

doi: 10.13241/j.cnki.pmb.2018.09.027

连续静脉-静脉血液透析滤过治疗多器官功能障碍综合征的临床疗效研究*

布合力其·麦麦提 莫颖 刘红艳 徐超 帕提古丽·阿斯讨拜 张蕾[△]

(新疆医科大学第五附属医院肾内科 新疆 乌鲁木齐 830011)

摘要 目的:探讨连续静脉-静脉血液透析滤过(continuous veno-venous hemodialysis filtration, CVVHDF)治疗多器官功能障碍综合征(MODS)的临床疗效。**方法:**选择我院ICU自2015年1月-2017年2月收治的MODS患者50例作为研究对象,根据随机抽签原则分为观察组与对照组,每组25例。对照组在常规内科治疗基础上给予机械通气治疗,观察组在对照组基础上采用CVVHDF治疗,两组治疗观察时间为30d。观察和比较两组ICU停留时间、呼吸机辅助时间、治疗后APACHE II评分与MODS评分、治疗前后血清IL-6与TNF- α 含量的变化及随访6个月的死亡情况。**结果:**治疗后,观察组ICU停留时间和呼吸机辅助时间均短于对照组($P<0.05$),APACHE II评分与MODS评分分别为 22.33 ± 2.49 分和 6.42 ± 1.98 分,均明显低于对照组(62.19 ± 7.45 分和 7.29 ± 1.67 分)($P<0.05$)。治疗后,两组的血清IL-6与TNF- α 含量都明显低于治疗前,且观察组的血清IL-6与TNF- α 含量均明显低于对照组($P<0.05$)。随访6个月,观察组与对照组的死亡率分别为4.0%和20.0%,观察组的死亡率低于对照组($P<0.05$)。**结论:**CVVHDF治疗MODS能有效清除患者炎症因子,缩短ICU停留时间和呼吸机辅助时间,降低患者的死亡率。

关键词:连续静脉-静脉血液透析滤过;多器官功能障碍综合征;炎症因子;机械通气

中图分类号:R459.7;R459.5 **文献标识码:**A **文章编号:**1673-6273(2018)09-1726-04

Clinical Effects of CVVHDF on the Patients with Multiple Organ Dysfunction Syndrome*

Buheliqiomaimaiti, MO Ying, LIU Hong-yan, XU Chao, PATIGULI·asitaobai, ZHANG Lei[△]

(Nephrology Department, The Fifth Affiliated Hospital of Xinjiang Medical University, Urumqi, Xinjiang, 830011, China)

ABSTRACT Objective: To investigate the clinical effect of CVVHDF on the patients with multiple organ dysfunction syndrome (MODS). **Methods:** 50 cases of patients with MODS in our hospital from January 2015 to February 2017 were selected as the subjects of study. All the patients were divided into the observation group and the control group with 25 patients in each group according to the principle of random ballot. The control group was treated with routine mechanical ventilation based on the routine medical treatment. The observation group was given mechanical ventilation and CVVHDF treatment on the basis of control group. The ICU standing time, ventilator assisted time, APACHE II score and MODS score after treatment, the serum IL-6 and TNF- α content before and after treatment, the death status of two groups were observed and compared. **Results:** After treatment, the stay time of ICU and the time of ventilator assistance in the observation group were shorter than those in the control group ($P<0.05$). The APACHE II score and MODS score in the observation group were 22.33 ± 2.49 points and 6.42 ± 1.98 points, which were significantly lower than those of the control group (62.19 ± 7.45 and 7.29 ± 1.67 points)($P<0.05$). After treatment, the serum IL-6 and TNF- α in both groups were significantly lower than those before treatment, and the serum IL-6 and TNF- α in the observation group were lower than those in the control group($P<0.05$). After a followed-up of 6 months, the mortality rates in the observation group and the control group were 4% and 20%, respectively. The mortality of observation group was lower than that of the control group ($P<0.05$). **Conclusion:** CVVHDF could effectively eliminate the inflammatory factors in treatment of MODS, shorten the ICU retention time and the ventilator assisted time, and reduce the mortality of patients.

