

• 短篇论著 •

高通量血液透析对尿毒症患者心肌损伤标志物和心功能指标的影响

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【摘要】目的 观察高通量血液透析(HFHD)对尿毒症患者心功能的影响。**方法** 采用前瞻性随机对照研究方法,选择2014年12月至2015年6月贵阳市第二人民医院收治的确诊为尿毒症并需维持性血液透析(MHD)治疗的60例患者和30例健康体检者。按随机数字表法将患者分为HFHD组(每周3次)和普通血液透析(HD)组(每周3次),每组30例;另外,所有患者每月均接受1次血液灌流(HP)和1次血液滤过(HF)治疗。所有患者于治疗前及治疗6个月取静脉血,检测血清B型脑钠肽(BNP)、心肌肌钙蛋白T(cTnT),并由专人进行心脏B超检查,记录左室舒张期末内径(LVEDD)、左室收缩期末内径(LVESD)、左室舒张期末容积(LVEDV)、左室收缩期末容积(LVESV)、左室后壁厚度(LVPWT)、室间隔厚度(IVST)、舒张早期与晚期最大血流比(E/A)、左室射血分数(LVEF)、左室重量指数(LVMI)。**结果** 与健康对照组比较,HD组和HFHD组治疗前BNP、cTnT、LVEDD、LVESD、LVESV、LVPWT、IVST均显著升高,LVEDV显著下降;而HD组与HFHD组上述各指标及E/A、LVEF、LVMI比较差异均无统计学意义。与治疗前比较,HD组治疗后BNP、LVPWT显著降低[BNP(ng/L):641.50±60.09比2676.20±454.30,LVPWT(mm):10.57±1.16比12.57±1.41,均P<0.05];HFHD组治疗后BNP、LVPWT下降较HD组更为显著[BNP(ng/L):253.10±48.77比641.50±60.09,LVPWT(mm):9.29±1.08比10.57±1.16,均P<0.05],另外HFHD组治疗后cTnT、IVST、LVMI较治疗前显著降低[cTnT(μg/L):0.014±0.005比0.028±0.011,IVST(mm):7.81±1.69比11.04±2.23,LVMI(g/m²):149.10±15.77比158.70±17.25,均P<0.05],LVEF显著升高(0.574±0.068比0.528±0.082,P<0.05)。**结论** HFHD改善尿毒症患者心功能较普通HD有明显优势。

【关键词】 血液透析;高通量; 尿毒症; B型脑钠肽; 心肌肌钙蛋白; 心功能

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【Abstract】Objective To investigate the effects of high flow hemodialysis (HFHD) on cardiac function in uremia patients. **Methods** A prospective randomized controlled study was conducted. Sixty patients who were diagnosed with uremia, taken maintenance hemodialysis (MHD) and 30 healthy controls admitted to the Second People's Hospital of Guiyang from December 2014 to June 2015 were enrolled. They were randomly divided into two groups: HFHD group (HFHD three times a week) and the routine hemodialysis group (HD group, HD three times a week), with 30 in each group. Patients in each group were received hemoperfusion and hemofiltration once a month. Before the treatment and 6 months after the treatment, venous blood from all the patients were collected for testing the brain natriuretic peptide (BNP), cardiac troponin T (cTnT) and the ultrasound cardiograph were done at the same period by a special person, the left ventricular end diastolic diameter (LVEDD), left ventricular end systolic diameter (LVESD), the left ventricular end diastolic volume (LVEDV), left ventricular end systolic volume (LVESV), left ventricular posterior wall thickness (LVPWT), interventricular septum thickness (IVST), early and late diastolic blood flow to the largest ratio (E/A), left ventricular ejection fraction (LVEF), left ventricular mass index (LVMI) were recorded. **Results** Compared with the health control group, BNP, cTnT, LVEDD, LVESD, LVESV, LVPWT, IVST were significantly increased, LVEDV were significantly lowered before treatment in the HD group and HFHD group. But no significant differences in

the above indexes and E/A, LVEF, LVMI between two groups were found. Compared with the data before treatment, the BNP, LVPWT were significantly lowered after treatment in HD group [BNP (ng/L): 641.50 ± 60.09 vs. 2676.20 ± 454.30 , LVPWT (mm): 10.57 ± 1.16 vs. 12.57 ± 1.41 , both $P < 0.05$]. The BNP, LVPWT were significantly lowered in HFHD group as compared with HD group [BNP (ng/L): 253.10 ± 48.77 vs. 641.50 ± 60.09 , LVPWT (mm): 9.29 ± 1.08 vs. 10.57 ± 1.16 , both $P < 0.05$]; in addition, the cTnT, IVST, LVMI were significantly lowered after the treatment in HFHD group compared with those before treatment [cTnT ($\mu\text{g}/\text{L}$): 0.014 ± 0.005 vs. 0.028 ± 0.011 , IVST (mm): 7.81 ± 1.69 vs. 11.04 ± 2.23 , LVMI (g/m^2): 149.10 ± 15.77 vs. 158.70 ± 17.25 , all $P < 0.05$], and the LVEF were significantly increased in HFHD group as compared with those before treatment (0.574 ± 0.068 vs. 0.528 ± 0.082 , $P < 0.05$).

