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高通量血液透析联合肾衰宁颗粒对尿毒症患者钙磷代谢、炎症反应以及营养状况的影响 *

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摘要 目的:探讨高通量血液透析(HFHD)联合肾衰宁颗粒对尿毒症患者钙磷代谢、炎症反应以及营养状况的影响。方法:选取2017年1月~2019年10月在我院接受血液透析治疗的尿毒症患者114例作为研究对象,按随机数字表法分成对照组和观察组,每组各57例,对照组给予HFHD,观察组在对照组基础上口服肾衰宁颗粒。两组均治疗3个月。比较两组患者治疗前后肾功能指标,包括尿素氮(BUN)、血肌酐(Scr)、肾小球滤过率(GFR);钙磷代谢相关指标血清钙、血清磷、甲状旁腺激素(PTH);炎症反应指标,包括降钙素原(PCT)、C反应蛋白(CRP)、白细胞介素-6(IL-6);营养状况指标,包括白蛋白(ALB)、血红蛋白(Hb)、血清总蛋白(TP)。结果:治疗后两组患者BUN、Scr、GFR、血清磷、PTH、PCT、CRP、IL-6较治疗前降低,血清钙、ALB、Hb、TP较治疗前升高,观察组患者BUN、Scr、GFR、血清磷、PTH、PCT、CRP、IL-6低于对照组,血清钙、ALB、Hb、TP高于对照组,差异均有统计学意义($P<0.05$)。结论:HFHD联合肾衰宁颗粒治疗尿毒症,可有效改善患者的钙磷代谢和肾功能,改善机体炎症状态及营养状况。

关键词:高通量血液透析;肾衰宁颗粒;钙磷代谢;炎症反应;营养状况;肾功能

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Effects of High-throughput Hemodialysis Combined with Shenshuaining Granules on Calcium and Phosphorus Metabolism, Inflammatory Response, and Nutritional Status in Patients with Uremia*

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ABSTRACT Objective: To investigate the effects of high-throughput hemodialysis (HFHD) combined with Shenshuaining granules on calcium and phosphorus metabolism, inflammatory response, and nutritional status in patients with uremia. **Methods:** The patients with uremia who underwent hemodialysis treatment in our hospital from January 2017 to October 2019 were selected as research objects, and randomly divided into control group and observation group, with 57 cases in each group. The control group was given HFHD and the observation group received Shenshuaining granules on the basis of the control group. Both groups were treated for 3 months. The renal function indexes, including urea nitrogen (BUN), blood creatinine (Scr), glomerular filtration rate (GFR). Related indexes of calcium and phosphorus metabolism including serum calcium, serum phosphorus and parathyroid hormone (PTH). Inflammatory response indicators, including procalcitonin (PCT), C-reactive protein (CRP), interleukin-6 (IL-6); Nutritional status indicators include albumin (ALB), hemoglobin (Hb), and total serum protein (TP) before and after treatment were compared between the two groups. **Results:** After treatment, BUN, Scr, GFR, serum phosphorus, PTH, PCT, CRP and IL-6 in the two groups were lower than before treatment, serum calcium, ALB, Hb and TP were higher than before treatment. BUN, Scr, GFR, serum phosphorus, PTH, PCT, CRP and IL-6 in the observation group were lower than those in the control group, Serum calcium, ALB, Hb and TP were higher than control group, with statistical differences ($P<0.05$). **Conclusions:** HFHD combine shenshuaining granules in the treatment of uremia, which could effectively improve calcium and phosphorus metabolism and renal function of uremia patients, and improve the inflammatory state and nutritional status of the body.

Key words: High-throughput hemodialysis; Shenshuaining granules; Calcium and phosphorus metabolism; Inflammation response; Nutritional status; Renal function

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前言

尿毒症是多种肾脏疾病的最终归宿,维持性血液透析是尿毒症患者维持生命的替代治疗方式,但长期治疗容易导致免疫紊乱和炎症指标异常增高,钙磷代谢紊乱,营养不良等症状,对患者心血管系统、内分泌系统有一定损害,严重影响患者预后^[1,2]。高通量血液透析(High-throughput hemodialysis, HFHD)可降低慢性肾脏病(Chronic kidney disease, CKD)患者体内有毒物质的积累,改善患者的氧化应激状态,降低全因死亡率和心血管病死亡率,是CKD的首选疗法之一^[3,4]。中医药在改善机体的水电解质紊乱状态,抑制机体微炎症状态,保护残余肾功能,改善血透患者的治疗质量,延缓病情进展上显示出其独特的优势^[5]。肾衰宁颗粒具有益气健脾、通腑泄浊、活血化瘀的功效,可改善慢性肾功能衰竭,纠正磷、钙代谢异常,降低机体炎症水平,改善患者营养状况,延缓病情进展^[6]。故本研究通过比较单独使用HFHD治疗及肾衰宁颗粒联合HFHD治疗的尿毒症患者钙磷代谢、炎症反应以及营养状况的变化情况,以期为

