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低钠透析联合血液透析滤过对终末期肾脏病合并顽固性高血压患者血压节律、钙磷代谢的影响

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摘要 目的:探讨低钠血液透析(hemodialysis,HD)联合血液透析滤过(Hemodiafiltration,HDF)对终末期肾脏病合并顽固性高血压的透析患者血压节律、钙磷代谢的影响。**方法:**将 62 例终末期肾脏病合并顽固性高血压患者随机分为治疗组和对照组,对照组应用常规 HD 治疗,每周 3 次,每次 4 h,治疗组低钠联合 HDF 治疗,每周 1 次,3 个月后进行效果评价。比较两组治疗前后血压昼夜节律、钙磷代谢变化及不良反应的发生情况。**结果:** 治疗后, 治疗组 24 h 收缩压 (systolic blood pressure,24 h SBP)、24 h 舒张压(diastolic blood pressure,24hDBP)、日间收缩压(day systolic blood pressure,dSBP)、日间舒张压(day diastolic blood pressure,dSBP)、夜间收缩压(night systolic blood pressure,nSBP)、夜间舒张压(night diastolic blood pressure,nSBP)均较治疗前明显下降,且明显低于对照组(P<0.05);对照组除 nSBP 外,其余血压指标治疗前后比较差异均无统计学意义(P>0.05)。治疗后,治疗组血 Ca 水平较治疗前明显升高,且显著高于对照组,而血 P、PTH 水平较治疗前明显降低,且均明显低于对照组(P<0.05)。治疗组和对照组不良反应发生率分别为 16.1%、12.9%,两组比较差异无统计学意义(P>0.05)。**结论:**低钠 HD 联合 HDF 治疗终末期肾脏病合并顽固性高血压患者可有效改善钙磷代谢并促进血压节律恢复。

关键词:低钠透析;血液透析滤过;顽固性高血压;血压节律;钙磷代谢

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Effect of Low Sodium Hemodialysis Combined with Hemodiafiltration on the Blood Pressure Rhythm and Calcium Phosphorus Metabolism in Patients with Resistant Hypertension

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ABSTRACT Objective: To explore the clinical effect of low sodium hemodialysis(HD) combined with hemodiafiltration(HDF) on the blood pressure rhythm and calcium phosphorus metabolism of patients with resistant hypertension. **Methods:** 62 uremia patients combined with resistant hypertension were randomly divided into two groups. The control group (n=31) was treated with traditional HD alone for 2h per time, 3 times per week, and combined group (n=31) was treated with low sodium HD and HDF, once per week. The effect was evaluated at 3 months after treatment, the changes of blood pressure circadian rhythm, calcium phosphate metabolism before and after treatment as well as the incidence of adverse reactions during HD were compared between two groups. **Results:** The indicators of blood pressure rhythm including 24h systolic blood pressure (24hSBP), 24h diastolic blood pressure (24hDBP), day systolic blood pressure (dSBP), day diastolic blood pressure (dSBP), night systolic blood pressure (nSBP), night diastolic blood pressure (nSBP) of treatment group were significantly reduced after treatment and were significantly lower than those of the control group (P<0.05). All the indicators of blood pressure rhythm except nSBP in control group showed no significant difference between before and after treatment (P>0.05). After treatment, the levels of blood Ca in the treatment group was obviously increased, the levels of blood P, PTH were obviously decreased compared with control group (P<0.05). The incidence of adverse reactions in treatment group and control group was 16.1% and 16.1% respectively, which showed no significant difference (P>0.05). **Conclusions:** Low sodium HD combined with HDF can effectively remove the toxic metabolites, promote the blood pressure rhythm recovery, regulate metabolism of calcium phosphate in treating the uremia patients with resistant hypertension.

