doi: 10.13241/j.cnki.pmb.2019.22.022

持续性血液滤过联合高流量吸氧治疗重症急性呼吸综合征的疗效及对血清炎症因子水平的影响*

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摘要 目的: 探讨持续性血液滤过联合高流量吸氧治疗重症急性呼吸综合征的疗效及对血清炎症因子水平的影响。**方法:** 选择2013年2月至2016年2月我院接诊的60例重症急性呼吸综合征患者,通过随机数表法将其分为观察组(n=30)和对照组(n=30)。观察组采用持续性血液滤过联合高流量吸氧进行治疗,对照组采用持续性血液滤过进行治疗。比较两组临床疗效、治疗前后动脉血氧分压(PaO_2)、动脉血二氧化碳分压($PaCO_2$)、氧合指数、氢离子浓度指数(pH)值、呼吸频率(RR)、心率(HR)、血清C反应蛋白(CRP)、白介素6(IL-6)、白介素8(IL-8)、肿瘤坏死因子α(TNF-α)水平的变化及不良反应的发生情况。**结果:** 治疗后,观察组有效率为76.67%,显著高于对照组(50.00%,$P<0.05$)。两组治疗后PaO_2、$PaCO_2$、氧合指数、pH值、RR、HR均较治疗前明显改善,观察组患者PaO_2、氧合指数明显高于对照组,$PaCO_2$、pH值、RR、HR、血清CRP、IL-6、IL-8及TNF-α水平均显著低于对照组($P<0.05$)。治疗期间,观察组患者不良反应总发生率(10.00%)显著低于对照组(36.67%,$P<0.05$);观察组死亡1例(3.33%),对照组死亡6例(20.00%),观察组病死率显著低于对照组($P<0.05$)。**结论:** 持续性血液滤过联合高流量吸氧治疗重症急性呼吸综合征患者的临床疗效及安全性明显优于单用持续性血液滤过治疗,可能与其更有效减轻炎症反应有关。

关键词: 持续性血液滤过;高流量吸氧;重症急性呼吸综合征;炎症因子

中图分类号: R459.5;R563 **文献标识码:** A **文章编号:** 1673-6273(2019)22-4303-05

Curative Efficacy of Continuous Blood Filtration Combined with High Flow Oxygen Uptake in the Treatment of Severe Acute Respiratory Syndrome and Its Effects on the Serum Inflammatory Factors Levels*

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ABSTRACT Objective: To study the curative efficacy of continuous blood filtration combined with high flow oxygen uptake in the treatment of severe acute respiratory syndrome and its effects on the inflammatory factors. **Methods:** 60 cases of patients with severe acute respiratory syndrome admitted to our hospital from February 2013 to February 2016 were selected and divided into the observation group (n=30) and the control group (n=30) by random number table method. The observation group was treated with continuous hemofiltration combined with high flow oxygen, while the control group was treated with continuous hemofiltration. Clinical efficacy, arterial partial oxygen pressure (PaO_2), arterial partial carbon dioxide pressure ($PaCO_2$), oxygenation index, hydrogen ion concentration index (pH), respiratory rate (RR), heart rate (HR), serum c-reactive protein (CRP), interleukin-6 (il-6), interleukin-8 (il-8), and tumor necrosis factor (TNF-α) were compared between the two groups. **Results:** After treatment, the effective rate of observation group was 76.67%, which was significantly higher than that of the control group (50.00%, $P<0.05$). After treatment, the PaO_2, $PaCO_2$, oxygenation index, pH value, RR and HR in both groups were significantly improved compared with those before treatment. The PaO_2 and oxygenation index in the observation group were significantly higher than those in the control group, and the levels of $PaCO_2$, pH value, RR, HR, serum CRP, IL-6, IL-8 and TNF-α were significantly lower than those in the control group ($P<0.05$). During the treatment, the total incidence of adverse reactions in the observation group (10.00%) was significantly lower than that in the control group (36.67%, $P<0.05$). One case died in the observation group (3.33%), and six cases died in the control group (20.00%). The fatality rate of the observation group was significantly lower than that of the control group ($P<0.05$). **Conclusion:** The clinical efficacy and safety of continuous hemofiltration combined with high-flow oxygen inhalation in the treatment of patients with severe acute respiratory syndrome are significantly better than that of continuous hemofiltration alone, which may be related to the effective reduction of inflammatory reactions.