Conclusion HFHD has obvious advantages than the routine HD in improving cardiac function of uremia patients.

【Key words】 High flow hemodialysis; Uremia; Brain natriuretic peptide; Cardiac troponin; Cardiac function

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血液透析(HD)是尿毒症患者重要的肾脏替代治疗方式之一,随着血液净化技术的迅速发展,越来越多的尿毒症患者选择维持性血液透析(MHD)作为肾脏替代治疗的主要方式。MHD患者最主要死亡原因为心血管疾病(CVD),包括动脉粥样硬化性心脏病、心脏结构改变、心力衰竭(心衰)等,CVD死者占MHD死亡患者的45%~60%^[1]。因此,如何减少心血管事件发生,改善MHD患者生存质量、延长生命显得尤为重要。高通量血液透析(HFHD)系指采用对溶质和水等物质具有很高通透性能的透析器进行HD的方法,近年来大量研究均表明,炎症是导致动脉粥样硬化的机制之一,而HFHD可以明显减少血膜反应、氧化应激和炎症反应,清除中大分子毒素^[2]。本研究旨在观察HFHD对尿毒症患者心肌肌钙蛋白T(cTnT)、B型脑钠肽(BNP)及心脏结构的影响,为MHD患者选择合理治疗方式提供理论依据。

1 资料及方法

1.1 病例的纳入及排除标准:采用前瞻性随机对照研究方法,选择2014年12月至2015年6月本院确诊为尿毒症并需MHD治疗的患者60例。同期选择30例健康体检者作为对照,均无高血压、高血脂、糖尿病、感染、心血管事件,近2周末服用过任何药物。

1.1.1 纳入标准:年龄>18岁;确诊为尿毒症且需MHD时间超过3个月;无急慢性感染、多器官功能衰竭,未服用降脂药及抗血小板聚集、抗凝药物。

1.1.2 排除标准:服用降脂药物及抗血小板聚集、抗凝药物;存在各种感染、恶性肿瘤;严重营养不良;严重心衰;风湿免疫疾病,如系统性红斑狼疮(SLE)、血管炎等。

1.2 伦理学:本研究符合医学伦理学标准,经医院伦理委员会批准,所有治疗获得患者家属知情同意。

1.3 分组及治疗:入选患者按随机数字表法分为HFHD组和普通HD组,每组30例。两组患者常规治疗相同,HFHD组使用德国费森尤斯4008s透析机,FX80聚砜膜透析器,超滤系数 $44 \text{ mL} \cdot \text{h}^{-1} \cdot \text{mmHg}^{-1}$,膜面积 1.8 m^2 ,每周3次;普通HD组使用德国费森尤斯4008s透析机,FX8聚砜膜透析器,超滤系数 $12 \text{ mL} \cdot \text{h}^{-1} \cdot \text{mmHg}^{-1}$,膜面积 1.0 m^2 ,每周3次。所有患者使用爱尔YTS100活性炭灌流器进行血液灌流(HP),每月1次;使用德国费森尤斯5008s血滤机进行血液滤过

(HF, FX800聚砜膜透析器,超滤系数 $63 \text{ mL} \cdot \text{h}^{-1} \cdot \text{mmHg}^{-1}$,膜面积 1.8 m^2),每月1次。本院血液净化中心水处理设备为DWA二级反渗系统。

1.4 检测指标及方法:于治疗前及治疗6个月采集患者静脉血,离心取血清,用电化学发光分析仪(德国罗氏411)检测BNP,用化学发光仪(美国贝克曼800)检测cTnT水平;同期由专人进行心脏B超检查,记录左室舒张期末内径(LVEDD)、左室收缩期末内径(LVESD)、左室舒张期末容积(LVEDV)、左室收缩期末容积(LVESV)、左室后壁厚度(LVPWT)、室间隔厚度(IVST)、舒张早期与晚期最大血流比(E/A)、左室射血分数(LVEF)、左室重量指数(LVMI,LVMI=左心室重量/体表面积)。

1.5 统计学方法:使用SPSS 17.0软件进行统计学分析,计量数据以均数±标准差($\bar{x} \pm s$)表示,两组间比较采用t检验,3组间比较采用F检验,组间两两比较采用SNK检验;计数资料比较采用 χ^2 检验。 $P < 0.05$ 为差异有统计学意义。