Key words: CVVHDF; Multiple organ dysfunction syndrome; Inflammatory factors; Mechanical ventilation

Chinese Library Classification(CLC): R459.7; R459.5 **Document code:** A

Article ID: 1673-6273(2018)09-1726-04

前言

多器官功能障碍综合征(MODS)为在原发病基础上出现导致2个或2个以上的器官现可逆性功能障碍的临床综合症

* 基金项目:新疆维吾尔自治区自然科学基金项目(2015211C179)

作者简介:布合力其·麦麦提(1984-),女,硕士研究生,主治医师,研究方向:肾脏病与血液净化学,

E-mail: yanxueping_1965@papmedline.club

[△] 通讯作者:张蕾(1963-),女,本科,主任医师,研究方向:肾脏病与血液净化,E-mail: zhanglei_1963@papmedline.club

(收稿日期:2017-10-15 接受日期:2017-10-31)

[12],在临床上具有病情凶险、病死率高等特征,缺乏有效的治疗手段[3,4]。研究表明致炎因素刺激机体释放大炎症介质,形成炎症介质瀑布样连锁反应,是导致 MODS 的根本原因[5,6],对于 MODS 的治疗应高度重视首发衰竭器官的处理[7-9]。连续静脉-静脉血液透析滤过(CVVHDF)可重建机体免疫平衡,但 CVVHDF 在人类多器官功能障碍中的治疗作用尚未被完全阐明[10-12]。有研究表明 CVVHDF 可有效清除患者体内各种毒性物质和炎症递质等,维持生理功能平衡,改善患者体内水电解质紊乱[13,14]。本试验将通过比较常规治疗与 CVVHDF 治疗 MODS 患者对机体免疫功能的影响,以期为 MODS 的治疗提供新的思路。现报道如下。

1 资料与方法

1.1 研究对象

表 1 两组一般临床特征对比

Table 1 Comparison of the general data between two groups

Groups	Cases(n)	Sex (Male/Female)	Age(Year)	Pathogenesis (shock/trauma/pancreatitis/intestinal obstruction)	APACHE II score (score)	Weight index (kg/m ²)
Control group	25	14/11	44.23± 0.44	10/6/7/2	77.10± 5.24	22.19± 2.48
Observation group	25	15/10	44.21± 0.34	11/7/6/1	77.83± 6.43	21.09± 3.11
P		>0.05	>0.05	>0.05	>0.05	>0.05

1.2 治疗方法

常规内科治疗基础上,对照组给予机械通气治疗;观察组在对照组基础上给予 CVVHDF 治疗。常规治疗包括营养支持、脏器支持治疗、抗感染及原发病治疗。CVVHDF 治疗时,选择 Prismaflex 床旁血液透析机和金宝 M-100 型滤器。治疗参数:置换液量:5-45 mL/kg/h,前稀释法输入;采用持续治疗方式,每 12 h 更换滤器一次;前 3 d 进行持续治疗,之后根据病情调整治疗剂量、频率;血流速度维持在 180-220 mL/min;使用低分子肝素或无肝素进行抗凝。置换液量 5-45 mL/Kg/h,前稀释法输入。两组开始治疗为观察起始时间,观察终点为 30 d 或治疗终点,包括痊愈、好转出院或死亡。

1.3 观察指标

(1)记录两组患者 ICU 停留时间和呼吸机辅助时间。(2)记录两组治疗后 APACHE II 评分、MODS 评分,评分越高,疾病

越严重。(3)炎症因子检测:治疗前后采 5-10 mL 血样,1200 r/min,离心 10 min,采用 ELISA 方法测定血清 IL-6、TNF-α 含量,试剂盒由美国 R&D 公司生产,长沙佳和生物有限公司提供。(4)记录与随访两组患者的半年死亡率情况。

表 2 两组 ICU 停留时间及呼吸机辅助时间对比(d,均数± 标准差)

Table 2 Comparison of the ICU duration and auxiliary time of the ventilator between two groups(d, $\bar{x} \pm s$)

Groups	Cases(n)	ICU stay length	Ventilator assisted time
Control group	25	10.63± 2.17	6.75± 1.84
Observation group	25	7.21± 1.92	3.43± 1.81
P		<0.05	<0.05