* 基金项目:陕西省自然科学基金项目(20131067)

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(收稿日期:2019-04-08 接受日期:2019-04-30)

Key words: Continuous blood filtration; High flow oxygen; Severe acute respiratory syndrome; Inflammatory cytokines
Chinese Library Classification(CLC): R459.5; R563 Document code: A
Article ID: 1673-6273(2019)22-4303-05

前言

重症急性呼吸综合征为一种由 SARS 冠状病毒引起的急性呼吸道传染病，主要传播方式为近距离液滴传播或与患者呼吸道分泌物接触[1,2]，具有起病迅速、传染性强等特点，临床表现为发热、乏力、咳嗽、气促等症状[3,4]。SARS 若得不到及时治疗，可导致急性呼吸窘迫综合征、多脏器功能障碍等，严重者甚至会导致患者死亡[5,7]。目前，临床上采用连续性的替代肾脏血液净化，通过具有一定孔径的生物过滤器缓慢、连续地去除体内多余的水，但是单一的持续性血液滤过难以达到预期效果[8-10]。

研究表明高流量吸氧治疗重症急性呼吸综合征有较好的疗效，且治疗更方便、安全[11,12]。高流量吸氧是指在大气压下通过佩戴特殊的吸氧面罩进行吸氧治疗的方法，其吸氧不进入高压仓，为重症急性呼吸综合征辅助治疗提供了新思路[13,14]。本研究旨在探讨持续性血液滤过联合高流量吸氧治疗重症急性呼吸综合征的临床效果及其可能机制，结果现报道如下。

1 资料与方法

1.1 一般资料

选取 2013 年 2 月至 2016 年 2 月我院收治的 60 例重症急性呼吸综合征患者，通过随机数表法将其分为 2 组，每组各 30 例。观察组中，男 17 例，女 13 例；年龄 31~68 岁，平均(47.58± 7.25)岁；对照组中，男 18 例，女 12 例；年龄 32~70 岁，平均(48.11± 6.81)岁。两组患者一般资料比较均无统计学差异(P>0.05)，具有可比性。

纳入标准：① 符合 SARS 的诊断与治疗诊断标准[15]且经影像学检查确诊；② 符合无创通气适应证；③ 无呼吸系统疾病者。排除标准：① 心电图提示严重心律失常、心肌缺血等，或动脉收缩压＜80 mmHg；② 心功能严重不全，或呼吸、心跳停止；③ 自主呼吸停止或十分微弱；④ 意识障碍；⑤ 气道分泌物过多、痰液十分粘稠，难以进行有效咳痰，误吸危险性高；⑥ 合并其余重要器官功能障碍。

1.2 治疗方法

所有患者入院后均给予抗感染、对症治疗等基础治疗。对照组使用日本旭化成医疗设备公司所购买的 ACH-10 型血液滤过机及 PANFLO-APF-10S 型血液滤过器，血流量 120 mL/min，超滤量为 2L/h，每次治疗总量为 16~20L。观察组在对照组的基础上使用经鼻高流量吸氧仪器和鼻塞导管，流量初始设置为 50 L/min，气道湿化温度 37℃。

1.3 观察指标

观察记录患者治疗前后 RR、HR 及血气指标；临床疗效评定标准：治愈：治疗后呼吸平稳，RR 为 15~20 次 /min，胸片显示正常；有效：治疗后呼吸平稳，RR 为 21~28 次 /min，胸片显示原斑片状阴影大部分消失；无效：临床症状无好转甚至加重。治愈 + 显有效 = 总有效率；采用 ELISA 检测血清 IL-6、IL-8 、TNF-α 及 CRP 水平，所有操作均严格按照仪器及试剂盒说明书进行；观察记录患者不良反应发生情况及 28d 病死率。