2 结 果

2.1 各组一般资料(表1):3组研究对象性别、年龄比较差异均无统计学意义(均 $P > 0.05$),说明基线资料均衡,具有可比性。

表1 各组研究对象一般资料比较

组别	例数 (例)	性别(例)		年龄 (岁, $\bar{x} \pm s$)
		男性	女性	
健康对照组	30	16	14	44 ± 16
普通HD组	30	15	15	46 ± 14
HFHD组	30	14	16	45 ± 16

注:HD为血液透析,HFHD为高通量血液透析

2.2 各组心功能指标比较(表2):与健康对照组比较,HD组和HFHD组治疗前BNP、cTnT、LVEDD、LVESD、LVESV、LVPWT、IVST均显著升高,LVEDV显著下降(均 $P < 0.05$);而HD组与HFHD组治疗前上述各指标及E/A、LVEF和LVMI比较差异均无统计学意义(均 $P > 0.05$)。与治疗前比较,HD组治疗后BNP、LVPWT显著降低;HFHD组治疗后BNP、cTnT、LVPWT、IVST、LVMI显著降低,LVEF显著升高,且HFHD组治疗后BNP、LVPWT下降较HD组更为显著(均 $P < 0.05$)。

表2 HFHD对尿毒症患者心功能的影响($\bar{x} \pm s$)

组别	时间	例数(例)	BNP(ng/L)	cTnT(μg/L)	LVEDD(mm)	LVESD(mm)	LVEDV(mL)	LVESV(mL)
健康对照组		30	67.56 ± 10.40	0.012 ± 0.004	46.77 ± 1.97	27.87 ± 2.12	122.98 ± 12.49	37.11 ± 4.03
普通 HD 组	治疗前	30	2 676.20 ± 454.30 ^a	0.037 ± 0.012 ^a	52.35 ± 2.53 ^a	33.57 ± 3.00 ^a	118.30 ± 11.46 ^a	38.66 ± 3.81 ^a
	治疗后	30	641.50 ± 60.09 ^b	0.032 ± 0.014	51.50 ± 3.20	32.71 ± 4.29	122.10 ± 13.72	37.90 ± 3.76
HFHD 组	治疗前	30	2 476.10 ± 594.10 ^a	0.028 ± 0.011 ^a	53.10 ± 2.83 ^a	33.24 ± 3.46 ^a	120.50 ± 11.93 ^a	39.07 ± 3.44 ^a
	治疗后	30	253.10 ± 48.77 ^{bc}	0.014 ± 0.005 ^b	52.47 ± 4.06	33.42 ± 4.67	118.50 ± 11.96	38.97 ± 3.49
组别	时间	例数(例)	LVPWT(mm)	IVST(mm)	E/A	LVEF	LVMI(g/m ²)	
健康对照组		30	8.23 ± 1.34	6.59 ± 1.37				
普通 HD 组	治疗前	30	12.57 ± 1.41 ^a	10.35 ± 2.13 ^a	1.02 ± 0.21	0.532 ± 0.083	160.60 ± 18.77	
	治疗后	30	10.57 ± 1.16 ^b	9.53 ± 1.64	1.00 ± 0.22	0.546 ± 0.088	159.80 ± 18.54	
HFHD 组	治疗前	30	12.25 ± 1.57 ^a	11.04 ± 2.23 ^a	1.11 ± 0.22	0.528 ± 0.082	158.70 ± 17.25	
	治疗后	30	9.29 ± 1.08 ^{bc}	7.81 ± 1.69 ^b	1.06 ± 0.21	0.574 ± 0.068 ^b	149.10 ± 15.77 ^b	

注:HD为血液透析, HFHD为高通量血液透析, BNP为B型脑钠肽, cTnT为心肌肌钙蛋白T, LVEDD为左室舒张期末内径, LVESD为左室收缩期末内径, LVEDV为左室舒张期末容积, LVESV为左室收缩期末容积, LVPWT为左室后壁厚度, IVST为室间隔厚度, E/A为舒张早期与晚期最大血流比, LVEF为左室射血分数, LVMI为左室重量指数;与健康对照组比较,^aP<0.05;与本组治疗前比较,^bP<0.05;与普通HD组同期比较,^cP<0.05;空白代表无此项