Key words: Low sodium hemodialysis; Hemodiafiltration; Resistant hypertension; Blood pressure rhythm; Calcium phosphorus metabolism

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前言

顽固性高血压是终末期肾脏病维持性血液透析(maintenance hemodialysis, MHD)患者常见的并发症，约 50~90%的终末期肾脏病患者合并高血压，且不易控制，而顽固性高血压可进一步诱发心脑血管并发症，严重影响患者的预后[1-3]。血液透析(HD)有助于清除终末期肾脏病小分子毒素，纠正水和电解质紊乱，改善内环境，但对患者的血流动力学影响较大[4-6]。目前，临床上主要通过限制钠盐摄入、控制干体质量、降压药物治疗等措施控制血压，但部分患者效果并不理想。有研究显示相对性低钠透析可提高水钠的清除力度，且对电解质、血浆渗透压的影响较小，有助于控制患者血压、减少透析的不良反应[7-10]，但其对终末期肾脏病合并顽固性高血压患者的疗效研究仍较少。因此，本研究采用低钠 HD 联合血液透析滤过(HDF)治疗终末期肾脏病合并顽固性高血压患者，探讨了其对血压昼夜节律、钙磷代谢的影响。

1 资料与方法

1.1 一般资料

选择 2014 年 1 月 ~2016 年 12 月在上海市第一人民医院宝山分院肾内科收治的接受 MHD 的终末期肾脏病合并顽固性高血压患者，共 62 例。入组标准：(1)符合终末期肾脏病、顽固性高血压的诊断标准。(2)MHD 时间大于 3 个月，近期无心血管不良事件发生；(3) 排除肾病高血压以外的继发性高血压，排除贫血、肿瘤，排除严重心律失常、心肌梗死、心衰等心血管并发症。其中，男 39 例，女 23 例；年龄 39~75(51.8± 4.1)岁；MHD 时间 8~41(20.7± 3.7)个月；体质量 51~78(56.1± 7.5)kg；原发病：慢性肾小球肾炎 29 例，糖尿病肾病 18 例，高血压肾病 11 例，系性红斑狼疮肾炎 4 例。将患者按照随机数字表法，分为治疗组和对照组，各 31 例。两组患者在性别、年龄、原发病、MHD 时间、体质量等比较均无统计学差异(P>0.05)，具有可比性。

1.2 诊断标准

1.2.1 终末期肾脏病 (End Stage of Renal Disease，ESRD) 终末期肾脏病在世界范围内发病率高达十万分之一，是慢性肾脏病(CKD)进展至 5 期后不得不进入替代治疗的阶段[11]。

1.2.2 终末期肾脏病顽固性高血压 经充分透析达干体质量，并联合 3 种以上降压药(利尿剂、α 或 β 受体阻滞剂、ACEI 抑制剂、钙拮抗剂)，运用最佳剂量后，仍不能将血压控制至正常范围(<140/90 mmHg)[12]。

1.3 治疗方法

治疗组采用低钠 HD 联合 HDF，对照组采用常规 HD 治疗。透析血流量 230~260 mL/min，透析液流量 500 mL/min，采用碳酸氢盐透析液，其中钾 2.0 mmol/L、钙 1.5 mmol/ L，治疗组和对照组钠离子浓度分别为 135 mmol/L、138 mmol/L。透析液温度 37℃。每周 3 次，每次 4 h，透析过程禁止饮食。治疗组在 HD 的同时给予 HDF 治疗，每周 1 次。HD 采用费森尤斯 4008b 血液透析机、HDF 采用费森尤斯 4008S 血液透析机，HD 采用费森尤斯 fx8 透析器(聚砜膜)，表面积 1.4 m^2，透析液流量 500 mL/min；HDF 采用日本旭化成 APS-15u 透析器 (聚砜膜)，表面积 1.5 m^2，透析液流量 500 mL/min。透析过程中如血压明显升高时可口含或口服降压药物，血压明显降低时可给予高渗葡萄糖静脉推注等。治疗期间，所有患者低盐饮食，降压药的服用方案与入组前一致，未做调整，治疗 3 个月后进行效果评价。

1.4 观察指标

1.4.1 动态血压监测 采用动态血压监测仪(美国 SPACELAB 公司)进行 24 h 动态血压监测，在透析前一天、治疗 3 个月后的清晨 7:00- 次日 7:00 各 1 次。采用袖带式，日间血压每隔 30 min、夜间每隔 60 min 测量 1 次，记录患者 24 h、日间、夜间的平均收缩压与舒张压(24hSBP、24hDBP、dSBP、dDBP、nSBP、nDBP)。监测数据中 24 h 无中断与可读数据需大于 90%。

