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脓毒症急性肾损伤患者血液净化时机选择对治疗期间微循环系统的影响研究*

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摘要 目的:探究脓毒症急性肾损伤患者血液净化时机选择对治疗期间微循环系统的影响。**方法:**选取 2016 年 2 月~2017 年 2 月期间来我院治疗的脓毒症急性肾损伤患者 200 例作为研究对象,依据急性肾损伤的诊断和分级(RIFLE)标准将脓毒症急性肾损伤患者分为 1 期(A 组,n=56)、2 期(B 组,n=70)、3 期(C 组,n=74),所有患者皆采取连续性肾脏替代疗法。观察不同时期治疗前后微循环的变化。**结果:**三组脓毒症急性肾损伤患者在性别、年龄、空腹血糖浓度、急性生理功能和慢性健康状况(APACHE)评分、体温、心率指标上差异无统计学意义($P>0.05$);治疗后,A 组患者微血管流动指数低于 B 组和 C 组,而灌注血管比例、灌注血管密度及总血管密度显著高于 B 组和 C 组($P<0.05$);A 组患者血液流态积分、襻周状态积分、管襻形态积分及总积分显著低于 B 组和 C 组($P<0.05$),而襻顶血管直径显著大于 B 组和 C 组($P<0.05$)。**结论:**在 RIFLE 诊断标准 1 期对脓毒症急性肾损伤患者实施血液净化,可以明显地改善治疗效果,促进微循环系统的恢复。

关键词:脓毒症;急性肾损伤;连续性肾脏替代疗法;血液净化时机;微循环

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Effect of Blood Purification Timing on Microcirculatory System during Treatment in Patients with Acute Kidney Injury Caused by Sepsis*

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ABSTRACT Objective: To explore the effect of blood purification timing on the microcirculatory system during treatment in patients with acute kidney injury caused by sepsis. **Methods:** A total of 200 patients with acute kidney injury caused by sepsis, who were treated in Affiliated Chinese Medicine Hospital of Xinjiang Medical University from February 2016 to February 2017 were chosen as study subjects. According to the criteria of RIFLE, the patients with acute kidney injury caused by sepsis were divided into stage 1 (group A, n=56), stage 2 (group B, n=70), and stage 3 (group C, n=74). All patients were treated with continuous renal replacement therapy (CRRT). The changes of microcirculation before and after treatment were observed. **Results:** There were no significant differences in sex, age, fasting blood glucose, acute physiology and chronic health evaluation (APACHE) score, body temperature and heart rate of the patients with acute kidney injury caused by sepsis among the three groups ($P>0.05$). After treatment, the microvascular flow index in group A was significantly lower than that in group B and group C ($P<0.05$), while the proportion of perfused vessels, the perfusion vessel density and the total vascular density was significantly higher than that in group B and group C ($P<0.05$). After treatment, the scores of blood flow state, loop weeks status, pipe loop integral and the total score in group A were significantly lower than those in group B and group C ($P<0.05$), while the diameter of the dome blood vessel was significantly larger than that in group B and group C ($P<0.05$). **Conclusions:** In the stage 1 of the RIFLE diagnostic criteria, blood purification can significantly improve the treatment effect and promote the recovery of microcirculation system in the patients with acute kidney injury caused by sepsis.

Key words: Sepsis; Acute kidney injury; Continuous renal replacement therapy; Blood purification timing; Microcirculation

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前言

脓毒症是一种临床上常见的疾病,是由感染性因素引起的全身炎症反应综合征,临床表现一般为发热、心跳过快、呼吸急

促及外周白细胞增多^[1]。在临床上主要采取早期目标指导性治疗和早期集束化治疗^[2],同时脓毒症也是导致急性肾损伤和多脏器功能障碍综合征、多脏器功能衰竭的常见原因^[3,4]。因此,及时治疗脓毒症以减少该病带来的并发症显得尤为重要。连续性

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肾脏替代治疗是目前治疗脓毒症急性肾损伤的最佳方式,其是模仿肾小球滤过原理,主要通过对流和弥散两种方式以及吸附机制达到清除炎症介质的目的,从而维持内环境的稳态,促进脓毒症患者的术后恢复^[5-7]。目前多数研究的内容是有关脓毒症急性肾损伤患者血液净化时机和方式的选择^[8,9],而关于血液净化时机和微循环之间的关系研究甚少,因此,本研究通过探讨脓毒症急性肾损伤患者血液净化时机选择对治疗期间微循环系统的影响,以期为临床上治疗脓毒症急性肾损伤提供参考,阐述如下。

