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高通量血液透析治疗慢性肾衰竭尿毒症的疗效及对尿毒症毒素、免疫球蛋白及肺功能指标的影响*

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摘要 目的:探讨高通量血液透析(HFHD)治疗慢性肾衰竭尿毒症的疗效及对尿毒症毒素、免疫球蛋白及肺功能指标的影响。**方法:**选取 90 例于 2012 年 1 月-2017 年 3 月期间在喀什地区第一人民医院治疗的慢性肾衰竭尿毒症患者,依据随机数字表法将其分为对照组(n=45)和观察组(n=45),对照组给予血液透析滤过(HDF)治疗,观察组给予 HFHD 治疗,两组均透析治疗 1 个月。对比两组患者透析前后症状缓解情况及尿毒症毒素、免疫球蛋白及肺功能指标水平,记录两组相关并发症的发生情况。**结果:**透析治疗结束后观察组患者缓解率为 91.11%(41/45),高于对照组的 73.33%(33/45)($P<0.05$)。两组患者透析后血磷(P)、血钾(K⁺)、甲状旁腺激素(PTH)、β₂-微球蛋白(β₂-MG)水平明显低于透析前,血钙(Ca²⁺)水平明显高于透析前($P<0.05$);观察组透析后 K⁺、Ca²⁺、P 等尿毒症毒素水平与对照组比较差异无统计学意义($P>0.05$),观察组透析后 PTH、β₂-MG 水平明显低于对照组($P<0.05$)。透析后,两组患者的免疫球蛋白 IgM、IgA、IgG 水平均较透析前上升,且观察组高于对照组($P<0.05$)。透析后,两组患者残气量(RV)均低于治疗前,最大肺活量(FVC)、肺活量(VC)、肺总量(TLC)均高于治疗前,且观察组 RV 低于对照组,FVC、VC、TLC 均高于对照组($P<0.05$)。观察组并发症发生率为 8.89%(4/45),低于对照组的 24.44%(11/45)($P<0.05$)。**结论:**HFHD 治疗慢性肾衰竭尿毒症能够安全有效地清除尿毒症毒素,缓解患者的临床症状,且能够提高患者的免疫功能和肺功能。

关键词:高通量血液透析;血液透析滤过;慢性肾衰竭尿毒症;尿毒症毒素;免疫球蛋白

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Therapeutic Effect of High Flux Hemodialysis on Chronic Renal Failure Uremia and Its Influence on Uremic Toxin, Immunoglobulin and Pulmonary Function*

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ABSTRACT Objective: To explore the effect of high flux hemodialysis(HFHD) on chronic renal failure uremia and its influence on uremic toxin, immunoglobulin and pulmonary function index. **Methods:** A total of 90 uremic patients with chronic renal failure, who were admitted to the First People's Hospital of Kashgar from January 2012 to March 2017, were selected and were randomly divided into control group (n=45) and observation group (n=45). The control group was treated with hemodiafiltration (HDF), the observation group was treated with HFHD. Both groups were treated with dialysis for one month. The remission of symptoms and the levels of uremic toxin, immunoglobulin and pulmonary function indexes before and after dialysis were compared between the two groups. The occurrence of related complications were recorded. **Results:** The remission rate of observation group was 91.11% after dialysis treatment, which was higher than 73.33% in the control group ($P<0.05$). The levels of serum phosphorus (P), potassium (K⁺), parathyroid hormone (PTH) and β₂-microglobulin (β₂-MG) in the two groups after dialysis were significantly lower than those before dialysis. The level of serum calcium (Ca²⁺) was significantly higher than that before dialysis ($P<0.05$). There were no significant differences in the levels of K⁺, Ca²⁺, P and other uremic toxins between the observation group and the control group after dialysis ($P>0.05$). The levels of PTH and β₂-MG in the observation group after dialysis were significantly lower than those in the control group ($P<0.05$). After dialysis, the levels of IgM, IgA and IgG in the two groups were higher than those before dialysis, the observation group was higher than the control group ($P<0.05$). After dialysis, the residual air volume (RV) in both groups was lower than that before treatment, and the maximum vital capacity (FVC), vital capacity (VC) and total lung volume (TLC) were higher than those before treatment, and the RV in the observation group was lower

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than that in the control group, the FVC, VC and TLC were higher than those of the control group ($P < 0.05$). The incidence of complications in the observation group was 8.89% (4/45), which was lower than 24.44% in the control group ($P < 0.05$). **Conclusion:** HFHD, in the treatment of patients with chronic renal failure uremia, can remove uremic toxin safely and effectively, alleviate clinical symptoms, and improve immune function and lung function of patients.