2.2 两组治疗后 APACHE II 评分与 MODS 评分对比

治疗后,观察组 APACHE II 评分为 22.33± 2.49 分,MODS 评分为 6.42± 1.98 分,均明显低于对照组 (62.19± 7.45 分和 7.29± 1.67 分)(P<0.05),见表 3。

2.3 两组治疗前后血清 IL-6 与 TNF-α 含量的变化对比

治疗后,两组的血清 IL-6 与 TNF-α 含量都明显低于治疗

前,且观察组的血清 IL-6 与 TNF-α 含量均明显低于对照组 (P<0.05),见表 4。

2.4 两组随访死亡情况

随访 6 个月,观察组与对照组的死亡率分别为 4.0%(1/25)和 20.0%(5/25),观察组的死亡率显著低于对照组(P<0.05)。

表 3 两组治疗后 APACHE II 评分与 MODS 评分对比(分,均数± 标准差)

Table 3 Comparison of the APACHE II score and MODS score between two groups after treatment(score, $\bar{x} \pm s$)

Groups	Cases(n)	APACHE II score	MODS score
Control group	25	22.33± 2.49	6.42± 1.98
Observation group	25	62.19± 7.45	7.29± 1.67
P		<0.05	<0.05

表 4 两组治疗前后血清 IL-6 与 TNF-α 含量变化对比(ng/ml,均数± 标准差)

Table 4 Comparison of the serum IL-6 and TNF-α content between two groups before and after treatment(ng/mL, $\bar{x} \pm s$)

Groups	Cases(n)	IL-6		P	TNF-α		P
		Before treatment	After treatment		Before treatment	After treatment	
Control group	25	12.93± 2.19	5.38± 1.98	<0.05	176.20± 22.84	89.02± 19.48	<0.05
Observation group	25	12.88± 1.94	8.22± 2.04	<0.05	174.20± 19.49	122.49± 20.11	<0.05
P		>0.05	<0.05		>0.05	<0.05	

3 讨论

MODS 是由于严重休克、感染或大手术后等原发病发生 24 小时后,患者机体同时或序贯的发生 2 个或以上器官或系统功能障碍的一种临床综合征,具有高动力型循环、高代谢、来势凶猛、死亡率高等特点,是危重患者死亡的主要原因之一^[15,16]。现代研究对于 MODS 提出的假说包括胃肠道假说、炎症失控假说、缺血-再灌注损伤假说、内毒素假说等^[17,18]。MODS 早期为全身炎症反应综合征,是一种常见的临床综合征,是机体对非感染或感染性致病因素的过度反应状态,而阻断或中和某种炎症介质的方法不能达到理想的治疗效果。连续血液净化是一种体外循环血液的净化方法,具有清除机体内过多水分、代谢废物作用,还可清除炎性介质、调节体内的免疫内稳定,可作为多器官功能支持的方法用于治疗 MODS。

CVVHDF 目前在重症医学领域应用越来越多,具有保护心肌和改善氧合的作用^[9]。有研究显示 CVVHDF 治疗 ARDS 时能有效降低动物气道峰压、提高动脉血氧分压、改善肺顺应性^[20]。本研究结果显示 CVVHDF 辅助治疗的患者 ICU 停留时间和呼吸机辅助时间均短于常规治疗的患者,其 APACHE II 评分与 MODS 评分分别为 22.33± 2.49 分和 6.42± 1.98 分,均较常规治疗的患者模型降低,表明 CVVHDF 能促进 MODS 患者康复,缩短 ICU 停留时间和呼吸机辅助时间。

MODS 可激活单核-巨噬系统等炎症细胞,启动机体的防御反应系统,释放一些列炎性细胞因子和炎症介质,启诱导炎症级联反应,导致全身性炎症反应^[21-23]。MODS 早期为致炎因子释放如 IL-6 与 TNF-α 等,通过瀑布式放大反应导致促炎症因子的泛滥^[24,25]。大多数炎症因子相对分子质量较大,为 6000~60000,甚至超过过滤过膜孔径,其与蛋白结合或以多具体形式存在于血液中,因此吸附方法称为炎症介质的一种主要清除方式。CVVHDF 可以非选择性地清除循环中大量可溶性的炎性介质,重建机体免疫内稳态,削弱或延缓疾病的病程。