1 资料及方法

1.1 一般资料

选取 2016 年 2 月~2017 年 2 月期间来我院治疗的脓毒症急性肾损伤患者 200 例作为研究对象。纳入标准:(1)所有患者均符合 2001 年国际脓毒症定义会议制定的脓毒症诊断的新标准^[10]和 2006 年急性肾损伤诊断与分类专家共识^[11];患者肾功能在 48 h 内肌酐升高绝对值 $>25 \text{ mmol/L}$ (0.3 mg/dl),或者是肌酐较之前升高 50%,或者是尿量减少(尿量 $<0.5 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$,时间超过 6 h);(2)所有患者均签署知情同意书,患者及其家属同意接受连续性肾脏替代治疗。排除标准:(1)合并慢性肾衰竭及终末期肾病患者;(2)需长期接受维持性透析治疗者;(3)合并脑梗或脑死亡者;(4)合并出血性疾病、恶性肿瘤、免疫缺陷性疾病等患者。该研究经我院伦理委员会批准实施。依据急性肾损伤的诊断和分级(RIFLE)标准将脓毒症急性肾损伤患者分为 A 组($n=56$)、B 组($n=70$)、C 组($n=74$),所有患者皆采取连续性肾脏替代疗法。三组临床资料比较差异均无统计学意义($P>0.05$),见表 1。

1.2 治疗方法

按照 2012 年脓毒症治疗指南^[12]中的相关治疗原则,所有患者均给予营养和呼吸支持、纠正酸中毒、应用抗生素、消除感染源、补液等治疗,在此基础上,三组患者再行连续性肾脏替代

疗法治疗。具体过程如下:在 24 h 内采用股静脉或颈内脉建立通路,采用 CBP 机,以根据 Port 配方配置的置换液实施连续性静脉-静脉血液滤过模式,置换液以 4000 mL/h 按照稀释方式输入,血流量控制在 250~300 mL/min。同时,对于无高分解代谢的患者,只需白天进行 10 h 左右的治疗;对于伴有高分解代谢的患者,则需在 24 h 内进行不间断的治疗;而对于伴有严重的高分解代谢患者,则还需行血液透析治疗。三组共 200 例患者均分别接受连续性肾脏替代疗法治疗 3~12 次,总次数为 678 次。抗凝治疗采用低分子肝素,如患者存在高危出血风险,则采用无抗凝血液滤过治疗。

1.3 观察指标

微循环系统变化:(1)舌下微循环变化主要通过旁流暗视野成像技术观察,采用丙泊酚对患者进行镇静治疗,当患者 Ramsay 镇静评分处于 3~4 分时进行图像采集,采集部位分别为舌下左、中、右三个位置,且每个部位的采集时间在 20 s 以上,以血管内径和红细胞流速计算出相关参数:包括微血管流动指数、灌注血管比例、灌注血管密度、总血管密度;(2)采用彩色甲襞微循环显微检查仪测定微循环状态相关指标:包括血液流态积分、襻周状态积分、管襻形态积分、总积分、襻顶血管直径。

1.4 统计学分析

研究所得数据均采用 SPSS 22.0 统计软件分析,性别比例等计数资料以 $[n(\%)]$ 表示,采用独立样本 χ^2 检验,舌下及甲襞微循环等计量资料以 $(\bar{x} \pm s)$ 的形式表示,采用 t 检验,多组比较采用单因素方差分析,组间两两比较采用 LSD 法进行分析,将 $\alpha=0.05$ 设置为检验标准。