1.4 统计学分析

以 spss18.0 软件包处理数据，计量资料均为正态分布，以均数± 标准差($\bar{x}\pm s$)表示，组间比较使用独立样本 t 检验，计数资料以率表示，组间比较采用 x^2 检验，以 P＜0.05 表示差异具有统计学意义。

2 结果

2.1 两组患者疗效比较

治疗后，两组总有效率分别为 76.67%、50.00%，观察组显著高于对照组(P<0.05)，详见表 1。

表 1 两组患者疗效比较[例(%)]

Table 1 Comparison of the clinical efficacy between the two groups[n(%)]

Groups	n	Effective	Valid	Invalid	Total effective rate
Observation group	30	12(40.00)	11(36.67)	7(23.33)	23(76.67)
Control group	30	7(23.33)	8(26.67)	15(50.00)	15(50.00)
u/x^2 value			u=2.032		4.593
P value			0.042		0.032

2.2 两组患者治疗前后血气指标的比较

治疗后，两组治疗后 PaO_2、$PaCO_2$、氧合指数、pH 值、RR、HR 均较治疗前明显改善，观察组患者 PaO_2、氧合指数明显高于对照组，$PaCO_2$、pH 值均低于对照组(P<0.05)，详见表 2。

2.3 两组患者治疗前后 RR 及 HR 的比较

治疗后，观察组患者 RR、HR 较对照组降低更显著(P<0.05)，详见表 3。

2.4 两组患者治疗前后血清炎症因子水平的比较

治疗后，两组患者血清 CRP、IL-6、IL-8 及 TNF-α 水平均显著治疗前，且观察组以上指标均明显低于对照组(P<0.05)，详见表 4。

2.5 两组患者不良反应发生情况的比较

两组患者不良反应总发生率分别为 10.00%、36.67%，观察组显著低于对照组(P<0.05)，详见表 5。

2.6 两组患者预后情况的比较

观察组死亡 1 例(3.33%)，对照组死亡 6 例(20.00%)，观察

组病死率显著低于对照组(P=0.044)。

表 2 两组患者治疗前后血气指标的比较($\bar{x}\pm s$)

Table 2 Comparison of the blood gas indexes between the two groups before and after treatment($\bar{x}\pm s$)

Groups	n	PaO_2(mmHg)		$PaCO_2$(mmHg)		Oxygenation index (mmHg)		pH	
		Before the treatment	After treatment	Before the treatment	After treatment	Before the treatment	After treatment	Before the treatment	After treatment
Observation group	30	55.28± 3.79	95.91± 5.72	30.05± 1.83	35.89± 3.42	196.04± 24.78	349.16± 46.75	7.42± 0.08	7.02± 0.11
Control group	30	55.34± 3.76	82.49± 6.38	30.11± 1.81	42.18± 3.71	195.79± 25.16	279.42± 43.12	7.41± 0.11	7.38± 0.13
t value		0.062	8.578	0.128	6.828	0.039	6.006	0.403	11.579
P value		0.951	0.000	0.899	0.000	0.969	0.000	0.689	0.000

表 3 两组患者治疗前后 RR 及 HR 的比较($\bar{x}\pm s$,次 /min)

Table 3 Comparison of the RR and HR between the two groups before and after treatment($\bar{x}\pm s$, Times/min)

Groups	n	RR		HR	
		Before the treatment	After treatment	Before the treatment	After treatment
Observation group	30	26.52± 3.34	19.52± 2.03	101.96± 9.89	80.17± 9.02
Control group	30	26.57± 3.29	23.57± 3.41	101.53± 10.04	95.28± 12.24
t value		0.058	5.590	0.167	5.443
P value		0.954	0.000	0.868	0.000

表 4 两组患者治疗前后血清炎症因子水平的比较($\bar{x}\pm s$)

