

doi: 10.13241/j.cnki.pmb.2018.08.022

血液透析联合血液灌流治疗对慢性肾衰竭患者肾功能、微炎症状态和血液净化效果的影响*

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摘要 目的:探讨血液透析(HD)联合血液灌流(HP)治疗对慢性肾衰竭(CRF)患者肾功能、微炎症状态和血液净化效果的影响。**方法:**选取2015年3月-2017年3月期间我院收治的CRF患者90例作为研究对象,采用随机数字表法分为对照组(n=45)和研究组(n=45),对照组在常规治疗的基础上给予HD治疗,研究组在对照组治疗的基础上给予HD联合HP治疗,对比两组治疗前后的肾功能、微炎症状态、血液净化效果。**结果:**治疗后研究组肌酐清除率(Ccr)较对照组增加,血尿素氮(BUN)、血肌酐(Cr)较对照组下降(P<0.05)。治疗后研究组白细胞介素(IL-6)、C反应蛋白(CRP)、肿瘤坏死因子- α (TNF- α)水平较对照组下降(P<0.05)。治疗后研究组同型半胱氨酸(Hcy)、甲状旁腺激素(PTH)及 β_2 -微球蛋白(β_2 -MG)水平较对照组下降(P<0.05)。研究组总不良反应发生率为4.44%(2/45),低于对照组的15.56%(7/45)(P<0.05)。**结论:**HD联合HP治疗CRF,能够有效改善患者肾功能和炎症反应,清除肾脏内的有毒物质,从而提升血液净化效果,且安全性较好。

关键词:血液透析;血液灌流;慢性肾衰竭;肾功能;微炎症状态;血液净化

中图分类号:R692.5;R459.5 **文献标识码:**A **文章编号:**1673-6273(2018)08-1511-04

Effect of Hemodialysis Combined with Hemoperfusion on Renal Function, Micro Inflammatory State and Blood Purification Effect in Patients with Chronic Renal Failure*

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ABSTRACT Objective: To investigate the effect of hemodialysis (HD) combined with hemoperfusion (HP) on renal function, micro inflammation state and blood purification in patients with chronic renal failure (CRF). **Methods:** 90 patients with CRF admitted in our hospital from March 2015 to March 2017 were selected as the subjects. They were divided into the control group (n=45) and the study group (n=45) by random number table methods. The control group was treated with HD on the basis of routine treatment. The study group was given HD combined with HP on the basis of treatment in the control group. The renal function, the micro inflammation state and the blood purification effect before and after the treatment were compared. **Results:** After treatment, the creatinine clearance (Ccr) in the study group was increased compared with the control group, the blood urea nitrogen (BUN) and the creatinine (Cr) were lower than those in the control group (P<0.05). After treatment, the levels of interleukin (IL-6), C reactive protein (CRP) and tumor necrosis factor- α (TNF- α) in the study group were lower than those in the control group (P<0.05). After treatment, the levels of homocysteine (Hcy), parathyroid hormone (PTH) and β_2 -microglobulin (β_2 -MG) in the study group were lower than those in the control group (P<0.05). The incidence of total adverse reactions in the study group was 4.44% (2/45), which was lower than 15.56% in the control group (7/45) (P<0.05). **Conclusion:** HD combined with HP in the treatment of CRF can effectively improve the renal function and inflammatory reaction, remove toxic substances in the kidneys, and improve the effect of blood purification, and the safety is good.

Key words: Hemodialysis; Hemoperfusion; Chronic renal failure; Renal function; Micro inflammatory state; Blood purification

Chinese Library Classification(CLC): R692.5; R459.5 **Document code:** A

Article ID: 1673-6273(2018)08-1511-04

前言

慢性肾衰竭(chronic renal failure, CRF)是由多种肾脏病症组成的晚期临床综合征,可导致患者出现贫血、恶心呕吐、口腔溃疡等症状,其显著的特征包括水电解质酸碱失衡、新陈代谢

紊乱及毒素潴留等^[1-3]。CRF病程极长,对患者的生存质量有很大的影响,已然成为威胁公共健康卫生的主要问题^[4]。对于慢性肾衰疾病的治疗,临床往往给予患者血液透析(hemodialysis, HD)治疗。作为CRF患者最为常见的治疗措施,HD是通过半透膜对血液中的代谢废物、多余水分进行清除,以实现酸碱

