

## • 论著 •

# 不同血液净化方式治疗多器官功能障碍综合征的临床疗效比较

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**【摘要】目的** 比较连续性静脉-静脉血液滤过(CVVH)和连续性静脉-静脉血液透析滤过(CVVHDF)两种不同净化方式对多器官功能障碍综合征(MODS)患者临床疗效的差异。**方法** 采用前瞻性观察性研究方法,选择2013年9月至2016年12月遵义医学院附属医院重症医学科收治的MODS患者70例,按治疗方法不同将患者分为两组,每组35例。CVVH组置换液及透析液流速均为1800 mL/h, CVVHDF组置换液和透析液流速均为2000 mL/h,两组血流速度均为150~180 mL/min。比较两组治疗前和治疗后24、48、72 h血肌酐(SCr)、尿素氮(BUN)、pH值、碳酸氢根( $\text{HCO}_3^-$ )、辅助性T细胞(Th1、Th2)和Th1/2比值的差异。**结果** 随时间延长,两组治疗后SCr、BUN均较治疗前降低,治疗后72 h达最低,且CVVHDF组治疗后的变化程度较CVVH组更显著[SCr( $\mu\text{mol/L}$ ):  $150.62 \pm 32.09$  比  $177.47 \pm 31.41$ , BUN( $\text{mmol/L}$ ):  $7.31 \pm 2.19$  比  $9.06 \pm 2.36$ , 均  $P < 0.05$ ],两组治疗后pH值、 $\text{HCO}_3^-$ 呈先升高后降低的趋势,治疗后48 h达峰值,与治疗前比较差异有统计学意义[CVVH组:pH值为 $7.42 \pm 0.08$ 比 $7.25 \pm 0.10$ ,  $\text{HCO}_3^-$ ( $\text{mmol/L}$ )为 $22.49 \pm 5.11$ 比 $15.65 \pm 4.16$ ;CVVHDF组:pH值为 $7.41 \pm 0.04$ 比 $7.24 \pm 0.11$ ,  $\text{HCO}_3^-$ ( $\text{mmol/L}$ )为 $23.24 \pm 4.78$ 比 $15.65 \pm 4.16$ , 均  $P < 0.05$ ]。治疗后72 h又有所降低(CVVH组:pH值、 $\text{HCO}_3^-$ 分别为 $7.37 \pm 0.07$ 、 $22.35 \pm 4.91$ , CVVHDF组pH值、 $\text{HCO}_3^-$ 分别为 $7.38 \pm 0.06$ 、 $22.53 \pm 4.58$ ),但仍明显高于治疗前,两组间各时间点比较差异均无统计学意义(均  $P > 0.05$ )。随治疗时间延长,两组治疗后Th1、Th1/2均逐渐升高,于治疗后72 h达高峰;Th2呈逐渐降低趋势,于治疗后72 h达最低,且治疗后CVVHDF组的变化较CVVH组更显著[Th1( $\times 10^{-2}$ ):  $1.51 \pm 0.12$ 比 $1.21 \pm 0.11$ , Th2( $\times 10^{-2}$ ):  $1.61 \pm 0.62$ 比 $1.70 \pm 0.18$ , Th1/2:  $0.91 \pm 0.14$ 比 $0.71 \pm 0.15$ , 均  $P < 0.05$ ]。**结论** CVVHDF和CVVH均能有效清除MODS患者体内的炎症介质和代谢产物,调整酸碱平衡并调节免疫功能,且CVVHDF较CVVH更为有效。

**【关键词】** 连续性静脉-静脉血液滤过; 连续性静脉-静脉血液透析滤过; 多器官功能障碍综合征

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**Comparison of therapeutic effects between different blood purification therapies for treatment of patients with multiple organ dysfunction syndrome Liu Anping, Yang Qian, Ye Peng, Yu Anyong, Xiao Xue**