目前,MODS 的病死率高达 40%左右^[27,28]。本研究随访 6 个月,观察组与对照组的死亡率分别为 4.0%(1/25) 和 20.0%(5/25),观察组的死亡率低于对照组(P<0.05),与 Liu F 等研究相似。从机制上分析,CVVHDF 使用生物相容性好、高通透性滤

器,有利于提高末梢血管阻力,稳定血压,更符合人体生理状态,对细胞因子的清除率明显增加,为营养及代谢支持创造条件,从而改善了组织的氧利用,提高患者的生存率^[29,30]。

总之,CVVHDF 治疗 MODS 患者有助于清除炎症因子,促进患者的康复,缩短 ICU 停留时间和呼吸机辅助时间,降低患者的死亡率。

参考文献(References)

- [1] Zhu Y, Cui Y, Zhang YC, et al. Efficacy of continuous blood purification in treatment of severe acute pancreatitis in children [J]. Chinese Journal of Pediatrics, 2017, 55(5): 338-342
- [2] Xu YP, Sui XL, Zhang AS, et al. Monocytes, endoplasmic reticulum stress and metabolomics in dogs with multiple organ dysfunction syndrome treated by continuous venovenous hemodiafiltration [J]. Oncotarget, 2017, 8(21): 34992-35008
- [3] Li M, Wang Z, Wang Y, et al. Part of plasmapheresis with plasma filtration adsorption combined with continuous hemodiafiltration in the treatment of severe acute liver failure [J]. Exp Ther Med, 2016, 12(4): 2582-2584
- [4] Fischler R, Meert AP, Sculier JP, et al. Continuous Renal Replacement Therapy for Acute Renal Failure in Patients with Cancer: A Well-Tolerated Adjunct Treatment [J]. Front Med (Lausanne), 2016, 3(3): 33
- [5] Yuan H, Chen S, Hu F, et al. Efficacy of Two Combinations of Blood Purification Techniques for the Treatment of Multiple Organ Failure Induced by Wasp Stings [J]. Blood Purif, 2016, 42(1): 49-55
- [6] Uldemolins M, Martin-Loeches I, Llauro-dó-Serra M, et al. Piperacillin population pharmacokinetics in critically ill patients with multiple organ dysfunction syndrome receiving continuous venovenous haemodiafiltration: effect of type of dialysis membrane on dosing requirements [J]. J Antimicrob Chemother, 2016, 71(6): 1651-1659
- [7] Şık G, Çıtak A. Fatal paraphenylenediamine poisoning due to black henna [J]. Turk J Pediatr, 2016, 58(3): 301-304
- [8] Kara OD, Dincel N, Kaplan Bulut I, et al. Success of continuous veno-venous hemodiafiltration treatment in children monitored in the intensive care units [J]. Ren Fail, 2014, 36(9): 1411-1415
- [9] Li MQ, Ti JX, Zhu YH, et al. Combined use of non-biological artificial liver treatments for patients with acute liver failure complicated by

