

doi: 10.13241/j.cnki.pmb.2018.05.018

序贯血液净化对严重创伤合并 MODS 患者炎症因子 以及血流动力学的影响 *

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摘要 目的:探讨序贯血液净化(SBP)对严重创伤合并多器官功能障碍综合征(MODS)患者血清炎症因子及血流动力学的影响。**方法:**选取 2015 年 7 月-2017 年 5 月第三军医大学新桥医院收治的严重创伤合并 MODS 患者 48 例,根据患者的治疗方式分为对照组 21 例以及观察组 27 例,其中对照组接受常规内科治疗,观察组在对照组的基础上进行 SBP 治疗,在治疗前后对两组患者的肝肾功能、血清炎症因子水平、血流动力学指标进行检测,并对比两组患者 ICU 住院时间、病死率、机械通气时间。**结果:**治疗后两组患者的总胆红素(TBIL)、直接胆红素(DBIL)、谷草转氨酶(AST)、谷丙转氨酶(ALT)、血尿素氮(BUN)、肌酐(Cr)水平均较治疗前降低,且治疗后观察组患者各指标低于对照组($P<0.05$);治疗后两组患者血清 C 反应蛋白(CRP)、白介素-6(IL-6)、白介素-1 β (IL-1 β)、肿瘤坏死因子- α (TNF- α)水平均较治疗前显著降低,且治疗后观察组患者各炎症因子水平显著低于对照组($P<0.05$);治疗后两组患者的心率(HR)、中心静脉压(CVP)较治疗前降低,平均动脉压(MAP)、心脏指数(CI)较治疗前升高,且治疗后观察组患者的 HR、CVP 显著低于对照组,MAP、CI 显著高于对照组($P<0.05$);观察组患者的 ICU 住院时间、机械通气时间均较对照组缩短,病死率较对照组明显降低($P<0.05$)。**结论:**SBP 应用于严重创伤合并 MODS 患者的治疗可以有效减轻患者的炎症反应,并可以显著改善患者血流动力学以及预后。

关键词:严重创伤;多器官功能障碍综合征;序贯血液净化;炎症因子;血流动力学

中图分类号:R641;R459.5 **文献标识码:**A **文章编号:**1673-6273(2018)05-884-05

Effect of Sequential Blood Purification on Inflammatory Factors and Hemodynamics in Patients with Severe Trauma Complicated with MODS*

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ABSTRACT Objective: To investigate the effect of sequential blood purification (SBP) on serum inflammatory factors and hemodynamics in patients with severe trauma complicated with multiple organ dysfunction syndrome (MODS). **Methods:** A total of 48 patients with severe trauma complicated with MODS, who were admitted to the Third Military Medical University Xinqiao Hospital during July 2015 to May 2017, were selected and divided into observation group($n=27$) and control group($n=21$). The control group was given routine medical treatment, the observation group was treated with SBP on the basis of the control group's therapy. The liver and kidney function, serum levels of inflammatory cytokines, hemodynamic indexes of the two groups of patients were detected before and after therapy. The ICU length of hospital stay, mortality, mechanical ventilation time of the two groups of patients were compared. **Results:** After treatment, the levels of total bilirubin (TBIL), direct bilirubin (DBIL), aspartate aminotransferase (AST), alanine aminotransferase (ALT), blood urea nitrogen (BUN), creatinine (Cr) of the two groups of patients decreased than those before treatment, and the indexes of the observation group were lower than those of the control group; serum C reactive protein (CRP), Interleukin -6 (IL-6), interleukin -1 beta (IL-1 beta), tumor necrosis factor alpha (TNF- α) levels of the two groups of patients were significantly lower than those before treatment, and the inflammatory factors of the observation group were lower than those of the control group ($P<0.05$). After treatment, heart rate (HR), central venous pressure (CVP) decreased than those before treatment; mean arterial pressure (MAP) and cardiac index (CI) were higher than those before treatment, and the indexes of the observation group were higher than those of the control group($P<0.05$). The ICU hospitalization time and mechanical ventilation time of the patients in the observation group was shorter than that in the control group, and the mortality rate was significantly lower than that in the control group ($P<0.05$). **Conclusion:** In the treatment of patients with severe trauma complicated with MODS, SBP can effectively reduce the inflammatory response of patients and significantly improve the

* 基金项目:第三军医大学第二附属医院临床科研项目(2014YLC33)

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(收稿日期:2017-07-20 接受日期:2017-08-12)

hemodynamics and the prognosis of the patients.