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**【Abstract】Objective** To compare the clinical therapeutic effects of continuous veno-venous hemofiltration (CVVH) and continuous veno-venous hemodiafiltration (CVVHDF) for treatment of patients with multiple organ dysfunction syndrome (MODS). **Methods** A prospective observation was conducted, seventy patients with MODS admitted to the Department of Critical Care Medicine of the Affiliated Hospital of Zunyi Medical College from September 2013 to December 2016 were enrolled, and they were divided into a CVVH group and a CVVHDF group according to different treatment, 35 cases in each group. In the CVVH group, the ultrafiltration fluid flow rate was set at 1800 mL/h, while in the CVVHDF group, the flow rate was set at 2000 mL/h for both substitution fluid and dialysate, and the blood flow of the two groups was 150–180 mL/min. The changes of creatinine (SCr), urea nitrogen (BUN), pH value,  $\text{HCO}_3^-$ , helper T cell (Th1, Th2) and Th1/Th2 ratio were compared between the two groups before and after treatment for 24, 48 and 72 hours. **Results** With the extension of time, SCr, BUN were reduced in both groups after treatment compared to those before treatment, 72 hours after treatment they reached the lowest value, and the degree of change in CVVHDF group was more significant than that in CVVH group [SCr ( $\mu\text{mol/L}$ ):  $150.62 \pm 32.09$  vs.  $180.41 \pm 30.52$ , BUN ( $\text{mmol/L}$ ):  $7.31 \pm 2.19$  vs.  $9.06 \pm 2.36$ , all  $P < 0.05$ ], after treatment; the pH value,  $\text{HCO}_3^-$  level in the two groups had a tendency at first elevated and then lowered, 48 hours after treatment they reached the peak values, compared with those before treatment, the differences were statistically significant [CVVH group: the pH value  $7.42 \pm 0.08$  vs.  $7.25 \pm 0.10$ ,  $\text{HCO}_3^-$  ( $\text{mmol/L}$ ) was  $22.49 \pm 5.11$  vs.  $15.65 \pm 4.16$ ; CVVHDF group: pH value  $7.41 \pm 0.04$  vs.  $7.24 \pm 0.11$ ,  $\text{HCO}_3^-$  ( $\text{mmol/L}$ )  $23.24 \pm 4.78$  vs.  $15.65 \pm 4.16$ , all  $P < 0.05$ ], 72 hours after treatment, they began reduced (CVVH group: pH value,  $\text{HCO}_3^-$  were  $7.39 \pm 0.09$ ,  $22.35 \pm 4.91$  respectively, CVVHDF group: pH value,  $\text{HCO}_3^-$  were  $7.38 \pm 0.06$ ,  $23.13 \pm 4.61$  respectively), but they were still significantly higher than those before treatment, and at each time point compared between the two groups, no statistical significant difference was seen (all  $P > 0.05$ ). With the extension of therapeutic time, Th1, Th1/Th2 in two groups were gradually elevated after treatment, and 72 hours after treatment they reached the peak values; Th2 showed a trend of gradual decrease and after 72 hours of treatment it reached the lowest value, and the changes in CVVHDF group were more significant than those in CVVH group [Th1 ( $\times 10^{-2}$ ):  $1.51 \pm 0.12$  vs.  $1.21 \pm 0.11$ ,

Th2 ( $\times 10^{-2}$ ):  $1.64 \pm 0.65$  vs.  $1.70 \pm 0.18$ , Th1/Th2:  $0.91 \pm 0.14$  vs.  $0.71 \pm 0.15$ , all  $P < 0.05$ ]. **Conclusion** Both CVVH and CVVHDF can effectively remove inflammatory mediators and metabolic products, adjust the balance of acid and base, regulate immune system in the body of patients with MODS, and the CVVHDF is more effective than CVVH.

**【Key words】** Continuous veno–venous hemofiltration; Continuous veno–venous hemodiafiltration; Multiple organ dysfunction syndrome