尿毒症患者的临床治疗提供方案参考。

1 资料与方法

1.1 研究对象

选取2017年1月~2019年10月在我院接受血液透析治疗的尿毒症患者114例,男63例,女51例,年龄31~63岁,平均(42.20 ± 3.29)岁。慢性肾小球肾炎41例,慢性肾盂肾炎12例,糖尿病肾病33例,高血压肾病28例。纳入标准:^①确诊为尿毒症^[7];^②患者治疗依从性好,维持规律的血液透析治疗;^③病情稳定,有残余肾功能;^④所有患者知情且签署同意书。排除标准:^①急性左心衰,肝、肺等脏器功能严重受损者;^②严重心脑血管疾病、消化道疾病、感染、恶性肿瘤、免疫系统疾病者;^③对治疗药物过敏者;^④HFHD禁忌症者。我院伦理委员会已批准本研究。114例患者按随机数字表法分成对照组和观察组,每组各57例。两组年龄、性别、基础疾病比较无统计学差异($P>0.05$),具有可比性,见表1。

表1 两组患者的基线资料比较

Table 1 Comparison of baseline data between the two groups

Groups	n	Age(years)	Gender(male / female)	Basic diseases			
				Chronic glomerulonephritis	Chronic pyelonephritis	Diabetic nephropathy	Hypertensive nephropathy
Control group	57	41.85±3.33	33/24	23	4	16	14
Observation group	57	42.54±3.28	30/27	18	8	17	14
t/ χ^2		0.809	0.319				
P		0.422	0.572				

1.2 治疗方法

透析过程中两组患者给予控制血糖、稳定血压、抗感染、低分子肝素抗凝、优质低蛋白饮食等对症治疗。对照组采用欧赛高OCI-HD200通量聚醚砜中空纤维膜血液透析器进行高通量血液透析,有效膜表面积为2.0 m²,超滤系数93 mL/hr·mm Hg,使用压力为66.3 Kpa,血室容量75 mL。每周2~4次规律透析治疗,每次4 h。观察组患者在上述治疗的基础上口服肾衰宁颗粒(山西德元堂药业有限公司,国药准字:Z20050503,规格:每袋装5 g),1袋/次,3~4次/天,两组患者均连续治疗3个月。

1.3 观察指标

两组患者均于治疗前和治疗3个月后采集空腹晨起静脉血5 mL,以转速3000 r/min,半径10 cm,离心15 min,取上层血清,置于冰箱中保存备用。采用迈瑞BS-380全自动生化分析仪检测肾功能指标尿素氮(Blood urea nitrogen, BUN)、血肌酐(Serum creatinine, Scr),钙磷代谢相关指标血清钙、血清磷、甲状旁腺激素(Parathyroid hormone, PTH),营养状况指标,包括白蛋白(Albumin, ALB)、血红蛋白(Hemoglobin, Hb)、血清总蛋白(Total serum protein, TP)。酶联免疫吸附法检测血清炎症因子指标降钙素原(procalcitonin, PCT)、C反应蛋白(C-reactive protein, CRP)、白细胞介素-6(interleukin-6, IL-6)。肾小球滤过率(glomerular filtration rate, GFR)_男=(140-年龄)×体重(kg)×1.23Scr, GFR_女=(140-年龄)×体重(kg)×1.03Scr。试剂均购

自深圳迈瑞生物电子有限公司,试验操作严格按照试剂说明书进行。

1.4 统计学方法

数据应用SPSS20.0统计软件分析。计数资料以比或率表示,采用卡方检验。计量资料以($\bar{x} \pm s$)表示,采用t检验。检验水准为 $\alpha=0.05$ 。

