACHEII score of observation group was lower ($P<0.05$), the urine output was higher ($P<0.05$). The levels of serum LAC, BUN, SCr, IL-6, CRP, TNF- α , CK-MB, cTnI and LDH of both groups were significantly lower than those before treatment ($P<0.05$), and the levels of above indicators in the observation group were significantly lower than those of the control group ($P<0.05$). **Conclusion:** Xuebijing injection combined with tigecycline can effectively improve the heart and kidney function and inhibit the inflammatory response in the treatment of patients with sepsis shock, the clinical efficacy is better compared with the use of Xuebijing injection alone.

Key words: Xuebijing injection; Tigecycline; Septic shock; LAC; Lactic acid; Renal function

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前言

脓毒症是感染导致的全身炎症反应综合征,主要发生在大手术、休克、感染、严重创伤后,进一步发展可能会导致多脏器功能衰竭及脓毒性休克^[1]。心肌损伤是脓毒症中较为常见的并发症。相关研究显示 15%以上的脓毒症患者存在难治性心功能衰竭,主要和心肌损伤密切相关^[2]。可见,尽早逆转心肌损伤,确保心脏泵血功能得以恢复,在抢救脓毒性休克患者中显得颇为

关键。近年来,血必净在脓毒症领域获得良好的治疗效果,然而关于其对脓毒性休克患者的心肌受损影响报道相对较少^[3]。替加环素作为新型的超广谱抗菌药物,对多耐药菌具有明显优势^[4]。本研究主要探讨了血必净注射液联合替加环素对脓毒症休克患者的临床疗效,现将结果报道如下。

1 资料与方法

1.1 临床资料

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选取 2015 年 9 月至 2016 年 8 月我院收治的 86 例脓毒症休克患者,纳入标准:①伴有全身炎症反应综合征;②在临床中伴有确切的感染;③收缩压不足 90 mmHg,或基于原有的基础值下降幅度至少为 40 mmHg;④伴有组织灌注不良的现象,如急性意识障碍或少尿 >1 h。排除标准:①既往慢性心功能不全者;②自身免疫性疾病;③结缔组织病;④慢性肾、肺、肝、凝血等器官系统疾病者;⑤对本次研究中的药物具有过敏史。本次研究已取得我院伦理委员会批准,及得到患者及家属同意。

根据患者入院顺序分为观察组和对照组,42 例每组。观察组中男性 22 例,女性 20 例;年龄为 48~85 岁,平均(67.54±4.87)岁;疾病类型:中枢神经感染严重 2 例,严重烧伤者 3 例,弥漫性腹膜炎者 3 例,急性梗阻坏死性胆管炎 3 例,多发伤 7 例,急性重症胰腺炎 8 例,重症肺炎 16 例;基础疾病:慢性支气管炎 6 例,糖尿病 10 例,心脏病 5 例。对照组中男性 25 例,女性 17 例;年龄为 47~86 岁,平均(67.62±4.91)岁;疾病类型:中枢神经感染严重 3 例,严重烧伤者 4 例,弥漫性腹膜炎者 2 例,急性梗阻坏死性胆管炎 4 例,多发伤 6 例,急性重症胰腺炎 7 例,重症肺炎 16 例;基础疾病:慢性支气管炎 7 例,糖尿病 11 例,心脏病 6 例。两组患者性别、年龄、疾病类型比较无明显差异($P>0.05$),具有可比性。

1.2 治疗方法

所有患者均需采取抗休克、补液、抗感染、营养支持、免疫、内环境平衡的维持、控制血糖、糖皮质激素等治疗,若伴有器官衰竭则需给予相应的支持治疗。对照组在常规治疗基础上加以 50 mL 的血必净注射液完成治疗(生产厂家:天津红日药业股份有限公司,规格:10 mL×5 支/盒,生产批号:20150205)给药方式为静脉滴注,2 次/天,连续治疗 7 天。观察组在对照组治疗基础上加以替加环素(生产厂家:美国惠氏公司,规格:50 mg/支,生产批号:20150305)完成治疗,初始剂量为 100 mg,维持剂

量为 50 mg,静脉滴注,维持时间为 30~60 min,2 次/天,连续治疗 7 天。

1.3 观察指标

使用急性生理学与慢性健康状况评价系统 II(APACHE II)^[5] 对患者病情及预后进行评估,APACHE II 评分由慢性健康状况、年龄评分、生理学评分组合而成,总分为 0~71 分,分数越低则表明患者病情较轻,预后较好。分析两组患者治疗前后尿量。比较两组患者治疗前后乳酸(LAC)、血尿素氮(BUN)、肌酐(Scr)、炎症因子水平、心肌酶指标,分别在治疗前后收集两组患者 3 mL 的空腹肘静脉血,放置在抗凝剂的试管中,摇动试管后混匀血液,转速 3000 r/min,离心 15 min,分离血清后,放置在 -50℃低温箱中待测,采取常规生化法检测 LAC、BUN、SCr 水平,使用酶联免疫吸附法检测白介素-6(IL-6)、C-反应蛋白(CRP)、肿瘤坏死因子- α (TNF- α)水平。采取日本日立 7600 型全自动生化分析仪检测肌酸激酶同工酶(CK-MB)、心肌肌钙蛋白 I(cTnI)、乳酸脱氢酶(LDH)水平。