Key words: Severe trauma; Multiple organ dysfunction syndrome; Sequential blood purification; Inflammatory factors; Hemodynamics

Chinese Library Classification(CLC): R641; R459.5 **Document code:** A

Article ID: 1673-6273(2018)05-884-05

前言

多器官功能障碍综合征 (Multiple organ dysfunction syndrome, MODS) 主要是指患者在经过大手术、严重感染、创伤等应激状态下, 引发患者的两个或两个以上器官、系统发生急性功能衰竭的临床综合征, 进行性、继发性、顺序性是 MODS 疾病的发病特点^[1]。目前临床上治疗严重创伤合并 MODS 的方法主要以营养支持、对症治疗、病因治疗等常规内科治疗方法为主, 虽然能够在一定程度上缓解患者的症状, 但临床疗效欠佳^[2]。炎性因子的大量释放所引发的全身炎症反应是导致 MODS 发生的重要原因, 因此有效的清除患者血清炎性因子是改善严重创伤合并 MODS 患者预后的关键^[3,4]。有研究显示^[5-7], 序贯血液净化 (Sequential blood purification, SBP) 治疗 MODS 能够有效的清除血清中的炎性因子, 并能够有效的稳定患者的血流动力学, 从而改善患者的预后。因此, 本研究通过探讨 SBP 应用于严重创伤合并 MODS 患者的血清炎性因子水平及血流动力学的影响, 以期为临床治疗严重创伤合并 MODS 提供数据参考, 现作如下报道。

1 资料与方法

1.1 一般资料

选取 2015 年 7 月 -2017 年 5 月第三军医大学新桥医院收治的严重创伤合并 MODS 患者 48 例为研究对象。纳入标准: ① 所有入选患者均符合符合 1991 年美国胸科医师学会与危重病学会联席会议 (ACCP/SCCM) 提出的 MODS 诊断标准^[8]; ② 均伴有严重创伤; ③ 患者家属均签署知情同意书。排除标准: ① 入组前 2d 接受抗凝药物治疗的患者; ② 伴有活动性出血的患者; ③ 伴有明显出血倾向的患者; 哺乳期及妊娠期患者; ④ 免疫功能不全或者长期接受免疫抑制剂治疗的患者。48 例患者根据是否接受 SBP 治疗分为观察组 27 例, 对照组 21 例。观察组患者中男 16 例, 女 11 例; 年龄 41-75 岁, 平均年龄 (58.89±9.71) 岁; 脑外伤 8 例, 普外伤 12 例, 烧伤 7 例。对照组患者中男 12 例, 女 9 例; 年龄 43-77 岁, 平均年龄 (59.73±10.14) 岁; 脑外伤 7 例, 普外伤 9 例, 烧伤 5 例。两组患者的一般资料对比无显著差异 ($P>0.05$), 本研究通过医院伦理委员会批准。

1.2 方法

对照组患者给予预防感染、维持酸碱平衡、吸氧、营养支持等常规治疗, 并针对患者的并发症及原发病进行对症治疗。观察组患者在对照组的基础上联合 SBP 治疗, SBP 治疗方法: 应用德国费森公司 ADM08/ABM08 连续性肾替代治疗床边机及 AV600S 血液过滤器进行治疗, 在患者右侧股静脉置管, 抗凝剂选用低分子肝素钙注射液 (深圳赛保尔生物药业有限公司, 国药准字 H20060190, 1.0 mL:5000AXa 单位), 初始剂量为 15U/kg, 以 8U/(kg·h) 维持, 置换液根据改良 Port 配方^[9]配制, 以