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多器官功能障碍综合征(MODS)是指机体遭受外界因素如严重创伤、休克、中毒、感染等打击24 h后同时或序贯出现两个或两个以上系统或器官功能障碍或衰竭的临床综合征<sup>[1]</sup>。机体遭受感染、创伤等刺激后,不仅释放炎症介质引起全身炎症反应综合征(SIRS),同时释放大量抗炎介质导致代偿性抗炎反应综合征(CARS),如不及时控制,病情恶化,最终导致MODS<sup>[2]</sup>。目前,MODS治疗效果不佳,病死率仍高达40%<sup>[3-4]</sup>。研究证实,SIRS/CARS失衡是导致MODS的重要因素<sup>[5]</sup>,辅助性T细胞1/2(Th1/2)参与机体免疫调节,Th1/2平衡可反映SIRS/CARS是否平衡,是判断机体炎症反应程度的重要指标之一<sup>[6]</sup>。连续性血液净化(CBP)是救治MODS的重要方法之一,可清除机体内炎症介质和内毒素,控制氮质血症,纠正酸碱平衡失调及维持水和电解质稳定,改善患者预后。曾有文献报道,CBP治疗能改善MODS患者Th1/2比值,使细胞免疫功能恢复<sup>[7]</sup>。本研究2013年9月至2016年12月对遵义医学附属医院70例MODS患者分别采用连续性静脉-静脉血液滤过(CVVH)和连续性静脉-静脉血液透析滤过(CVVHDF)治疗,比较两种血液净化方式治疗前后血生化指标、血气分析指标、细胞因子的变化,观察两种不同血液净化方式对MODS患者的疗效。

## 1 资料与方法

**1.1 研究对象的选择:**采用前瞻性观察性研究方法,选择2013年9月至2016年12月本院重症医学科收治的MODS患者70例,诊断均符合MODS标准<sup>[8]</sup>。患者中男性38例,女性32例;年龄18~65岁,平均( $47.7 \pm 9.4$ )岁。

**1.2 伦理学:**本研究符合医学伦理学标准,并经遵义医学院附属医院伦理委员会批准,所有治疗和检测方法均取得患者或家属知情同意。

**1.3 研究分组:**将患者按治疗方法不同分为CVVH组和CVVHDF组,每组35例。70例MODS患者性别、年龄、不同病因患者数、不同器官功能障碍患者数等一般资料在CVVH组和CVVHDF组间比较差异均无统计学意义(均 $P > 0.05$ ;表1),说明两组资料均衡,在可比性。

表1 70例MODS患者治疗前临床资料在CVVH组和CVVHDF组间的比较

项目	CVVH组(35例)	CVVHDF组(35例)
年龄(岁, $\bar{x} \pm s$ )	47.1 ± 9.6	48.3 ± 9.1
性别(例)		
男性	20	18
女性	15	17
病因分类(例)		
感染性休克	13	14
心肺复苏术后	4	5
重症胰腺炎	8	7
多发性创伤	7	7
肠梗阻	3	2
器官功能障碍数(例)		
5个	4	5
4个	6	7
3个	20	18
2个	5	5

**1.4 治疗方法:**采用瑞士金宝PRISMA-FLEX智能化床旁血液净化仪和M100滤器(AN69膜,面积 $1.2 \text{ m}^2$ )进行血液净化,股静脉留置双腔导管作为血管通路。置换液和透析液均采用统一配方,根据患者病情及时调整血糖及电解质浓度,采用低分子肝素钙抗凝,治疗过程中每8~12 h更换滤器管路一套。CVVH组置换液及透析液流速均为1800 mL/h, CVVHDF组置换液及透析液流速均为2000 mL/h,两组血流速度均为150~180 mL/min。

## 1.5 观察指标及方法

**1.5.1 两组肾功能指标测定:**于血液净化治疗前和治疗后24、48、72 h取两组患者静脉血,采用日本Beckman Coulter K.K公司生产的全自动生化分析仪(商品名:AU5800系列)检测血肌酐(SCr)、尿素氮(BUN)水平。

**1.5.2 两组pH值、碳酸氢根( $\text{HCO}_3^-$ )水平测定:**于血液净化治疗前和治疗后24、48、72 h取两组患者动脉血,采用丹麦雷度ABL800血气分析仪检测pH值、 $\text{HCO}_3^-$ 水平。

**1.5.3 两组免疫功能指标测定:**于血液净化治疗前和治疗后24、48、72 h取两组患者静脉血4 mL经单个核细胞分离、丙二醇甲醚酯酸酯(PMA)及蛋白转运抑制剂(BFA)刺激、二氧化碳( $\text{CO}_2$ )孵箱培养4~6 h,加入CD3、CD8、 $\gamma$ 干扰素(IFN- $\gamma$ )、白细

表2 两组治疗前后肾功能指标及pH值、 $\text{HCO}_3^-$ 水平比较( $\bar{x} \pm s$ )