Key words: High flux hemodialysis; Hemodiafiltration; Chronic renal failure uremia; Uremic toxin; Immunoglobulin

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前言

慢性肾衰竭是指各种肾脏病导致的肾脏功能减退、丧失等一系列症状和代谢紊乱所组成的临床综合征,该病的终末期为慢性肾衰竭尿毒症^[1]。目前我国慢性肾衰竭发病率约为 100/百万人口,男女发病率分别是 55%和 45%,高发年龄为 40-50 岁,近年来慢性肾衰竭尿毒症的发病率呈现逐年递增的趋势,引起广泛关注^[2]。肾功能衰竭导致机体代谢产生的相关毒素无法有效排出体外,使其在体内蓄积,进而引起体内多脏器损害,降低患者生存质量,甚至危及患者生命,影响患者远期存活率^[3,4]。血液透析是挽救慢性肾衰竭尿毒症患者生命最常用的治疗方式,其有多种透析模式,不同的透析模式对毒素的清除能力存在较大差异^[5]。目前临床上使用较为广泛的血液透析方式有血液透析滤过(hemodiafiltration, HDF)及高通量血液透析(high-flux hemodialysis, HFHD)两种,其中 HFHD 以清除中大分子尿毒症毒素为主,而 HDF 以清除小分子尿毒症毒素为主^[6,7]。本研究采用 HFHD 治疗慢性肾衰竭尿毒症患者,疗效满意,现整理报道如下。

1 资料与方法

1.1 一般资料

选取 90 例于 2012 年 1 月-2017 年 3 月期间在喀什地区第一人民医院治疗的慢性肾衰竭尿毒症患者,纳入标准:① 所有患者均被确诊为慢性肾衰竭尿毒症,符合《内科学》中诊断标准^[8],即血肌酐(serum creatinine, SCr) $> 707 \mu\text{mol/L}$;② 患者及其家属均知情且签署了知情同意书;③ 入组前未进行血液透析治疗者。排除标准:① 合并心衰、恶性高血压、原发性甲状腺等疾病者;② 近期发生过感染性疾病及急性心血管病变者;③ 听力障碍等无法配合者。依据随机数字表法将其分为对照组($n=45$)和观察组($n=45$),对照组男 24 例,女 21 例,年龄 29~73 岁,平均(45.73 ± 4.61)岁;尿毒症发病时间 1-11 个月,平均(6.51 ± 2.37)个月;肾衰竭病史 1-10 年,平均(3.69 ± 1.25)年;观察组男 25 例,女 20 例,年龄 31~72 岁,平均(44.56 ± 5.97)岁;尿毒症发病时间 1-9 个月,平均(6.08 ± 2.14)个月;肾衰竭病史 1-11 年,平均(3.74 ± 1.35)年;两组患者一般资料比较无显著差异($P > 0.05$),均衡可比,研究经我院伦理委员会审批通过。

1.2 治疗方法

两组均接受常规的血压控制和血脂控制,贫血患者给予促红细胞生成素治疗。两组均使用 Fresenius 公司型号为 4008B 的透析机,聚砜膜血液透析器,碳酸氢盐透析液,低分子肝素钠抗凝,建立颈内静脉透析导管通路。观察组实施 HFHD 治疗,