- multiple organ dysfunction syndrome [J]. *World J Emerg Med*, 2014, 5(3): 214-217
- [10] Xu C, Fan K, Xie L, et al. Evaluation of optimized continuous venovenous hemodiafiltration therapy efficiency in severe burn patients with sepsis[J]. *Burns Trauma*, 2014, 2(3): 125-129
- [11] Li MQ, Li JQ, Shi ZX, et al. Efficacy of various combined blood purification techniques for treating patients with non-viral acute liver failure[J]. *Cell Biochem Biophys*, 2014, 68(3): 571-575
- [12] Eremenko AA, Pavlov MV, Kolpakov PE, et al. The influence of continuous veno-venous haemodiafiltration start time on multiple organ dysfunction syndrome treatment results in cardiac surgery patients [J]. *Anesteziol Reanimatol*, 2013, 8(2): 63-66
- [13] Raj VM, Alladin A, Pfeiffer B, et al. Therapeutic plasma exchange in the treatment of exertional heat stroke and multiorgan failure[J]. *Pediatr Nephrol*, 2013, 28(6): 971-974
- [14] Chen J, Liu J, Yu C, et al. Continuous veno-venous hemodiafiltration alleviates multiple organ dysfunction syndrome in dogs [J]. *Immunopharmacol Immunotoxicol*, 2012, 34(6): 1001-1009
- [15] Masui-Ito A, Okamoto R, Ikejiri K, et al. Tocilizumab for uncontrollable systemic inflammatory response syndrome complicating adult-onset Still disease: Case report and review of literature [J]. *Medicine (Baltimore)*, 2017, 96(29): e7596
- [16] Hazeldine J, Naumann DN, Toman E, et al. Prehospital immune responses and development of multiple organ dysfunction syndrome following traumatic injury: A prospective cohort study[J]. *PLoS Med*, 2017, 14(7): e1002338
- [17] Cabrera CP, Manson J, Shepherd JM, et al. Signatures of inflammation and impending multiple organ dysfunction in the hyperacute phase of trauma: A prospective cohort study [J]. *PLoS Med*, 2017, 14(7): e1002352
- [18] Wan J, He W, Zhu Y, et al. Stratified analysis and clinical significance of elevated serum triglyceride levels in early acute pancreatitis: a retrospective study[J]. *Lipids Health Dis*, 2017, 16(1): 124
- [19] Veach RA, Liu Y, Zienkiewicz J, et al. Survival, bacterial clearance and thrombocytopenia are improved in polymicrobial sepsis by targeting nuclear transport shuttles[J]. *PLoS One*, 2017, 12(6): e0179468
- [20] Matsushita Y, Ishigami M, Matsubara K, et al. Multifaceted therapeutic benefits of factors derived from stem cells from human exfoliated deciduous teeth for acute liver failure in rats [J]. *J Tissue Eng Regen Med*, 2017, 11(6): 1888-1896
- [21] Ning Y, Kim JK, Min HK, et al. Cholesterol metabolites alleviate injured liver function and decrease mortality in an LPS-induced mouse model[J]. *Metabolism*, 2017, 1(71): 83-93
- [22] Huang HC, Tsai HJ, Wang CC, et al. Levosimendan mitigates coagulopathy and organ dysfunction in rats with endotoxemia [J]. *J Chin Med Assoc*, 2017, 80(7): 432-441
- [23] Zharkova O, Celhar T, Cravens PD, et al. Pathways leading to an immunological disease: systemic lupus erythematosus[J]. *Rheumatology (Oxford)*, 2017, 56(suppl_1): i55-i66
- [24] José FF, Kerbauy LN, Perini GF, et al. A life-threatening case of TAFRO syndrome with dramatic response to tocilizumab, rituximab, and pulse steroids: The first case report in Latin America[J]. *Medicine (Baltimore)*, 2017, 96(13): e6271
- [25] Qian C, Ren Y, Xia Y. Sodium tanshinone IIA sulfonate attenuates hemorrhagic shock-induced organ damages by nuclear factor-kappa B pathway[J]. *J Surg Res*, 2017, 3(209): 145-152
- [26] Sauaia A, Moore FA, Moore EE. Postinjury Inflammation and Organ Dysfunction[J]. *Crit Care Clin*, 2017, 33(1): 167-191
- [27] Yang PC, Ho CM, Hu RH, et al. Prophylactic liver transplantation for high-risk recurrent hepatocellular carcinoma [J]. *World J Hepatol*, 2016, 8(31): 1309-1317
- [28] Wada T, Gando S, Ono Y, et al. Disseminated intravascular coagulation with the fibrinolytic phenotype predicts the outcome of patients with out-of-hospital cardiac arrest[J]. *Thromb J*, 2016, 21(14): 43
- [29] Liu F, Wang HM, Wang T, et al. The efficacy of thymosin $\alpha 1$ as immunomodulatory treatment for sepsis: a systematic review of randomized controlled trials[J]. *BMC Infect Dis*, 2016, 15(16): 488
- [30] Martínez ML, Ferrer R, Torrents E, et al. Impact of Source Control in Patients With Severe Sepsis and Septic Shock[J]. *Crit Care Med*, 2017, 45(1): 11-19