2 结果

2.1 两组肾功能指标比较

治疗前两组BUN、Scr、GFR比较无差异($P>0.05$),两组治疗后上述指标较治疗前降低,并且观察组低于对照组($P<0.05$)。见表2。

2.2 两组治疗前后钙、磷、PTH比较

两组患者治疗前血清钙、血清磷、PTH比较无差异($P>0.05$),治疗后两组患者较治疗前血清磷、PTH降低,血清钙升高,观察组血清磷、PTH较对照组低,血清钙高于对照组($P<0.05$)。见表3。

2.3 两组炎症反应指标比较

两组患者治疗前IL-6、CRP、PCT比较无差异($P>0.05$),治疗后两组IL-6、CRP、PCT较治疗前降低,观察组较对照组低($P<0.05$)。见表4。

表 2 两组患者肾功能指标比较($\bar{x} \pm s$)
Table 2 Comparison of renal function indexes between the two groups($\bar{x} \pm s$)

Groups	n	BUN(mmol/L)		Scr(mmol/L)		GFR(mL/min)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Control group	57	24.35± 5.19	14.39± 2.65*	464.38± 110.85	310.53± 85.45*	43.61± 6.72	25.14± 3.53*
Observation group	57	25.27± 5.41	10.37± 1.84*	466.83± 114.52	231.68± 74.39*	41.27± 6.28	16.73± 2.75*
t		0.926	9.408	0.116	5.255	1.921	14.189
P		0.356	0.000	0.908	0.000	0.057	0.000

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

表 3 两组患者治疗前后钙、磷、PTH 比较($\bar{x} \pm s$)
Table 3 Comparison of calcium, phosphorus and PTH between the two groups before and after treatment($\bar{x} \pm s$)

Groups	n	Calcium(mmol/L)		Phosphorus(mmol/L)		PTH(ng/L)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Control group	57	1.93± 0.56	2.27± 0.72*	2.26± 0.53	1.80± 0.36*	357.17± 52.18	235.26± 31.52*
Observation group	57	1.90± 0.63	2.61± 0.86*	2.23± 0.48	1.53± 0.31*	353.28± 50.26	174.16± 26.35*
t		0.269	2.289	0.317	4.291	0.405	11.228
P		0.789	0.024	0.752	0.000	0.686	0.000

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

表 4 两组患者炎症反应指标比较($\bar{x} \pm s$)
Table 4 Comparison of inflammatory response indexes between the two groups($\bar{x} \pm s$)

Groups	n	IL-6(pg/mL)		CRP(mg/mL)		PCT(ng/mL)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Control group	57	84.25± 21.26	28.36± 4.31*	24.58± 4.61	10.87± 2.76*	0.70± 0.21	0.44± 0.17*
Observation group	57	85.31± 23.67	20.14± 3.531*	26.11± 4.97	5.45± 1.83*	0.68± 0.15	0.32± 0.12*
t		0.252	11.140	1.704	12.357	0.585	4.354
P		0.802	0.000	0.091	0.000	0.680	0.000

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

2.4 两组患者营养状况相关指标比较

两组患者治疗前 ALB、Hb、TP 比较无差异($P<0.05$),治疗

后两组 ALB、Hb、TP 较治疗前升高, 观察组高于对照组($P<0.05$)。见表 5。

表 5 两组患者营养状况相关指标比较($\bar{x} \pm s$)
Table 5 Comparison of nutrition related indicators between the two groups($\bar{x} \pm s$)

Groups	n	ALB(g/L)		Hb(g/L)		TP(g/L)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Control group	57	30.35± 4.36	36.27± 5.72*	86.25± 8.65	107.27± 10.26*	61.34± 6.18	67.83± 7.29*
Observation group	57	31.28± 4.74	43.58± 7.18*	84.23± 7.57	128.36± 11.39*	60.53± 6.67	76.11± 8.42*
t		1.207	6.012	1.327	10.387	0.673	5.613
P		0.230	0.000	0.187	0.000	0.503	0.000

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

3 讨论

尿毒症患者代谢废物及毒素在体内蓄积、水电解质平衡及酸碱平衡遭到破坏、机体中的营养元素也会不断减少,影响机体其他脏器系统正常运作,严重危害患者健康,导致患者生活

质量下降,预期寿命缩短^[8-10]。维持性血液透析作为一种主要肾脏替代治疗方法延续着尿毒症患者的生命。HFHD 具有良好的生物相容性以及较大的透析膜孔径,可以显著提高尿毒症患者血液中大分子有毒物质的清除效果,降低心脑血管疾病病死率,改善患者近期预后^[11-13]。然而血液透析仅能够清除患者体内