超滤系数 $46 \text{ mL}/(\text{mmHg} \cdot \text{h})$,膜面积 1.3 m^2 ,透析时间 4h,3 次/周;对照组进行 5 次血液透析治疗后给予一次 HDF 治疗, HDF 超滤系数 $55 \text{ mL}/(\text{mmHg} \cdot \text{h})$,膜面积 1.8 m^2 ,透析时间 4h。两组均透析治疗 1 个月。

1.3 疗效评价与观察指标

1.3.1 治疗效果 明显缓解:透析后不适症状基本消失,尿素氮(Urea nitrogen, BUN)、SCr 等肾功能相关指标至少改善 60%;缓解:透析后不适症状消退或减少, BUN、SCr 等肾功能相关指标至少改善 30%;无效:透析后不适症状无明显变化, BUN、SCr 等肾功能改善不足 30%,或病情恶化。缓解率 = (明显缓解例数 + 缓解例数) / 总例数 $\times 100\%$ ^[9]。

1.3.2 尿毒症毒素、免疫球蛋白及肺功能指标检测 两组患者均在进行透析治疗前与透析治疗结束后从患者透析管路动脉端取血标本 4 mL 送检,利用预先装有 EDTA 的抗凝采血管保存样品,以 3000 rpm 离心 10 min,离心结束后将离心得到的上层血清装入 EP 管中,放置于 -20°C 保存以及备用。采用日立全自动生化分析仪检测血磷(P^+)、血钾(K^+)、血钙(Ca^{2+})水平,采用酶联免疫吸附法测定甲状旁腺激素(parathyroid hormone, PTH)、 β_2 -微球蛋白(β_2 -microglobulin, β_2 -MG)水平,试剂盒均购于生工生物工程(上海)股份有限公司。采用间接免疫荧光法检测免疫球蛋白 IgM、IgA、IgG 水平,采用 2200 型全自动肺功能仪测定两组患者肺功能,包括残气量(residual volume, RV)、最大肺活量(forced vital capacity, FVC)、肺活量(vital capacity, VC)、肺总量(total lung volume, TLC)。

1.3.3 并发症发生情况 记录两组患者透析后相关并发症的发生情况。

1.4 统计学方法

采用 SPSS21.0 进行统计分析,尿毒症毒素、免疫球蛋白及肺功能指标等计量资料以均数 $\pm$ 标准差($\bar{x} \pm s$)表示,实施 t 检验;以率表示计数资料,实施 χ^2 检验,检验水准 $\alpha = 0.05$ 。

2 结果

2.1 两组患者缓解率比较

透析治疗结束后观察组患者缓解率为 91.11%(41/45),高于对照组的 73.33%(33/45)($P < 0.05$),详见表 1。

2.2 两组患者透析前后尿毒症毒素水平比较

两组患者透析后 K^+ 、 P^+ 水平明显低于透析前, Ca^{2+} 水平明显高于透析前($P < 0.05$),但透析前、透析后两组 K^+ 、 Ca^{2+} 、 P^+ 水平比较差异均无统计学意义($P > 0.05$);两组患者透析前 PTH、 β_2 -MG 水平差异无统计学意义($P > 0.05$),两组患者透析后 PTH、 β_2 -MG 水平较透析前明显降低,且观察组低于对照组($P < 0.05$),详见表 2。

表 1 两组患者缓解率比较[n(%)]

Table 1 Comparison of remission rates between two groups[n(%)]

Groups	n	Obvious remission	Remission	Invalid	Remission rates
Control group	45	8(17.78)	25(55.56)	12(26.67)	33(73.33)
Observation group	45	10(22.22)	31(68.89)	4(8.99)	41(91.11)
χ^2			4.865		
P			0.027		

表 2 两组患者透析前后尿毒症毒素水平比较($\bar{x} \pm s$)Table 2 Comparison of uremic toxin levels between two groups before and after dialysis($\bar{x} \pm s$)