* 基金项目:陕西省社会发展科技攻关项目(2016SF-239)

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(收稿日期:2017-12-23 接受日期:2018-01-18)

平衡的维持。其治疗方法为经外周血管置管,将体内血液引出体外,经过血液净化装置,再输入体内^[5-7]。已有研究指出 HD 联合血液灌流(hemoperfusion,HP)治疗 CRF 患者能够获得良好的临床疗效,且不良反应少,而 CRF 的发生发展与同型半胱氨酸(homocysteine,Hcy)、甲状旁腺激素(parathyroid hormone,PTH)及 β_2 -微球蛋白(β_2 -microglobulin, β_2 -MG)等指标异常有关,因此,有效控制血液净化指标对于患者病情改善具有重要的临床意义^[8-10]。本次研究选取 2016 年 3 月-2017 年 3 月期间我院收治的 CRF 患者 90 例作为研究对象,通过分析 HD 联合 HP 治疗对 CRF 患者肾功能、微炎症状态和血液净化效果的影响,旨在为临床治疗 CRF 提供参考依据。

1 资料与方法

1.1 一般资料

选取 2016 年 3 月-2017 年 3 月期间我院收治的 CRF 患者 90 例作为研究对象,纳入标准:①所选 CRF 患者参照《内科学》中关于肾衰竭的诊断标准(即血肌酐(creatinine,Cr)水平超过 $130\mu\text{mol/L}$;肌酐清除率(creatinine clearance,Ccr)低于 80mL/min)^[11];②自愿参与研究并签署知情同意书。排除标准:①患有泌尿系统感染者以及既往行透析治疗者;②伴有恶性肿瘤疾病者。采用随机数字表法分为两组,其中对照组及研究组均为 45 例。对照组男性 23 例,女性 22 例;年龄 41-79 岁间,平均(50.34 ± 3.26)岁;病程 1-15 年,平均(7.24 ± 2.25)年。研究组男性 25 例,女性 20 例;年龄 39-78 岁间,平均(50.45 ± 3.43)岁;病程 1-14 年,平均(7.19 ± 2.43)年。两组一般资料经统计检验后显示无统计学差异($P>0.05$)。本研究获得我院伦理委员会的批准。

1.2 方法

给予两组患者调节酸碱平衡、抗感染以及调节电解质、控制血压等对症治疗,均给予优质低蛋白、低磷饮食,补充足量维生素及必需氨基酸。在常规治疗的基础上,对照组患者给予 HD 进行治疗,治疗仪器为透析机(德国费森尤斯,4008B)与空心纤维透析器(德国费森尤斯低通量透析器,FX10),血液量最小为 200mL/min ,最大为 250mL/min ,每次透析时间为 4h,每

周透析 3 次,持续透析 90d。研究组在对照组的基础上给予 HP 治疗,HD 方法与对照组一致,HP 方法为:治疗过程中所选取的仪器为一次性血管灌流器(珠海健帆,HA130 树脂血液灌流器),然后将血流灌流器及透析器进行串联,首进行 2 次灌流,然后再进行 HD,血液量最小为 200mL/min ,最大为 250mL/min ,透析液流量设置为 500mL/min ,每周 HD 治疗 3 次,HD+HP 治疗 1 次,持续治疗 90d。

1.3 观察指标

1.3.1 肾功能指标检测 于治疗前后患者处于早晨空腹状态下取其 5 mL 静脉血作为标本,经 3000 转/min,温度设定 4°C ,离心 10 min 后将血浆和血清分开,检测肾功能变化指标,包括血尿氮(blood urine nitrogen,BUN)、Ccr 与 Cr。

1.3.2 炎症因子检测 炎症因子包括白细胞介素-6(IL-6)、C 反应蛋白(C reactive protein,CRP)、肿瘤坏死因子- α (tumor necrosis factor- α ,TNF- α)等指标。对两组患者治疗前后的清晨空腹静脉血标本进行采集,对其进行离心处理之后将其保存好,采用酶联免疫吸附法进行测定。