稀释方式注入, 流量控制在 3000 mL/h, 血液流量控制在 150-200 mL/min, 1 次/d, 12 h/次, 连续治疗 5 d, 滤器 24 h 更换 1 次。

1.3 评价指标

1.3.1 肝肾功能 于治疗前、治疗后 2d 抽取患者的空腹静脉血 2 mL, 应用美国贝克曼 AU5800 全自动生化分析仪检测肝功能指标谷丙转氨酶 (Alanine aminotransferase, ALT)、谷草转氨酶 (Aspartate transaminase, AST)、总胆红素 (total bilirubin, TBIL)、直接胆红素 (bilirubin direct, DBIL) 及肾功能指标血尿素氮 (Blood urea nitrogen, BUN)、血肌酐 (creatinine, Cr)。

1.3.2 炎性因子 于治疗前及治疗后 2 d 抽取患者的空腹静脉血 5 mL, 应用离心机以 1500 r/min 的转速离心 10 min, 离心半径为 10 cm, 待血清分离后, 置于 -70℃ 环境中保存待检。血清中 C 反应蛋白 (C reactive protein, CRP) 水平应用免疫比浊法检测, 白介素 -6 (Interleukin -6, IL-6)、白介素 -1β (Interleukin -1β, IL-1β)、肿瘤坏死因子 -α (Tumor necrosis factor -α, TNF-α) 应用酶联免疫吸附法检测, 试剂盒由石家庄麦迪克试剂公司提供。

1.3.3 血流动力学指标 应用迈瑞多功能监护仪 IMEC12 记录治疗前、治疗后 2 d 患者的血流动力学指标: 中心静脉压 (central venous pressure, CVP)、心率 (heart rate, HR)、平均动脉压 (mean arterial pressure, MAP)、心脏指数 (cardiac index, CI)。

1.3.4 临床指标 对比两组患者 ICU 住院时间、病死率、机械通气时间。

1.4 统计学分析

采用 SPSS20.0 统计学软件, 肝功能、肾功能指标等计量资料以 ($\bar{x} \pm s$) 的形式表示, 采用 t 检验分析, 一般资料等计数资料以 % 的形式表示, 采用 χ^2 检验分析, 以 $P<0.05$ 为差异有统计学意义。

2 结果

2.1 两组肝功能指标对比

治疗前, 两组患者的肝功能指标对比无显著差异 ($P>0.05$), 治疗后两组患者的 TBIL、DBIL、AST、ALT 水平均较治疗前降低, 且治疗后观察组患者各指标均明显低于对照组 ($P<0.05$), 见表 1。

2.2 两组肾功能比较

治疗前, 两组患者的肾功能指标对比无显著差异 ($P>0.05$), 治疗后两组患者的 BUN、Cr 水平均较治疗前降低, 且治疗后观察组患者 BUN、Cr 水平低于对照组 ($P<0.05$), 见表 2。

2.3 两组炎性因子对比

治疗前, 两组患者的炎性因子水平对比无显著差异 ($P>0.05$), 治疗后两组患者血清 CRP、IL-6、IL-1β、TNF-α 水平均较治疗前降低, 且治疗后观察组患者各炎性因子水平低于对照组 ($P<0.05$), 见表 3。

表 1 两组肝功能对比

Table 1 Comparison of liver function between the two groups

Groups	n	TBIL($\mu\text{mol/L}$)		DBIL($\mu\text{mol/L}$)		AST(U/L)		ALT(U/L)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Observation group	27	52.49 $\pm$ 11.57	24.94 $\pm$ 7.12*	31.82 $\pm$ 7.68	10.82 $\pm$ 2.33*	170.37 $\pm$ 41.52	53.49 $\pm$ 12.54*	186.14 $\pm$ 50.33	61.40 $\pm$ 15.42*
Control group	21	53.20 $\pm$ 12.29	39.27 $\pm$ 9.28*	32.12 $\pm$ 8.29	22.18 $\pm$ 5.76*	175.17 $\pm$ 44.59	74.19 $\pm$ 20.42*	183.10 $\pm$ 52.17	85.19 $\pm$ 23.13*
t		0.985	9.718	0.182	11.372	1.043	6.847	0.812	8.165
P		0.431	0.022	0.097	0.015	0.076	0.036	0.754	0.029

Note: Compared with before treatment in the same group, *P<0.05.