1.4 统计学处理

选取 SPSS 11.5 软件包对本次实验数据予以处理,以($\bar{x}\pm s$)表示计量资料,组间比较采用 t 检验,以[n(%)]表示计数资料,组间比较予以 χ^2 检验,以 $P<0.05$ 为差异具有统计学意义。

2 结果

2.1 两组患者治疗前后的 APACHEII 评分、尿量比较

治疗前,两组患者 APACHEII 评分、尿量比较差异无统计学意义($P>0.05$);治疗后,两组患者 APACHEII 评分均较治疗前显著降低($P<0.05$),尿量较治疗前均显著增加($P<0.05$),和对照组相比,观察组的 APACHEII 评分较低($P<0.05$),尿量较多($P<0.05$),见表 1。

表 1 两组患者治疗前后的 APACHEII 评分、尿量比较($\bar{x}\pm s$)

Table 1 Comparison of the APACHEII score, urine volume between two groups before and after treatment($\bar{x}\pm s$)

Item	Observation group(n=43)		Control group(n=43)	
	Before treatment	After treatment	Before treatment	After treatment
APACHE II scale(points)	23.87±2.46	12.32±1.37**	23.82±2.41	17.38±1.96*
Urine volume (ml/h)	21.38±2.05	102.35±11.37**	21.32±2.01	72.46±7.21*

Note: Compared with before treatment, * $P<0.05$; Compared with control group after treatment, ** $P<0.05$.

2.2 两组患者治疗前后血清 LAC、BUN、SCr 水平的比较

治疗前,两组患者血清 LAC、BUN、SCr 水平比较差异无统计学意义($P>0.05$);治疗后,两组患者血清 LAC、BUN、SCr 水平

较治疗前显著降低($P<0.05$),和对照组相比,观察组的血清 LAC、BUN、SCr 水平较低($P<0.05$),见表 2。

表 2 两组患者治疗前后血清 LAC、BUN、SCr 水平的比较($\bar{x}\pm s$)

Table 2 Comparison of the serum LAC, BUN, SCr levels between two groups before and after treatment ($\bar{x}\pm s$)

Item	Observation group(n=43)		Control group(n=43)	
	Before treatment	After treatment	Before treatment	After treatment
LAC(mmol/L)	5.92±0.86	3.26±0.12	5.94±0.85	4.57±0.25
BUN(mmol/L)	33.87±4.58	13.87±1.32	33.89±4.52	24.61±2.79
SCr(mmol/L)	354.35±36.98	164.32±13.87	353.98±37.01	258.97±23.15

Note: Compared with before treatment, * $P<0.05$; Compared with control group after treatment, ** $P<0.05$.

2.3 两组患者治疗前后血清炎症因子水平的比较

治疗前,两组患者血清 IL-6、CRP、TNF- α 水平比较差异无统计学意义($P>0.05$);治疗后,两组患者血清 IL-6、CRP、TNF- α

水平均较治疗前显著降低($P<0.05$),和对照组相比,观察组的血清 IL-6、CRP、TNF- α 水平较低($P<0.05$),见表 3。

表 3 两组患者治疗前后血清炎症因子水平的比较($\bar{x} \pm s$)

Table 3 Comparison of the serum inflammatory factor levels between two groups before and after treatment ($\bar{x} \pm s$)

Item	Observation group(n=43)		Control group(n=43)	
	Before treatment	After treatment	Before treatment	After treatment
IL-6(ng/L)	324.56 $\pm$ 31.48	234.56 $\pm$ 22.76	324.51 $\pm$ 31.49	276.98 $\pm$ 25.87
CRP(mg/L)	76.98 $\pm$ 7.47	23.56 $\pm$ 2.43	76.95 $\pm$ 7.51	36.87 $\pm$ 3.52
TNF- α (mg/L)	61.36 $\pm$ 6.37	26.87 $\pm$ 2.52	61.42 $\pm$ 6.39	39.57 $\pm$ 3.47

Note: Compared with before treatment, * $P<0.05$; Compared with control group after treatment, [#] $P<0.05$.