1.4.2 钙磷代谢指标检测 分别于治疗前、后采集空腹静脉血 3 mL，利用自动生化分析仪测定血钙(Ca)、血磷(P)，利用化学发光法测定甲状旁腺激素(PTH)水平。

1.4.3 不良反应 记录两组透析治疗期间低血压、低血糖、心律失常、心力衰竭等不良反应的发生情况。

1.5 统计学方法

采用 SAS 8.2 版统计学软件。计量资料以均数± 标准差($\bar{x}\pm s$)表示，组间比较采用成组和配对 t 检验，计数资料以例数表示，采用 x^2 检验，P<0.05 视为差异有统计学意义。

2 结果

2.1 两组治疗前后血压节律变化的比较

两组治疗前 24hSBP、24hDBP、dSBP、dDBP、nSBP、nDBP 比较差异均无统计学意义(P>0.05)；治疗后，治疗组 24hSBP、24hDBP、dSBP、dDBP、nSBP、nDBP 均明显下降，且明显低于对照组，差异有统计学意义(P<0.05)。对照组除 nSBP 外，其余血压节律指标治疗前后比较差异均无统计学意义(P>0.05)。见表 1。

2.2 两组治疗前后钙磷代谢指标比较

治疗前，两组血 Ca、P、PTH 水平比较差异均无统计学意义(P>0.05)；治疗后，治疗组血 Ca 水平较治疗前明显升高，且显著高于对照组，而血 P、PTH 水平较治疗前明显降低，且与对照组比较差异均有统计学意义(P<0.05)。见表 2。

2.3 两组不良反应发生情况的比较

两组治疗期间的主要不良反应为低血压、低血糖、心律失常、心力衰竭等，治疗组和对照组不良反应发生率分别为 16.1%(5/31)、12.9%(4/31)，二者比较差异无统计学意义(P>0.05)，见表 3。

3 讨论

目前，终末期肾脏病合并顽固性高血压在国内外尚无相关指南或专家共识，普遍认为是患者经充分透析达到干体质量，并足量联用 3 种或以上降压药后仍无法将血压控制在目标值水平[13-15]。相关研究显示 86%终末期肾脏病患者存在高血压，仅 30%左右患者的血压能得到有效控制，其余患者即使应用降压药物后血压仍无法达标[16-18]。我们在临床实践中发现完全消除 HD 患者的水钠潴留相当困难，主要原因有三个方面：一是肾功能衰竭导致患者尿量减少甚至无尿；二是间断性的短时间(4 h)透析不符合正常的生理规律，无法完全清除水钠潴留；三是我国人群的饮食习惯普遍高钠，难以长期严格限制钠盐(<3 g/d)摄入[19,20]。终末期肾脏病顽固性高血压的发病机制尚不十分清

表 1 两组治疗前后血压节律变化比较($\bar{x}\pm s$)

Table 1 Comparison of the blood pressure rhythm before and after treatment between two groups

Index	Control group(N=31)		Treatment group(N=31)	
	Before treatment	After treatment	Before treatment	After treatment
24hSBP	166.2± 13.7	164.64± 10.5	164.6± 12.8	136.3± 10.9[◎◇]
24hDBP	103.3± 18.4	99.1± 17.6	105.4± 8.3	82.5± 7.2[◎◇]
dSBP	171.1± 12.5	167.4± 12.2	172.6± 11.8	141.3± 10.4[◎◇]
dDBP	106.3± 18.5	102.1± 17.7	107.8± 8.3	95.7± 8.2[◎◇]
nSBP	163.6± 10.2	155.2± 9.4[◎]	164.1± 10.5	134.4± 9.8[◎◇]
nDBP	99.5± 8.4	95.3± 6.8	100.4± 9.1	77.5± 6.2[◎◇]

Note: Compared within groups before treatment ◎ P<0.05; Compared between groups after treatment, ◇ P<0.05.