表 2 两组肾功能对比

Table 2 Comparison of renal function between the two groups

Groups	n	BUN(mmol/L)		Cr($\mu\text{mol/L}$)	
		Before treatment	After treatment	Before treatment	After treatment
Observation group	27	23.09 $\pm$ 8.15	8.69 $\pm$ 2.37*	685.25 $\pm$ 137.10	139.47 $\pm$ 41.16*
Control group	21	23.13 $\pm$ 8.19	13.42 $\pm$ 2.80*	672.78 $\pm$ 129.36	204.65 $\pm$ 58.92*
t		1.158	7.815	0.527	10.337
P		0.076	0.032	0.913	0.019

Note: Compared with before treatment in the same group, *P<0.05.

表 3 两组炎症因子对比

Table 3 Comparison of inflammatory factors between the two groups

Groups	n	CRP(pg/mL)		IL-6(pg/mL)		IL-1 β (pg/mL)		TNF- α (pg/mL)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Observation group	27	72.89 $\pm$ 13.57	8.26 $\pm$ 2.53*	45.52 $\pm$ 4.33	8.87 $\pm$ 2.11*	18.19 $\pm$ 5.32	3.71 $\pm$ 1.14*	30.36 $\pm$ 6.58	4.24 $\pm$ 1.32*
Control group	21	70.49 $\pm$ 14.14	17.12 $\pm$ 3.83*	45.72 $\pm$ 5.18	25.29 $\pm$ 2.19*	18.42 $\pm$ 5.76	10.12 $\pm$ 4.83*	29.28 $\pm$ 7.98	10.47 $\pm$ 2.76*
t		0.932	7.327	0.758	9.186	0.428	6.872	0.172	4.869
P		0.097	0.021	0.175	0.019	0.376	0.028	0.149	0.035

Note: Compared with before treatment in the same group, *P<0.05.

2.4 两组血流动力学指标对比

CI 较治疗前升高, 且治疗后观察组患者的 HR、CVP 低于对照

治疗前, 两组患者的血流动力学指标对比无显著差异

组, MAP、CI 高于对照组(P<0.05), 见表 4。

(P>0.05), 治疗后两组患者的 HR、CVP 较治疗前降低, MAP、

表 4 两组血流动力学指标对比

Table 4 Comparison of hemodynamic indexes between the two groups

Groups	n	HR(times/min)		CVP(cmH ₂ O)		MAP(mmHg)		CI(L/mm $\cdot$ m ²)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Observation group	27	130.16 $\pm$ 9.44	80.25 $\pm$ 5.43*	22.82 $\pm$ 3.57	7.03 $\pm$ 2.03*	70.23 $\pm$ 4.12	93.27 $\pm$ 5.27*	2.25 $\pm$ 0.37	3.42 $\pm$ 0.53*
Control group	21	129.45 $\pm$ 10.12	98.67 $\pm$ 7.57*	22.79 $\pm$ 3.41	11.64 $\pm$ 3.43*	70.69 $\pm$ 4.18	81.14 $\pm$ 6.37*	2.24 $\pm$ 0.34	2.63 $\pm$ 0.39*
t		0.119	8.913	0.097	6.318	0.054	7.572	0.079	6.129
P		0.136	0.025	0.476	0.042	0.865	0.033	0.614	0.045

Note: Compared with before treatment in the same group, *P<0.05.