组别	时间	例数(例)	SCr(μmol/L)	BUN(mmol/L)	pH值	$\text{HCO}_3^-$ (mmol/L)
CVVH组	治疗前	35	347.24±33.25	21.21±2.59	7.25±0.10	15.65±4.16
	治疗后24 h	35	258.15±34.59 <sup>a</sup>	15.42±2.40 <sup>a</sup>	7.36±0.06 <sup>a</sup>	19.32±4.34 <sup>a</sup>
	治疗后48 h	35	239.47±32.38 <sup>a</sup>	11.65±2.28 <sup>a</sup>	7.42±0.08 <sup>a</sup>	22.49±5.11 <sup>a</sup>
	治疗后72 h	35	177.47±31.41 <sup>a</sup>	9.06±2.36 <sup>a</sup>	7.37±0.07 <sup>a</sup>	22.35±4.91 <sup>a</sup>
CVVHDF组	治疗前	35	350.28±35.30	22.34±2.38	7.24±0.11	15.08±4.29
	治疗后24 h	35	200.71±33.28 <sup>ab</sup>	12.05±2.41 <sup>ab</sup>	7.37±0.17 <sup>a</sup>	20.58±4.37 <sup>a</sup>
	治疗后48 h	35	179.52±34.43 <sup>ab</sup>	9.88±2.48 <sup>ab</sup>	7.41±0.04 <sup>a</sup>	22.36±4.60 <sup>a</sup>
	治疗后72 h	35	150.62±32.09 <sup>ab</sup>	7.31±2.19 <sup>ab</sup>	7.38±0.06 <sup>a</sup>	22.53±4.58 <sup>a</sup>

注:与治疗前比较,<sup>a</sup>P<0.05;与CVVH组比较,<sup>b</sup>P<0.05

胞介素-4(IL-4)等抗体(均购自美国Cahag公司)进行细胞内外荧光染色处理后,采用流式细胞仪(美国BD公司生产)检测淋巴细胞中Th1、Th2和Th1/2比值。

**1.6 统计学分析:**使用SPSS 18.0统计软件处理数据,正态分布的计量资料以均数±标准差( $\bar{x} \pm s$ )表示,采用t检验,各时间点比较采用重复测量分析;计数资料以例表示,采用 $\chi^2$ 检验, $P<0.05$ 为差异有统计学意义。

## 2 结果

**2.1 两组治疗前后肾功能指标比较(表2):**随时间延长,两组治疗后SCr、BUN均较治疗前降低,治疗后72 h达最低,且CVVHDF组治疗后的变化程度较CVVH组更显著(均 $P<0.05$ )。

**2.2 两组治疗前后pH值、 $\text{HCO}_3^-$ 水平比较(表2):**两组治疗后pH值、 $\text{HCO}_3^-$ 呈先升高后降低的趋势,治疗后48 h达峰值,治疗后72 h又有所降低,但仍明显高于治疗前,两组间各时间点比较差异均无统计学意义(均 $P>0.05$ )。

**2.3 两组治疗前后免疫功能指标比较(表3):**随时间延长,两组治疗后Th1、Th1/2均逐渐升高,于治疗后72 h达高峰, Th2呈逐渐降低趋势,于治疗后72 h达最低,且CVVHDF组的变化较CVVH组治疗后更显著(均 $P<0.05$ )。

表3 两组治疗前后免疫功能指标比较( $\bar{x} \pm s$ )

组别	时间	例数 (例)	Th1		Th1/2
			( $\times 10^{-2}$ )	( $\times 10^{-2}$ )	
CVVH组	治疗前	35	0.62±0.16	2.57±0.33	0.24±0.03
	治疗后24 h	35	0.85±0.19 <sup>a</sup>	2.27±0.30 <sup>a</sup>	0.37±0.09 <sup>a</sup>
	治疗后48 h	35	1.15±0.17 <sup>a</sup>	1.89±0.19 <sup>a</sup>	0.61±0.11 <sup>a</sup>
	治疗后72 h	35	1.21±0.11 <sup>a</sup>	1.70±0.18 <sup>a</sup>	0.71±0.15 <sup>a</sup>
CVVHDF组	治疗前	35	0.60±0.22	2.59±0.38	0.23±0.05
	治疗后24 h	35	0.89±0.11 <sup>ab</sup>	2.28±0.31 <sup>ab</sup>	0.39±0.12 <sup>ab</sup>
	治疗后48 h	35	1.34±0.15 <sup>ab</sup>	1.78±0.14 <sup>ab</sup>	0.75±0.08 <sup>ab</sup>
	治疗后72 h	35	1.51±0.12 <sup>ab</sup>	1.61±0.52 <sup>ab</sup>	0.91±0.14 <sup>ab</sup>