2 结果

2.1 三组患者的临床资料比较

三组患者的性别、年龄、空腹血糖、急性生理功能和慢性健康状况(APACHE)评分、体温、心率对比经统计分析差异无统计学意义($P>0.05$)。见表 1。

表 1 三组患者的临床资料比较

Table 1 Comparison of clinical data of patients among three groups

Groups	Male[n(%)]	Age (years old)	Fasting blood glucose(mmol/L)	APACHE score (points)	Temperature($^{\circ}\text{C}$)	HR (bpm)
Group A($n=56$)	34(60.71)	49.23 $\pm$ 3.72	5.41 $\pm$ 0.85	19.57 $\pm$ 4.15	38.83 $\pm$ 1.27	119.51 $\pm$ 10.77
Group B($n=70$)	36(51.43)	50.18 $\pm$ 3.85	5.43 $\pm$ 0.74	19.25 $\pm$ 5.46	39.12 $\pm$ 1.10	120.55 $\pm$ 11.45
Group C($n=74$)	36(48.65)	50.15 $\pm$ 4.17	5.40 $\pm$ 0.80	19.23 $\pm$ 5.14	39.05 $\pm$ 1.17	120.65 $\pm$ 10.78
χ^2/F	0.985	0.569	0.013	0.044	0.503	0.100
P	0.321	0.568	0.987	0.957	0.606	0.905

2.2 三组脓毒症急性肾损伤患者在治疗前后的舌下微循环变化情况比较

治疗前,三组舌下微循环指标比较差异无统计学意义($P>0.05$);三组患者在治疗后微血管流动指数显著下降,灌注血管比例、灌注血管密度及总血管密度均显著升高,差异具有统计学意义($P<0.05$)。在治疗后,A 组患者微血管流动指数低于 B 组和 C 组,而灌注血管比例、灌注血管密度及总血管密度显著高于 B 组和 C 组($P<0.05$);B 组患者微血管流动指数显著

低于 C 组($P<0.05$),灌注血管比例、灌注血管密度及总血管密度显著高于 C 组($P<0.05$)。见表 2。

2.3 三组脓毒症急性肾损伤患者在治疗前后的甲襞微循环状态的变化

三组患者在治疗前的甲襞微循环状态指标差异无统计学意义($P>0.05$)。治疗后三组血液流态积分、襻周状态积分、管襻形态积分及总积分均较治疗前显著降低,而襻顶血管直径显著增大,差异有统计学意义($P<0.05$);在治疗后,A 组患者血液流

态积分、襻周状态积分、管襻形态积分及总积分显著低于 B 组 (P<0.05), 而襻顶血管直径显著大于 B 组和 C 组 (P<0.05), B 组患者血液流态积分、襻周状态积分、管襻形态积分及总积分显著低于 C 组 (P<0.05), 襻顶血管直径显著大于 C 组 (P<0.05)。见表 3。

表 2 三组脓毒症急性肾损伤患者在治疗前后的舌下微循环变化情况比较($\bar{x} \pm s$)Table 2 Comparison of sublingual microcirculation of patients with acute kidney injury caused by sepsis before and after treatment among three groups ($\bar{x} \pm s$)

Groups	Microvascular flow index		Proportion of perfused vessels(%)		Perfused vessel density (mm/mm ²)		Total Vascular Density (mm/mm ²)	
	Before	After	Before	After	Before	After	Before	After
	treatment	treatment	treatment	treatment	treatment	treatment	treatment	treatment
Group A(n=56)	6.72± 4.10	3.72± 3.05*	5.07± 2.97	7.34± 1.79*	34.12± 2.97	40.16± 1.77*	1.40± 0.90	2.87± 1.66*
Group B(n=70)	6.50± 4.07	4.56± 1.96* ^a	4.93± 2.57	6.33± 3.01* ^a	33.85± 2.67	37.65± 2.11* ^a	1.49± 0.32	2.25± 0.87* ^a
Group C(n=74)	6.30± 4.13	6.16± 1.68* ^{ab}	4.18± 2.14	5.41± 2.85* ^{ab}	33.01± 2.83	34.08± 1.96* ^{ab}	1.54± 0.89	1.65± 1.24* ^{ab}
F	0.168	20.396	2.423	8.413	2.853	158.068	0.567	14.866
P	0.846	<0.001	0.091	<0.001	0.060	<0.001	0.568	<0.001

Note: compared with group A, ^aP<0.05; compared with group B, ^bP<0.05; compared with before treatment, *P<0.001.