毒素,无法完成机体诸多激素内分泌生理调节过程,需辅助其他手段进一步治疗,以提高临床疗效。

肾衰宁颗粒的组成成分中丹参、牛膝、红花活血化瘀,通经止痛,改善肾血流,与改善慢性肾功能衰竭患者的贫血有关;大黄则可通腑泄浊、解毒清热、祛瘀泻火,促进肠道排出体内毒素,改善氮质血症,从组织形态和生理方面延缓慢性肾功能衰竭进展;太子参益气健脾、扶正增元,提高机体免疫力,改善了肾功能和贫血,甘草能调和诸药、清里解表,诸药合用,攻补兼备,具有滋补脾肾,化瘀通络、祛风扶本之效,多靶点、多层次维持内环境稳定,改善和恢复肾功能状况,减轻微炎症反应,改善患者营养状况,延缓病情进展^[14-16]。

Scr、BUN、GFR 是临床诊断肾脏疾病和评估肾功能情况的重要指标^[17-19]。治疗后两组患者 Scr、BUN、GFR 均降低,但观察组 Scr、BUN、GFR 低于对照组,表明 HFHD 联合肾衰宁颗粒治疗尿毒症效果优于单独 HFHD 治疗,在缓解肾小球高滤过状态、保护残存肾功能方面具有优势,对尿毒症患者肾功能具有较好的保护作用。研究显示,肾衰宁颗粒促进氮质代谢产物的排泄,降低 BUN 和 Scr 水平,减少基底膜损伤,增加肾血液量,改善肾功能,对于辅助治疗慢性肾衰竭有一定的疗效且相对安全^[20]。

高磷血症可引起尿毒症患者残余肾功能进一步恶化,加重低钙血症,刺激 PTH 分泌增加^[21,22]。本文中治疗后两组患者 BUN、Scr、GFR、血磷、PTH 较治疗前降低,且观察组低于对照组,血清钙较治疗前升高,且观察组高于对照组,提示 HFHD 联合肾衰宁颗粒可改善尿毒症患者残余肾功能,增加对血清磷、血清钙水平的调节能力,降低 PTH 的分泌。肾衰宁颗粒能够有效改善维持性血液透析患者钙磷代谢和肾功能^[23]。

尿毒症毒素和微生物的刺激、氧化应激损伤、血管通路各接口的感染等引起尿毒症患者微炎症状态,增加营养不良、动脉粥样硬化、贫血及死亡风险^[24,25]。IL-6 是机体内主要的促炎性细胞因子,可特异性反映慢性肾衰竭程度和微炎症状态^[26]。CRP 水平升高诱发肾脏微血管病变和加剧肾组织损伤,可作为透析患者长期预后指标之一^[27]。肾损伤患者血清中 PCT 表达显著增加,且随病情的严重程度而变化^[28]。本文研究显示,治疗后两组 IL-6、CRP、PCT 较治疗前低,且观察组低于对照组,提示 HFHD 联合肾衰宁颗粒治疗可减少患者体内促炎性细胞因子分泌,减轻肾小球基底膜损害,有助于清除组织代谢产物及肾脏功能的改善。肾衰宁颗粒中丹参可以降低内皮素的生成量,进而抑制机体的炎症反应。袁继福等^[29]采用肾衰宁颗粒治疗糖尿病肾病,降低血糖,可使微炎症状态和氧化应激反应明显减轻,肾功能明显改善。

定期血液透析会导致蛋白质和氨基酸丢失、脂肪量和肌肉量降低,促红细胞生成素分泌减少。营养状况是透析患者最重要的生存指标之一,营养不良会增加患者死亡风险。ALB、Hb、TP 是评估透析患者营养状况的常用指标。治疗后两组患者 ALB、Hb、TP 较治疗前升高,观察组高于对照组,说明 HFHD 后服用肾衰宁颗粒能够促进患者 ALB 合成,提高患者 ALB、Hb、TP 浓度,有助于改善患者的能量代谢和营养状况。肾衰宁颗粒增加 ALB 浓度,进而改善尿毒症患者的营养状况^[30]。

综上所述,HFHD 联合肾衰宁颗粒治疗尿毒症,可改善患者肾功能,减轻机体内微炎症反应,改善其钙磷代谢和营养状

况,延缓肾功能衰竭的病情进展,效果优于单一 HFHD 治疗。

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