注:与治疗前比较,<sup>a</sup>P<0.05;与CVVH组比较,<sup>b</sup>P<0.05

## 3 讨论

MODS病因多,发病机制复杂,机体在炎症、内毒素、缺血/再灌注(I/R)损伤等刺激下出现的SIRS/CARS失衡是其主要发病机制<sup>[9]</sup>。其中全身炎症介质失控性释放已成为大多数人的观点<sup>[10-11]</sup>,

无论是炎症介质释放过多引起的免疫亢进,还是抗炎介质的释放过多引起的免疫抑制,都会引起SIRS/CARS失衡,最终发展为MODS。研究证实, Th1、Th2参与机体免疫调节, Th1/2保持动态平衡,当机体遭受感染、创伤及中毒等因素刺激时,体内Th1/2平衡被打破,从而出现Th1分化减少或Th2分化增多的不稳定状态,是机体发生MODS的重要环节<sup>[12]</sup>; Th1/2失衡是判断机体炎症反应程度的重要指标之一,且可判断SIRS/CARS失衡的方向,因此调节Th1/2平衡对MODS的免疫调控有重要意义。

CBP已由原来意义的肾脏替代演变成具有多种功能的器官支持系统<sup>[13]</sup>。现已将该技术广泛应用于临床各种危重症中,以清除患者体内过多的炎症介质、细胞因子、内毒素等从而发挥重要的作用<sup>[14-15]</sup>。目前临床最常用的CBP方法有CVVH、CVVHDF、高容量血液滤过(HVHF)等。CVVH以对流的方式滤过清除血液中的水分和中大分子炎症介质,早期应用可减轻患者病情,改善MODS患者血液生化指标,维持水和电解质及内环境稳定、改善预后<sup>[16-20]</sup>。CVVHDF是在CVVH基础上进行的透析,弥补了CVVH对小分子溶质清除不足的缺点,增加了氮质等的清除率,通过连续缓慢对流和弥散来清除过量促炎和抗炎细胞因子,以维持免疫平衡<sup>[21]</sup>。李勇等<sup>[22]</sup>曾采用HVHF和CVVHDF两种不同CBP治疗脓毒症,发现两者均能清除体内炎症介质,而HVHF较CVVHDF更有效。

本研究表明,两组治疗后SCr、BUN均较治疗前明显降低,pH值、 $\text{HCO}_3^-$ 与治疗前比较均呈先升高后降低的趋势,但两组间比较差异均无统计学意义,说明两种CBP方式在清除体内小分子物质和维持酸碱平衡等方面均能发挥有效作用,CVVHDF是在滤过基础上加用了透析技术,对氮质及SCr等小分子物质的清除效果更好,如MODS患者合并肾脏功能较差时,采用CVVHDF患者获益更大;两组治疗后Th1、Th1/2均较治疗前明显升高,Th2较治疗前明显

降低,提示CVVH、CVVHDF均能清除MODS患者体内的炎症因子,阻断Th1向Th2的漂移,调节Th1/2平衡,改善SIRS/CARS失衡,从而提高机体的细胞免疫功能,改善MODS病情;治疗后48 h Th1上升和Th2下降幅度以CVVHDF组更明显,提示CVVHDF能更好地清除患者体内炎症介质。在调节酸碱平衡、维持水和电解质稳定方面两者疗效相当。

本研究证实,CBP是治疗MODS的有效方式之一,可清除机体内炎症介质和内毒素以及控制氮质血症,纠正酸碱平衡失调,维持水和电解质稳定;而CVVHDF在清除小分子物质及炎症介质方面较CVVH更为有效。但本研究因样本量小,病种复杂,未进行存活率的比较,因此,CVVHDF与CVVH对存活率的影响还需要进行大样本、多中心的临床研究加以证实。

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