表 2 两组治疗前后钙磷代谢指标比较($\bar{x}\pm s$)

Table 2 Comparison of the calcium phosphorus metabolism before and after treatment between two groups

Index	Control group(N=31)		Treatment group(N=31)	
	Before treatment	After treatment	Before treatment	After treatment
Ca(mmol/L)	1.78± 0.37	1.74± 0.25	1.72± 0.38	2.03± 0.29[◎◇]
P(mmol/L)	1.63± 0.44	1.51± 0.36	1.74± 0.43	1.35± 0.32[◎◇]
PTH(pg/mL)	551.13± 116.86	527.43± 102.72	549.60± 121.23	417.22± 180.43[◎◇]

Note: Compared within groups before treatment ◎ P<0.05; Compared between groups after treatment, ◇ P<0.05.

表 3 两组不良反应发生情况的比较(例)

Table 3 Comparison of the incidence of adverse reactions between two groups

Groups	N	Hypotension	Hypoglycemia	Cardiac arrhythmia	Heart failure
Treatment group	31	3	0	1	1
Control group	31	2	1	1	0

楚,主要与钠潴留、血管内收缩物质的增加、舒活血管物质的减少有关，与此同时 HD 期间患者体内血管紧张素 - 肾素 - 醛固酮系统(RAS)激活、以及内皮素浓度增加、血钙降低也可能对高血压造成影响[21,22]。因此,控制 HD 患者的高血压,改善钙磷代谢,对于减少心血管疾病并发症的发生和改善预后具有十分重要的意义。

HD 作为一种传统的血液净化手段对血液中小分子物质的清除效果较好,但对中、大分子则效果欠佳,且对减轻 MHD 患者水钠潴留帮助不大,同时由于炎性介质种类繁多、网络复杂,单纯依靠 HD 的清除效果并不令人满意。故即使充分透析后,顽固性高血压也无法得到有效控制[23]。HDF 是在 HD 基础上采用高通透性滤过膜,利用弥散、对流及吸附等多种机制对不同大小的物质都能进行有效清除，综合了 HD 和血液滤过的优点,更好地模拟肾小球的过滤功能,从而达到最佳血液净化的目的[24,25]。为了尽可能最大限度消除水钠潴留,控制血压,本研究在降压药物的基础上,采用相对低钠透析(135 mmol/L),结果显示:治疗组在治疗后血压得到有效控制,且明显低于对照组,且并未增加低血压、低血糖、心律失常、心力衰竭等并发症的发生。低于正常血钠浓度的低钠透析液易引发 HD 过程中恶心、呕吐、低血压等不良反应,而相对低钠 HD 则通过将透析液中钠离子浓度调整至正常范围内的相对低水平,可在确保电解质及血浆渗透压稳定的前提下,促进体内水钠的清除[26]。翟丽惠等[27]显示透析液钠离子浓度在 132 mmol/L 对高血压患者的血清钠离子浓度及心率无显著影响。因此,选择合理的透析液钠离子浓度对维持机体的容量平衡和调节血压节律至关重要。

钙磷代谢障碍是终末期肾脏病 MHD 患者的主要表现,机制复杂,涉及到低钙、磷潴留、PTH 作用等多种因素之间的相互作用等[28]。由肾小球滤过减少、肾小管内在特性改变导致机体的高磷血症,可诱发转移性钙化与组织损伤,是 MHD 患者的一种较为顽固的症状。本研究结果表明,常规血液透析无法有效降低患者血 P、PTH 水平,而低钠 HD 联合 HDF 则可有效降低患者血 P、PTH 水平、纠正低钙血症，从而缓解患者全身症状。张继波等[29]研究显示,低钠 HD 比传统 HD 能较好改善 MHD 患者矿物质和钙磷代谢紊乱，长期治疗有助于改善骨代谢。Flanigan 等[30]研究认为有相当比例的 HD 患者未能满意的控制钙磷代谢紊乱,可联合血液透析滤过及低钠 HD 等透析方式来加强对钙磷的控制。