Groups	n	K ⁺ (mmol/L)		Ca ²⁺ (mmol/L)		P ⁻ (mmol/L)		PTH(mg/L)		β 2-MG(mg/L)	
		Before dialysis	After dialysis	Before dialysis	After dialysis	Before dialysis	After dialysis	Before dialysis	After dialysis	Before dialysis	After dialysis
Control group	45	5.92 $\pm$ 0.95	3.68 $\pm$ 0.89*	2.01 $\pm$ 0.32	2.43 $\pm$ 0.21*	2.67 $\pm$ 0.31	1.42 $\pm$ 0.87*	680.46 $\pm$ 55.34	472.49 $\pm$ 35.08*	19.78 $\pm$ 3.92	11.83 $\pm$ 3.05*
		6.09 $\pm$ 1.12	3.73 $\pm$ 0.65*	2.13 $\pm$ 0.29	2.52 $\pm$ 0.33*	2.62 $\pm$ 0.25	1.28 $\pm$ 0.68*	679.56 $\pm$ 54.06	453.02 $\pm$ 30.82*	19.66 $\pm$ 4.25	10.15 $\pm$ 2.63*
t		-0.776	-0.304	-1.864	-1.543	0.842	0.851	0.078	2.797	0.139	2.798
P		0.440	0.762	0.066	0.126	0.402	0.397	0.938	0.006	0.890	0.006

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

2.3 两组患者透析前后免疫球蛋白水平比较

透析前两组患者免疫球蛋白 IgM、IgA、IgG 水平比较差异均无统计学意义($P>0.05$);透析后,两组患者的免疫球蛋白

白 IgM、IgA、IgG 水平均较透析前上升,且观察组高于对照组($P<0.05$),详见表 3。

表 3 两组患者透析前后免疫球蛋白水平比较($\bar{x} \pm s$)Table 3 Comparison of immunoglobulin levels before and after dialysis between two groups($\bar{x} \pm s$)

Groups	n	IgA(g/L)		IgM(g/L)		IgG(g/L)	
		Before dialysis	After dialysis	Before dialysis	After dialysis	Before dialysis	After dialysis
Control group	45	0.65 $\pm$ 0.23	1.43 $\pm$ 0.71*	0.73 $\pm$ 0.21	1.22 $\pm$ 0.46*	8.51 $\pm$ 0.93	12.93 $\pm$ 1.72*
Observation group	45	0.69 $\pm$ 0.32	1.81 $\pm$ 0.72*	0.75 $\pm$ 0.16	1.68 $\pm$ 0.77*	8.32 $\pm$ 1.17	14.22 $\pm$ 1.43*
t		-0.681	-2.521	-0.508	-3.440	0.853	-3.869
P		0.498	0.014	0.613	0.001	0.396	0.000

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

2.4 两组患者透析前后肺功能指标比较

透析前,两组患者肺功能指标比较无统计学差异($P>0.05$);透析后,两组患者 RV 均低于治疗前,FVC、VC、TLC 均高于治

疗前,且观察组 RV 低于对照组,FVC、VC、TLC 均高于对照组($P<0.05$),详见表 4。

表 4 两组患者透析前后肺功能指标比较($\bar{x} \pm s$)Table 4 Comparison of pulmonary function before and after dialysis between two groups($\bar{x} \pm s$)

Groups	n	VC(V/L)		FVC(V/L)		TLC(V/L)		RV(V/L)	
		Before dialysis	After dialysis	Before dialysis	After dialysis	Before dialysis	After dialysis	Before dialysis	After dialysis
Control group	45	2.82 $\pm$ 0.92	3.30 $\pm$ 0.33*	2.91 $\pm$ 0.82	3.43 $\pm$ 0.42*	5.41 $\pm$ 0.18	6.04 $\pm$ 0.72*	2.20 $\pm$ 0.16	1.73 $\pm$ 0.42*
Observation group	45	2.80 $\pm$ 0.73	4.21 $\pm$ 0.71*	3.05 $\pm$ 0.10	3.82 $\pm$ 0.35*	5.42 $\pm$ 0.36	6.95 $\pm$ 0.23*	2.23 $\pm$ 0.15	1.47 $\pm$ 0.18*
t		0.114	-7.797	-1.137	-4.785	-0.167	-8.076	-0.918	3.817
P		0.909	0.000	0.259	0.000	0.868	0.000	0.361	0.000