2.5 ICU 住院时间、病死率、机械通气时间对比

均较对照组降低,差异均有统计学意义($P<0.05$),见表 5。

观察组患者的 ICU 住院时间、病死率以及机械通气时间

表 5 两组 ICU 住院时间、病死率、机械通气时间对比

Table 5 Comparison of ICU hospitalization time, fatality rate and mechanical ventilation time between the two groups

Groups	n	ICU stay(d)	Case fatality rate [n(%)]	Mechanical ventilation time(d)
Observation	27	10.03± 2.76	6(22.22)	5.42± 1.63
Control group	21	15.91± 3.37	8(38.10)	7.73± 2.29
t/x ²		9.765	12.331	6.312
P		0.027	0.012	0.032

3 讨论

严重创伤合并 MODS 是由多种因素所引发的临床综合征,炎症反应是引发该病的重要原因,当机体遭受严重创伤、休克或者感染等因素时,便会释放大量的炎性介质,使机体内环境发生紊乱,导致器官功能被损坏,进而引发 MODS,因此有效的降低 MODS 患者血液中的炎性因子水平,并抑制炎性因子的释放,是治疗严重创伤合并 MODS 患者的关键方法^[10-12]。在临床以往常规治疗中以营养支持、对症治疗为主,但是由于严重创伤 MODS 患者的 CVP 往往处于较高的水平,严重限制了输液剂量,导致营养物质及治疗药物药效不能够充分发挥,并不能达到理想的治疗效果^[13-15]。近年来,较多文献显示严重创伤合并 MODS 患者经 SBP 治疗后可取得较好的疗效,sBP 主要是指将体内的溶质和水连续缓慢的清除的治疗方式^[16-18]。SBP 具有强大的吸附、对流的作用,可以将机体内的抗炎介质、促炎介质水平通过对流、吸附、弥散的方式降低,进而恢复单核细胞的反应性及改善血流动力学,进而减轻全身炎症反应,改善 MODS 患者的预后^[19,20]。

有研究显示,MODS 的发生与发展也可以促进肝肾功能的进一步恶化,而 SBP 治疗 MODS 的特点在于既能有效的稳定患者在治疗期间的血流动力学,又能最大限度的降低对患者肾脏血流灌注的影响,使患者残余的肝肾功能得到保留,并在一定程度上对肝肾功能的恢复发挥了促进作用^[21-23]。本研究结果显示,观察组与对照组患者的肝肾功能在治疗后均得到有效的改善,且观察组患者的肝肾功能指标改善更显著,说明 SBP 可有效的促进 MODS 患者肝肾功能的改善。IL-1 β 、IL-6 及 TNF- α 均为致炎因子,CRP 为机体发生组织损伤或感染时在血浆中的水平发生急剧上升的一类蛋白质,在机体发生炎症反应时,细胞因子则会促进肝脏释放大量的 CRP^[24,25]。在本研究对两组患者治疗前后炎性因子水平分析中显示,观察组患者的炎性因子水平较对照组降低更显著,说明 SBP 治疗 MODS 对炎症介质的清除作用更显著,分析其主要原因是因为 SBP 可以通过吸附和滤过的作用,将患者血液中可溶性的炎性介质有效的清除。同时在对两组患者血流动力学指标分析中显示,观察组患者的血流动力学指标改善程度优于对照组,说明 SBP 治疗 MODS 可有效稳定患者的血流动力学,与文献报道一致^[26-28]。分析其原因主要是因为 SBP 在清除溶质和水的同时,有效的确保了血浆的再充盈,进而使 MODS 患者血管调节功能障碍得到了改善,稳定了血流动力学^[29,30]。在两组患者 ICU 住院时间、病死率及机械通气时间对比中显示,观察组患者的 ICU 住院

时间、机械通气时间均较对照组缩短,病死率较对照组明显降低,说明 SBP 治疗严重创伤合并 MODS 患者可有效缩短患者的治疗时间,降低病死率,改善患者预后。

综上所述,SBP 治疗严重创伤合并 MODS 患者可有效降低炎性因子水平,并能改善患者血流动力学,确保组织灌注,改善患者肝功能及预后,具有显著的疗效。

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