综上所述，低钠 HD 联合 HDF 治疗终末期肾脏病合并顽固性高血压可实现优势互补，可有效清除体内毒性代谢产物,促进血压节律恢复,调节钙磷代谢。鉴于本研究病例数有限,观察时间尚短,该方案对终末期肾脏病合并顽固性高血压患者远期预后的影响有待进一步深入研究。

参 考 文 献(References)

[1] López-Huamanrayme E, Atamari-Anahui N, Pereira-Victorio CJ. Poor sleep quality in patients with resistant hypertension: is there an association?[J]. Rev Esc Enferm USP, 2016, 50(2): 194-195

[2] Marshall MR, Hawley CM, Kerr PG, et al. Home hemodialysis and mortality risk in Australian and New Zealand populations [J]. Am J Kidney Dis, 2011, 58(5): 782-793

[3] Nishimura M, Tokoro T, Nishida M, et al. Sympathetic overactivity and sudden cardiac death among hemodialysis patients with left ventricular hypertrophy[J]. Int J Cardiol, 2010, 142(1): 80-86

[4] Schlaich MP, Schultz C, Shetty S. Renal denervation for resistant hypertension: closing in on potential confounders[J]. J Hypertens, 2016, 34(8): 1505-1506

[5] Baigent C, Landray MJ, Reith C, et al. The effects of lowering LDL cholesterol with simvastatin plus ezetimibe in patients with chronic kidney disease (Study of Heart and Renal Protection): a randomised placebo-controlled trial[J]. Lancet, 2011, 377(9784): 2181-2192

[6] Palmer SC, Craig JC, Navaneethan SD, et al. Benefits and harms of statin therapy for persons with chronic kidney disease: a systematic review and meta-analysis[J]. Ann Intern Med, 2012, 157(4): 263-275

[7] Kim SM, Kim M, Lee EK, et al. The effect of zinc deficiency on salt taste acuity,preference, and dietary sodium intake inhemodialysis patients[J]. Hemodial Int, 2016, 20(3): 441-446

[8] Prka I, Balenovic D, Cavri G, et al. Importance of standardized stepwise screening in patients with resistant hypertension [J]. Acta Med Croatica, 2014, 68(2): 111-115

[9] Titze J, Müller DN, Luft FC. Taking another "look" at sodium[J]. Can J Cardiol, 2014, 30(32): 473-475

[10] Simon D, Ola C, Ole S, et al. The effects of low-sodium peritoneal dialysis fluids on blood pressure, thirst and volume status[J]. Nephrol Dial Transplant, 2009, 24(5): 1609-1617

[11] Hall Y N, Chertow G M. End stage renal disease [J]. Clinical Evidence, 2006, 46(15): 1171

[12] 张秀安,吴彼得,连学坚,等. 血液透析及与血液透析滤过联合治疗终末期肾脏病顽固性高血压疗效比较[J].现代诊断与治疗, 2011, 22(1): 19-21
Zhang Xiu-an, Wu Bi-de, Lian Xue-jian, et al. Comparison on Effects of Hemodialysis and Its Combination with Hemo-diafiltration on Intractable Hypertension[J]. Mod Diagn Treat, 2011, 22(1): 19-21

[13] Dlesk A, Kamensky G, Stefanik M, et al. Treatment efficiency of resistant hypertension in cardiologist's office [J]. BratislLek Listy, 2014, 115(1): 25-29

[14] Jair MM, Liz YB, Sumi S, et al. Effect of Lowering Dialysate Sodium Concentration on Interdialytic Weight Gain and Blood Pressure in Patients Undergoing Thrice-Weekly In-center Nocturnal Hemodialysis: A Quality Improvement Study [J]. Am J Kidney Dis, 2011, 58(6): 956-963

[15] Manfred H, Angelo K, Rajiv S, et al. Dialysate Sodium Concentration and the Association with Interdialytic Weight Gain, Hospitalization, and Mortality[J]. Clin J Am Soc Nephrol, 2012, 7(1): 92-100