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

2.5 两组患者并发症发生情况对比

观察组患者出现 3 例低血压, 1 例肌肉痉挛, 并发症发生率为 8.89%(4/45); 对照组患者出现 8 例低血压, 3 例肌肉痉挛, 并发症发生率为 24.44%(11/45); 与对照组比较, 观察组并发症发生率降低($\chi^2=3.920$, $P=0.048$)。

3 讨论

慢性肾衰竭尿毒症是各种病因导致的慢性肾脏病的最终结局, 由于肾功能衰竭, 肾脏无法将机体产生的代谢废物充分降解和排泄, 严重影响患者的身体健康^[10, 11]。尿毒症毒素根据分子量大小的差异, 分为小分子毒性物质, 中分子毒性物质与大分子毒性物质, 有些毒素在正常浓度时对人体无害, 一旦发生慢性肾衰竭尿毒症, 使毒素无法排出, 进而在机体堆积导致浓度升高后便会产生毒性作用^[12-14]。肾脏替代治疗是目前改善慢性肾功能衰竭患者临床症状和体征的重要治疗措施, 主要包括血液透析、腹膜透析及肾脏移植^[15-17], 临床上最常用的肾脏替代治疗方式是血液透析, 它能够有效纠正机体电解质和酸碱平衡紊乱, 清除患者体内代谢废物、激素、毒素等, 而 HFHD、HDF 是血液透析最常见的方式。

本研究结果表明, 观察组透析后缓解率高于对照组, 且并发症发生率低于对照组, 提示 HFHD 能有效的缓解患者的临床症状, 减少并发症, 这与徐皖东^[18]等人的报道一致。HDF 和 HFHD 均有一定的清除尿毒症毒素的作用, 但这两种血液透析方式对不同尿毒症分子清除效率不尽相同。本研究中 HFHD 与 HDF 皆可清除小分子尿毒症毒素 K^+ 、 Ca^{2+} 、 P 等, 并且两种透析方式治疗效果无明显差异, 但是观察组透析后 PTH、 β_2 -MG 水平明显低于对照组, 提示 HFHD 清除慢性肾衰竭尿毒症患者 PTH 和 β_2 -MG 等中大分子尿毒症毒素能力优于 HDF, 可能是由于 HFHD 生物膜对中大分子物质渗透性好, 能弥补 HDF 不能完全清除中大分子尿毒症毒素的不足^[19, 21]。尿毒症使患者体内不断蓄积水和毒性代谢物质, 进而导致肺间质性水肿, 肺血管静水压升高明显, 导致肺大气道、小气道的通气功能异常^[22, 23]。HDF 能够使机体内过多的水分与毒性代谢物排出, 恢复体内酸碱平衡, 纠正电解质紊乱, 减轻肺水肿, 使患者的肺水肿功能得到改善, 增加肺总量^[24, 25]。HFHD 可以使体内更多的水分与毒素物质排出, 减轻肺部损伤, 进而增加肺总量, 减轻肺间质水肿^[26, 27]。本研究结果表明, 观察组对患者的肺功能改善情况优于对照组, 说明 HFHD 对慢性肾衰竭尿毒症患者的肺功能改善效果更明显。尿毒症患者体内堆积的毒性物质会造成免疫系统的损伤, 使免疫球蛋白水平降低, HFHD 治疗后能够排出体内过多的毒素, 排出血液中的毒素有利于患者免疫功能的改善, 提高免疫球蛋白功能^[28, 29]。进行透析治疗后, 两组患者的免疫球蛋白水平均明显提高, 而观察组患者可以清除体内更多的毒素, 使机体的免疫功能得到更大的提高, 可能是由于 HFHD 治疗可以提高相关免疫球蛋白指标, 增强免疫功能, 从而提高免疫球蛋白 IgM、IgA、IgG 水平^[30]。

综上所述, HFHD 可有效地清除慢性肾衰竭尿毒症患者体内蓄积的尿毒症毒素, 有效改善患者的肺功能, 提高免疫功能, 减少并发症, 安全性高。

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