表 3 三组脓毒症急性肾损伤患者在治疗前后的甲襻微循环状态的变化($\bar{x} \pm s$)Table 3 Comparison of nail fold microcirculation of patients with acute kidney injury caused by sepsis before and after treatment among three groups ($\bar{x} \pm s$)

Groups	Blood flow state score (points)		Loop weeks status score (points)		Pipe loop integral score (points)		Total score (points)		Diameter of dome blood vessel(mm)	
	Before	After	Before	After	Before	After	Before	After	Before	After
	treatment	treatment	treatment	treatment	treatment	treatment	treatment	treatment	treatment	treatment
Group A (n=56)	2.39± 0.31	1.45± 0.28*	1.91± 0.18	0.56± 0.14*	1.79± 0.19	0.43± 0.17*	3.04± 0.41	1.63± 0.32*	15.83± 1.23	22.78± 1.25*
Group B (n=70)	2.42± 0.51	1.75± 0.28* ^a	1.84± 0.18	0.78± 0.14* ^a	1.80± 0.16	0.60± 0.18* ^a	3.13± 0.22	1.95± 0.32* ^a	15.94± 1.89	20.35± 1.80* ^a
Group C (n=74)	2.47± 0.33	1.96± 0.18* ^{ab}	1.90± 0.21	1.04± 0.06* ^{ab}	1.83± 0.21	1.03± 0.15* ^{ab}	3.15± 0.32	2.21± 0.13* ^{ab}	15.94± 1.89	18.05± 1.28* ^{ab}
F	0.679	67.603	2.604	273.328	0.825	230.857	2.061	75.857	0.081	164.430
P	0.508	<0.001	0.076	<0.001	0.440	<0.001	0.130	<0.001	0.922	<0.001

Note: compared with group A, ^aP<0.05; compared with group B, ^bP<0.05; compared with before treatment, *P<0.001.

3 讨论

脓毒症是一种炎症反应,患者机体内过量的炎症介质经血流动力学异常作用而遍布全身,从而将造成包括肾脏在内的多种脏器发生损伤^[13,14]。有研究表明,脓毒症导致的急性肾损伤的临床发病率较高,并且死亡率高达 50%左右,严重影响着患者的生命健康^[15]。因此对于脓毒症急性肾损伤的治疗就显得尤为重要。近几年,许多临床工作者对脓毒症所致的急性肾损伤的发病机制^[16-18]、诊断技术^[19,20]、治疗方法^[21,22]、预防措施^[23,24]进行了大量的研究。

既往大量研究提示采用连续性肾脏替代疗法治疗脓毒症肾损伤患者,可抑制机体炎症反应,改善体内感染情况,有效地改善脓毒症肾损伤患者的肾功能以及微循环,并且能明显地提高患者的预后效果^[25-27]。张任等^[28]的研究则发现在 RLFLE 诊断标准 1 期(即早期)就实施连续性肾脏替代疗法效果显著,可以有效地提高脓毒症所导致的急性肾损伤患者的存活率,改善

患者的肾功能,强调了针对脓毒症肾损伤患者治疗时机的关键性。

本研究为进一步探究脓毒症肾损伤患者不同时机血液净化对微循环系统的影响,对不同分期的脓毒症肾损伤患者治疗前后疗效进行了比较,结果提示:RLFLE 不同分期患者在治疗后舌下微循环指标微血管流动均较治疗前显著下降,灌注血管比例、灌注血管密度及总血管密度则显著升高;同时,甲襻微循环指标血液流态积分、襻周状态积分、管襻形态积分及总积分指标评分显著降低,而襻顶血管直径显著增大,提示了连续性肾脏替代疗法能够显著改善脓毒症肾损伤患者的微循环状态,且在疾病的不同分期疗效均显著。考虑可能的机制为血液净化能够快速有效地清除脓毒症肾损伤患者体内的炎性介质及内毒素,纠正酸中毒及机体高凝状态,从而改善患者的微循环状态^[29,30]。同时,脓毒症肾损伤患者不同分期各项微循环指标在血液净化治疗前无明显差异,而在治疗后却出现显著差异,且治疗时机越提前,患者的微循环改善效果越显著,提示了对脓毒症肾损伤患者血液净化时机的选择十分重要。早期对该类患者

进行肾脏替代疗法能够显著改善患者的微循环状态,对各重要脏器良好的血流灌注有着重要意义。本研究仅针对血液净化治疗脓毒症肾损伤患者微循环状态的变化及其时机的选择进行了研究,今后需进一步进行血液净化对机体炎症反应、各脏器灌注状态改善等研究,综合考虑脓毒症肾损伤患者血液净化时机的选择,制定出最合理的治疗方案,为临床治疗标准的完善提供可靠的依据。

综上所述,早期(RLFE 诊断标准 1 期)对脓毒症急性肾损伤患者实施血液净化,可以明显地改善治疗效果,促进微循环系统的恢复。

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