2.4 两组患者治疗前后血清心肌酶水平的比较

治疗前,两组患者血清 CK-MB、cTnI、LDH 水平比较差异无统计学意义($P>0.05$);治疗后,两组患者血清 CK-MB、cTnI、

LDH 水平较治疗前显著降低($P<0.05$),和对照组相比,观察组的血清 CK-MB、cTnI、LDH 水平较低($P<0.05$),见表 4。

表 4 两组患者治疗前后血清心肌酶水平的比较($\bar{x} \pm s$)

Table 4 Comparison of the serum myocardial enzymes between two groups before and after treatment ($\bar{x} \pm s$)

Item	Observation group(n=43)		Control group(n=43)	
	Before treatment	After treatment	Before treatment	After treatment
CK-MB(U/L)	397.65 $\pm$ 35.27	84.67 $\pm$ 8.36	397.61 $\pm$ 35.31	178.43 $\pm$ 15.16
cTnI(ug/L)	3.16 $\pm$ 0.45	1.03 $\pm$ 0.26	3.17 $\pm$ 0.46	1.97 $\pm$ 0.32
LDH(U/L)	603.76 $\pm$ 61.85	274.87 $\pm$ 21.54	603.75 $\pm$ 61.82	416.95 $\pm$ 34.85

Note: Compared with before treatment, * $P<0.05$; Compared with control group after treatment, [#] $P<0.05$.

3 讨论

脓毒症易引发多器官功能不全,特别是脓毒症休克的死亡率较高^[6]。目前,关于脓毒症休克的发病机制尚未完全阐明,既往研究表明细胞因子变化在脓毒症休克的发生发展过程中发挥着极其重要的作用^[7,8],特别是炎症介质会导致患者体内炎症反应长时间为高水平状态。一旦炎症反应失控时,细胞因子难以表达,组织受损,器官功能会相应的受到影响^[9,10]。因此,控制炎症反应能缓解脓毒症休克患者器官功能障碍和组织受损程度,进而有利于患者身体健康状况的改善^[11]。

血必净注射液主要由丹参、川芎、赤芍、红花组合而成,具备清热凉血、活血化瘀的作用^[12],可调节免疫功能、改善微循环、保护血管内皮细胞功能^[13]。相关研究显示血必净注射液能有效降低脓毒症而引发的多器官功能障碍死亡率,因此在治疗脓毒症中的作用已得到认可^[14]。替加环素为米诺环素的衍生物,肝肾安全性较为可靠,当患者发生轻中度肝损害或肾功能不全时,无需调整剂量。此外,替加环素具备广谱抗菌活性,能覆盖大多数厌氧菌、革兰阴性和革兰阳性需氧^[15,16],尤其是对耐药致病菌如糖肽类抗生素敏感性降低的葡萄球菌、耐万古霉素肠球菌、耐青霉素肺炎链球菌、耐甲氧西林金黄色葡萄球菌、超广谱 β -内酰胺酶的产酸克雷伯菌、肺炎克雷伯菌、大肠埃希菌均具有较高的活性^[17-19],因此常常应用在多药耐药菌中。当前,替加环素已广泛应用在骨关节感染、血液病继发感染、呼吸机相关肺炎、老年社区获得性肺炎中。血必净注射液联合替加环

素治疗的脓毒症休克患者 APACHE II 评分显著降低,尿量明显增加,且效果优于单纯血必净注射液治疗,提示在血必净联合替加环素治疗脓毒症休克的临床疗效优于单纯血必净注射液治疗。

循环中的 LAC 属于无氧酵解代谢的中间产物,可敏感反映细胞是否缺氧和机体外周组织灌注情况,观察 LAC 动态变化有助于评估患者的预后^[20]。本研究结果显示血必净联合替加环素治疗的脓毒症休克患者血清 LAC、BUN、Scr 水平均显著降低,效果优于单纯血必净治疗,提示血必净注射液联合替加环素治疗脓毒症休克患者能有效改善肾功能,促使效血容量的恢复,进而增强氧输送。此外,相关研究显示脓毒症休克的发生、发展过程和炎症因子存在着密切关联性,IL-6 对免疫反应、免疫应答、急性期反应均发挥着重要作用^[21,22]。CRP 是在组织感染或受损过程中而迅速产生的急性蛋白,在急性炎症、组织损伤后,其水平会迅速上升。本次研究结果显示血必净注射液联合替加环素治疗的脓毒症休克患者血清 IL-6、CRP、TNF- α 水平均显著降低,且降低的效果优于单纯血必净治疗者。心肌受损是脓毒症休克中的早期并发症,临床表现为心律失常、心力衰竭、低血压,其他脏器功能会相应的受损,CK-MB、cTnI、LDH 为反映心肌受损的严重程度的重要评判指标^[23,24]。本次研究结果表明患者经血必净注射液联合替加环素治疗后血清 CK-MB、cTnI、LDH 水平显著降低,效果优于单纯血必净治疗者,表明血必净联合替加环素能有效改善患者心功能。

总之,血必净注射液联合替加环素治疗脓毒症休克患者能

有效改善患者病情严重程度,提高患者心肾功能并抑制炎症反应,临床疗效较单用血必净注射液更好。

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