[16] Gijón-Conde T, Graciani A, López-García E, et al. Impact of ambulatory blood pressure monitoring on control of untreated, undertreated, and resistant hypertension in older people in spain [J]. J Am Med Dir Assoc, 2015, 16(8): 668-673

[17] Parker T, Hakim R, Nissenson AR, et al. Dialysis at a crossroads: 50 years later[J]. Clin J Am Soc Nephrol, 2011, 6(2): 457-461

[18] Koc Y, Unsal A, Kayabasi H, et al. Impact of volume status on blood pressure and left ventricle structure in patients undergoing chronic hemodialysis[J]. Ren Fail, 2011, 33(4): 377-381

[19] Li H, Wang SX. Improvement of hypertension and LVH in maintenance hemodialysis patients treated with sustained-release isosorbide mononitrate[J]. J Nephrol, 2011, 24(2): 236-245

[20] Inal S, Erten Y, Akbulu G, et al. Salt intake and hypervolemia in the development of hypertension in peritoneal dialysis patients [J]. Adv Perit Dial, 2012, 28(12): 10-15

[21] Chen Xi, Yu Da-chuan, Sun Xiao-li, et al. Clinical treatment countermeasures Maintenance hemodialysis patients of high blood pressure[J]. Chinese Journal of Gerontology, 2012, 32(5): 2150-2151

[22] Marshall MR, Dunlop JL. Are dialysate sodium levels too high Semin Dial[J]. Semin Dial, 2012, 25(3): 277-283

[23] Santos SF, Peixoto AJ. Revisiting the dialysate sodium prescription as a tool for better blood pressure and interdialytic weight gain management in hemodialysis patients [J]. Clin J Am Soc Nephrol, 2008, 3(2): 522-530

[24] EftimovskaOtovicN, Stojceva-Taneva O, Grozdanovski R, et al. Clinical effects of standard and individualized dialysate sodium in patients on maintenance hemodialysis [J]. Open Access Maced J Med Sci, 2016, 4(2): 248-252

[25] Gao Zeng-hui, Yang Dong-hua. Clinical observation of hemodialysis filtration treatment of maintenance hemodialysis patients with resistant hypertension[J]. China Practical Medical, 2015, (6): 147-148

[26] 赵艺欣,刘静,李明旭,等.低钠透析联合血液透析滤过对终末期肾脏病合并顽固性高血压患者血压节律、心功能及毒性代谢产物的影响[J].临床和实验医学杂志, 2017, 16(4): 375-378
Zhao Yi-xin, Liu Jing, Li Ming-xu, et al. Effect of low - sodium dialysis combined with hemodiafiltration on the blood pressure rhythm,cardiac function as well as toxic and side metabolites in patients with uremia and resistant hypertension[J]. Journal of Clinical and Experimental Medicine, 2017, 16(4): 375-378

[27] Zhai Li-hui, Li Jun. The short-term effect observation of Adjustable sodium dialysis in 76 cases of maintenance hemodialysis patients with high blood pressure [J]. Shaanxi Medical Journal, 2011, 40(1): 72-73

[28] 白石,吕红红,杨峰, 等.不同血液透析方法对终末期肾病患者钙磷代谢的影响[J].现代生物医学进展, 2012, 12(28): 5484-5486
Bai Shi, Lv Hong-hong, Yang Feng, et al. Different Hemodialysis for End-stage Renal Disease Patients Effects on Calcium Phosphorus Metabolism[J]. Progress in Modern Biomedicine, 2012, 12(28): 5484-5486

[29] 张继波,熊有明,覃娜莎, 等.低钠透析联合血液透析滤过对终末期肾脏病合并顽固性高血压患者血压昼夜节律变化的影响[J].广东医学, 2014, 35(24): 3857-3860
Zhang Ji-bo, Xiong You-ming, Qin Na-sha, et al. Effect of low sodium hemodialysis combined with hemodiafiltration on the blood pressure rhythm in patients with end stage renal disease [J]. Guangdong Medicine, 2014, 35(24): 3857-3860

[30] Flanigan MJ. Role of sodium in hemodialysis [J]. Kidney Int Suppl, 2012, 76(23): S72-S78