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

Groups	n	CRP(mg/L)		IL-6(ng/L)		IL-8(ng/L)		TNF-α(ng/L)	
		Before the treatment	After the treatmen	Before the treatment	After the treatment	Before the treatment	After the treatment	Before the treatment	After the treatmen
Observation group	30	38.08± 12.36	10.15± 6.46	26.03± 8.71	10.24± 7.19	19.10± 7.86	9.72± 5.91	19.02± 5.57	7.56± 2.93
Control group	30	37.89± 10.23	20.52± 8.74	25.69± 8.72	17.35± 7.56	18.97± 7.80	16.24± 7.96	19.21± 6.87	12.95± 4.15
t value		0.065	5.226	0.151	3.733	0.064	3.602	0.118	5.811
P value		0.949	0.000	0.880	0.000	0.949	0.001	0.907	0.000

表 5 两组患者不良反应发生情况的比较[例(%)]

Table 5 Comparison of the incidence of adverse reactions between the two groups[n(%)]

Groups	n	Allergy	Drop in blood pressure	shock	The total incidence of
Observation group	30	1(3.33)	1(3.33)	1(3.33)	3(10.00)
Control group	30	2(6.67)	5(16.67)	4(13.33)	11(36.67)
x^2 value		0.351	2.963	1.964	5.963
P value		0.554	0.085	0.161	0.015

3 讨论

重症急性呼吸综合征是一种以变种冠状病毒引起的急性炎症和损伤为特征的新型传染病，发病急且病情严重，其发病机制与炎症因子、如 IL-6、IL-8、TNF-α 等的大量释放密切相关[16-18]。因此，在治疗重症急性呼吸综合征患者时，临床上应注意加强患者的抗炎治疗[19-21]。持续性血液滤过是体外血液过滤模拟体内肾小球和小管的过滤和再吸收，主要是通过一个小型滤器达到模仿肾小球的功能，因为本质为血液滤过，连续进行时比血滤更加高效、阻力更低[22-24]。高流量吸氧是一种新型的无创吸氧疗法，可提供低水平正压通气，打开肺泡，改善通气功能，且具有多种优势，包括提高恒定氧浓度、降低鼻咽部阻力，

提高气道导通性和防御功能、增加肺泡对氧气的吸收等[25,26]。

本研究结果显示使用持续性血液滤过联合高流量吸氧治疗的患者总有效率为 76.67%，明显高于单独使用持续性血液滤过治疗，提示持续性血液滤过联合高流量吸氧治疗重症急性呼吸综合征效果更加显著[27]。分析原因可能是无效上呼吸道的高流量冲洗，减轻呼吸肌肉工作，减轻呼吸综合征症状。高流量吸氧能明显改善患者的血气指标。本研究结果显示使用持续性血液滤过联合高流量吸氧治疗的患者 PaO_2、氧合指数明显高于使用持续性血液滤过的患者，$PaCO_2$、pH 值明显低于使用持续性血液滤过的患者[28]，分析原因是因为高流量吸氧可提高恒定的氧浓度，可产生持续低水平的气道正压，提高呼吸末肺容积，复张塌陷的肺泡，改善肺通气血流比值，从而改善氧合。

研究表明高流量吸氧辅助治疗可通过改善患者的炎症反应提高其临床疗效[29]。本研究也显示持续性血液滤过联合高流量吸氧治疗的患者的 RR、HR 改善程度也均优于单独使用持续性血液滤过的患者。此外，使用持续性血液滤过联合高流量吸氧治疗的患者的 CRP、IL-6、IL-8 及 TNF-α 水平明显低于单独治疗的患者，分析是因为连续血液滤过联合大流量氧气吸入可有效清除血液中的炎性因子，提高患者肺毛细血管通透性。本研究结果还显示联合治疗后患者不良反应的总发生率明显低于单一治疗，提示持续性血液滤过联合高流量吸氧能减少不良反应的发生，安全性更高，这与 Mcritchie D[30]等的研究结果相似。治疗后，持续性血液滤过联合高流量吸氧治疗的患者死亡率为 3.33%，明显低于单纯使用持续性血液滤过治疗患者，可能是因为气道内气体冲刷所产生的呼气末正压较低，可避免肺泡塌陷，提高通气量与血流的比值，对远期预后的改善具有积极作用。

综上所述，持续性血液滤过联合高流量吸氧治疗重症急性呼吸综合征患者的临床疗效及安全性明显优于单用持续性血液滤过治疗，可能与其更有效减轻炎症反应有关。

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