1.3.3 血液净化指标检测 采用酶联免疫吸附法检测治疗前后患者 Hcy、PTH 及 β_2 -MG 等指标。

1.3.4 不良反应 观察患者治疗过程中出现的不良反应,包括头晕头痛、皮疹、胃肠道反应等。

1.4 统计学方法

本次研究采用 SPSS19.0 软件进行数据分析,肾功能指标、炎症因子、血液净化指标等计量资料以($\bar{x}\pm s$)表示,两组比较采用 t 检验;性别比例、不良反应率等计数资料以率(%)表示,两组比较采用 χ^2 检验,检验水准为 $\alpha=0.05$ 。

2 结果

2.1 两组肾功能比较

治疗前,两组 BUN、Ccr、Cr 等相关指标比较无统计学差异($P>0.05$)。治疗后,两组 Ccr 较治疗前增加,Cr、BUN 较治疗前下降,且研究组 Ccr 较对照组增加,Cr、BUN 较对照组下降($P<0.05$),见表 1。

表 1 两组治疗前后肾功能指标对比($\bar{x}\pm s$)

Table 1 Comparison of renal function indexes before and after treatment between the two groups($\bar{x}\pm s$)

Groups	Ccr(mL/min)		Cr($\mu\text{mol/L}$)		BUN(mmol/L)	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Control group (n=45)	27.65 $\pm$ 7.15	34.26 $\pm$ 5.98*	835.4 $\pm$ 65.85	366.4 $\pm$ 58.63*	26.14 $\pm$ 6.75	14.74 $\pm$ 4.63*
Study group(n=45)	27.48 $\pm$ 7.01	40.89 $\pm$ 7.24*	826.8 $\pm$ 58.36	327.1 $\pm$ 65.47*	26.38 $\pm$ 7.11	10.42 $\pm$ 4.34*
t	0.093	3.941	0.326	2.448	0.134	5.627
P	0.926	0.000	0.744	0.017	0.893	0.000

Note:Compared with before treatment,* $P<0.05$.

2.2 两组炎症因子比较

治疗前,两组 TNF- α 、IL-6、CRP 水平比较无统计学差异($P>0.05$);治疗后,两组炎症因子均较治疗前下降,且研究组显著低于对照组($P<0.05$),见表 2。

2.3 两组血液净化指标比较

治疗前,两组 Hcy、PTH 及 β_2 -MG 水平比较无统计学差异($P>0.05$);治疗后,两组血液净化指标水平均较治疗前下降,且研究组显著低于对照组($P<0.05$),详细数据见表 3。

表 2 两组治疗前后的炎性指标对比($\bar{x} \pm s$)Table 2 Comparison of inflammatory indicators before and after treatment between the two groups($\bar{x} \pm s$)

Groups	TNF- α (ng/L)		IL-6(ng/L)		CRP(mg/L)	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Control group (n=45)	55.26 $\pm$ 7.28	33.69 $\pm$ 2.25*	187.98 $\pm$ 1.28	154.25 $\pm$ 5.52*	23.69 $\pm$ 2.85	13.96 $\pm$ 3.25*
Study group(n=45)	56.52 $\pm$ 6.28	22.39 $\pm$ 1.85*	188.87 $\pm$ 1.36	120.54 $\pm$ 5.24*	23.96 $\pm$ 3.58	7.79 $\pm$ 2.25*
t	0.987	5.287	1.210	4.987	1.028	5.124
P	0.469	0.000	0.354	0.001	0.410	0.000

Note: Compared with before treatment, *P<0.05.

表 3 两组治疗前后的血液净化指标比较($\bar{x} \pm s$)Table 3 Comparison of blood purification indicators before and after treatment between the two groups($\bar{x} \pm s$)

Groups	Hcy(ng/L)		PTH(ng/L)		β 2-MG(mg/L)	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Control group (n=45)	35.96 $\pm$ 3.28	26.58 $\pm$ 2.85*	61.28 $\pm$ 2.57	34.69 $\pm$ 4.28*	5.98 $\pm$ 0.87	3.36 $\pm$ 0.57*
Study group(n=45)	36.98 $\pm$ 3.58	20.85 $\pm$ 2.74*	60.28 $\pm$ 3.28	21.85 $\pm$ 2.87*	5.87 $\pm$ 0.74	1.85 $\pm$ 0.17*
t	0.879	6.587	1.163	8.541	1.036	10.41
P	0.457	0.000	0.339	0.000	0.524	0.000

Note: Compared with before treatment, *P<0.05.