3 讨论

终末期肾病患者的首位死因仍是CVD,其中以心衰为主^[3]。研究发现,左室舒张功能衰竭患者的病死率较左室收缩功能衰竭者高,且左室舒张功能障碍的发生早于收缩功能障碍^[4],故及早发现心功能异常,重视左室舒张功能减退,探索相关影响因素,早期有效干预,可改善患者预后。有研究发现,HD 1年以上的MHD患者大部分存在心脏结构改变和(或)心功能减退,其中69%发生左室舒张功能减退,82%发生左室心肌肥厚,其原因与高血压、糖尿病、容量超负荷状态、血管钙化、贫血及HD治疗等因素相关^[5]。慢性肾脏病(CKD)患者普遍存在的微炎症状态能加速动脉粥样硬化的发展,且炎症是慢性肾衰竭(CRF)患者发生心血管事件的独立危险因素^[6]。心、肾功能相互影响,肾功能越差,失代偿性心力衰竭(DHF)患者预后越差,肾功能下降与心衰严重程度和心衰致死事件的发生率密切相关^[7]。

cTnT是目前心肌损伤特异性最高的标志物。cTnT升高可反映左室肥厚、心脏收缩功能减退^[8]。终末期CKD患者若cTnT水平升高,则提示患有心脏疾病的可能性较大^[9]。终末期肾衰竭患者血清cTnT水平升高,则心肌结构和功能明显损伤^[8]。de Lemos等^[10]研究发现,血清cTnT水平与年龄和BNP水平呈正相关,与肾功能水平呈负相关。BNP能很好地反映心功能变化^[11],是预测心血管事件及死亡的危险因子^[12-13]。BNP主要由心室肌细胞合成和分泌,是调节人体体液平衡的重要激素,心室负荷和室壁张力的改变是刺激BNP分泌的主要条件,在心室负荷过重或扩张时增加,因此反映心室功能改变更敏感、更具特异性,其血浆水平受血容量影响,水钠潴留血容量增加时,BNP释放增加^[14-15]。N末端B型钠尿肽前体(NT-proBNP)主要通过肾脏排泄,肾功能是影响其血清水平的重要因素^[16],而尿毒症患者因常合并水钠潴留、血容量升高、心脏扩大等,BNP水平显著升高。本研究结果也显示,尿毒症患者cTnT、BNP较健康者明显升高。终末期肾衰竭患者cTnT升高的机制尚未明确,可能与以下因素有关:①肾脏排泄减少,尿毒症毒素

蓄积致心肌损伤;②慢性炎症反应及水、电解质紊乱致慢性心肌损伤;③血管内皮功能障碍致心肌微小损伤等。另外,HD患者因容量负荷波动及微循环结构改变等可致心肌损伤发生率增加。有研究表明,严重感染/感染性休克患者血浆BNP升高^[17],心肌抑制可能是主要原因^[18-19]。

MHD患者心血管系统改变主要表现为左室功能减退、左室扩大、左室肥厚。HD患者左室舒张功能减退的原因多是由于水钠潴留和高血压引起的血流动力学改变,进而出现心肌肥厚,左室舒张顺应性降低,左心室充盈减少等心脏结构改变^[20]。LVMI是超声评测左室肥厚的有效指标。左室肥厚与尿毒症及HD时持续的负荷增加有关,左室肥厚患者易发生心衰、心律失常、脑血管意外。研究表明,HFHD治疗1年后,患者左心房内径(LAD)、LVEDD、LVPWT、LVMI呈下降趋势^[21]。本研究显示,HFHD治疗6个月BNP、cTnT、LVPWT、IVST、LVMI显著减低,LVEF明显升高,且HFHD在改善尿毒症患者心功能方面较普通HD有明显优势,表明HFHD可减少上述心血管事件的发生,从而降低病死率。

MHD患者往往存在严重的骨矿物质代谢紊乱,高甲状旁腺激素、高纤维细胞生长因子-23(FGF-23)可对心脑血管有显著影响,且MHD患者存在微炎症状态、高同型半胱氨酸血症等情况^[22-23]。上述物质和炎性因子均为中大分子,普通透析手段对其清除有限;而HFHD联合HP能更有效地清除中大分子毒素^[24]。国外一项荟萃分析显示,与低通量透析比较,HFHD可减少心血管相关病死率^[25]。此外,HFHD患者的生活质量评分较普通HD患者高^[26]。

HFHD系指采用对溶质和水等物质具有很高通透性能的透析器进行HD的方法,应用高通量高生物相容性膜透析器可以明显减少血膜反应、氧化应激和炎症反应,可能减轻对心肌细胞的损伤,延缓心肌细胞肥大及心室重构,从而改善心脏的舒张功能^[27]。以弥散作用清除小分子毒素,以对流作用清除低分子蛋白,同时以吸附的形式清除中大分子溶质。HFHD通过对中分子的清除可以改善MHD患者的血压、贫血、微炎症状态、钙磷代谢紊乱,通过清除心血管相关蛋

白结合毒素等,进而减轻对心血管的损伤,改善心血管的结构及功能,减少CVD。HFHD设备为常规透析机,治疗费用低,有更好的性价比,故在临床推广实施较为容易。

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