2.4 两组不良反应比较

另外,治疗过程中研究组出现头晕头痛 1 例,胃肠道反应 1 例,对照组出现头晕头痛 2 例,皮疹 3 例,胃肠道反应 2 例,研究组总不良反应发生率为 4.44%(2/45),低于对照组的 15.56%(7/45),差异有统计学意义(P<0.05)。

3 讨论

CRF 是一种以肾实质损害、肾脏萎缩为主要症状的临床疾病,由于患者在长期患病过程的肾功能会大大降低,导致体内聚集大量的代谢废物、毒素无法正常排除,常存在酸碱失衡、电解质紊乱等现象,会对其他器官功能造成较大的损伤^[12-14]。病情逐渐进展至终末期,代谢产物大量蓄积,水钠潴留,电解质及酸碱平衡紊乱,会对其他器官功能造成损伤,而疾病病程长,则对患者的生活质量造成严重影响^[15,16]。以往临床上常规 HD 治疗的主要原理为弥散,可以有效清除患者体内的小分子物质和部分中分子毒素,成本相对较低,作用效果较为明显,易于被患者所接受,但是在在大分子毒素、脂溶性毒素及炎症介质的清除上存在有较大难度^[17,18]。HP 工作的原理是通过吸附作用清除患者体内的炎症介质、脂溶性毒素,达到清除部分结合性大分子毒素以血液净化的效果。单独 HD 极易导致患者体内积聚大量大分子毒物,极易发生多种不良反应,另外由于体内微生物和内毒素等的刺激而激活单核巨噬细胞系统,导致机体释放促炎症细胞因子,而 HD 联合 HP 治疗,可有效弥补其中不足,可保持体内酸碱平衡,有效将小分子毒素进行清除,控制炎症因子,又能降低不良反应^[19-21]。

本次研究结果显示,治疗前,两组 BUN、Ccr、Cr、TNF- α 、IL-6、CRP 等相关指标对比无明显差异(P>0.05);治疗后,两组

相关指标均得到显著改善,且研究组显著优于对照组(P<0.05)。这提示与单一 HD 相比,联合治疗能够有效弥补 HD 存在的不足,可有效改善患者肾功能和炎症指标,从而改善患者的微炎症状态^[22,23]。CRP 属于急性反应期蛋白,通常将其看作感染的重要衡量指标,其由 IL-6 调节,患者机体创伤越严重,CRP 浓度越高。TNF- α 属于多肽细胞因子,可引起炎症反应,在细菌感染过程中发挥重要作用,可促进 IL-6 的释放,提高血管的通透性^[24-26]。治疗前,两组 Hcy、PTH 及 β 2-MG 水平比较无明显差异(P>0.05);治疗后,两组相关指标都发生显著改善,且研究组显著优于对照组(P<0.05),研究组总不良反应发生率为 4.44%,低于对照组的 15.56%(P<0.05)。这提示,联合两种治疗方法可有效清除血液中的毒物,具有良好的血液净化效果,且安全性较好。Hcy 属于含硫氨基酸,可以和血浆蛋白结合成二聚体,致使患者内皮细胞损伤程度更加严重,损伤速度更快。PTH 本质上属于直链多肽,其中含有较多的氨基酸,数量多达 48 个,可对患者机体中的钙磷代谢进行有效调节^[27,28]。倘若患者机体中积聚大量的 PTH,形成大量毒素,则对患者产生严重影响,比如导致免疫力下降、肾小管发生损伤等,进而导致患者极易发生 CRF。 β 2-MG 是机体中的毒素,本质上属于大分子多肽,久而久之,往往积聚在患者上消化道及心血管,增加患者消化道出血、异位钙化等情况的风险,甚至造成患者丧失生命^[29,30]。三个指标的水平往往是衡量血液净化效果的重要标志,本研究结果说明 HD 联合 HP 治疗能够提升患者的血液净化效果。

综上所述,HP 具有较大的吸附容量,而且吸附速度较快,然而此种治疗难以有效对水电解质进行调整。给予 HD 联合 HP 治疗 CRF,能够有效弥补 HD 单独治疗存在的不足,改善患

者肾功能和炎性指标,清除机体的各类不同有毒物质,且安全性较好。

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