

doi: 10.3978/j.issn.2095-6959.2017.03.012

View this article at: http://dx.doi.org/10.3978/j.issn.2095-6959.2017.03.012

超滤量及透析液钙浓度对透析前后血钙的影响

郑美洁¹, 林小洁¹, 黄坤², 王铠¹

(民航总医院 1. 透析中心; 2. 消化内科, 北京 100123)

[摘要] 目的: 观察不同超滤量及透析液钙浓度对透析前后血钙的影响。方法: 将92名血液透析患者按照使用透析液的Ca²⁺浓度分为Ca-1.25组和Ca-1.5组, 每组再按照透析超滤量分为两个亚组, Ca-1.25组分为A, B组, Ca-1.5组分为C, D组, A组、C组超滤量<3 kg, B组、D组超滤量≥3 kg。检测透析前后各组血清总钙、血磷、透前甲状旁腺激素(plasma parathyroid hormone, PTH)浓度并进行相关分析。结果: 各组透析后血钙浓度较透析前升高, 差异具有统计学意义($P<0.01$), B组、D组透析前后血钙变化分别较A组、C组明显, 差异具有统计学意义($P<0.01$), Ca-1.5组血钙较Ca-1.25组高, 两组透析前后血钙变化差异无统计学意义。A, B组及C, D组中血磷及PTH均无差异, Ca-1.25组血磷及PTH均高于Ca-1.5组, 差异具有统计学意义($P<0.05$)。结论: 使用1.25和1.5 mmol/L的Ca²⁺透析液均会使钙向体内转运, 超滤量与钙转运量成正比, 与血磷变化无关, 且使用1.5 mmol/L的Ca²⁺透析液的患者血钙更易达到正常水平, 不刺激PTH分泌。

[关键词] 血液透析; 透析液; 超滤量; 钙转运

Effect of ultrafiltration volume and dialysate calcium concentration on serum calcium in pre- and post-hemodialysis

ZHENG Meijie¹, LIN Xiaojie¹, HUANG Kun², WANG Kai¹

(1. Blood Purification Center; 2. Department of Gastroenterology, Civil Aviation General Hospital, Beijing 100123, China)

Abstract **Objective:** To investigate the effect of different ultrafiltration volume and dialysate calcium concentration on serum calcium in pre- and post-hemodialysis in maintenance hemodialysis patients. **Methods:** Ninety-two patients were divided into Ca-1.25 group and Ca-1.5 group according to their dialysate calcium concentration, and they were divided into subgroups according to ultrafiltration volume respectively, A, B subgroups belong to Ca-1.25 group, and C, D subgroups belong to Ca-1.5 group, patients with ultrafiltration volume less than 3.0 kg were as subgroup A in Ca-1.25 group and subgroup C in Ca-1.5 group, patients with ultrafiltration volume equal or greater than 3.0 kg were as subgroup B in Ca-1.25 group and subgroup D in Ca-1.5 group. To measure serum calcium, serum phosphate and plasma parathyroid hormone (PTH) concentrations in pre- and post-hemodialysis respectively were detected and analyzed. **Results:** Serum calcium concentrations were higher in post- than that in

收稿日期 (Date of reception): 2016-12-13

通信作者 (Corresponding author): 王铠, Email: wangkaicaac@126.com

pre-hemodialysis, the difference was statistically significant ($P < 0.01$), variations of them were more obvious in B and D subgroups than those in A and C subgroups, the difference was statistically significant ($P < 0.01$), and there were no significant differences in Ca-1.25 group and Ca-1.5 group, and in Ca-1.5 group they were higher than in Ca-1.25 group. Serum phosphate and PTH were no differences in A and B subgroups, C and D subgroups, and were higher in Ca-1.25 group than in Ca-1.5 group, $P < 0.05$. **Conclusion:** Calcium mass transfers from dialysate to blood during the hemodialysis using dialysate containing 1.25 mmol/L or 1.5 mmol/L calcium, ultrafiltration volumes are positively related with variations of serum calcium concentrations, but no relation with variations of serum plasma concentrations, and using dialysate containing 1.5 mmol/L calcium make patients more healthy.

Keywords hemodialysis; dialysate; ultrafiltration volume; calcium transport

慢性肾脏病矿物质和骨代谢异常(chronic kidney disease-mineral and bone disorder, CKD-MBD)对于维持性血液透析(maintenance hemodialysis, MHD)患者的生活质量有着重要影响。随着肾功能下降,毒素在体内蓄积,活性维生素D代谢异常,导致MHD患者普遍存在钙磷代谢紊乱及甲状旁腺激素(parathyroid hormone, PTH)分泌异常^[1-2]。如何改善这一状况一直是国内外学者研究的热点,但对于透析过程中超滤量是否影响血钙的变化未有较多关注,本研究回顾了单次透析前后不同超滤量及不同钙浓度透析液及对血钙的影响。

1 对象与方法

1.1 对象

将于民航总医院透析中心接受MHD治疗的92例患者纳入本次研究,纳入标准:年龄18~80岁,性别不限,24 h尿量 < 100 mL,病情稳定且一般状况良好,规律血液透析3次/周,4 h/次,透析通路均为动静脉内瘘。排除标准:现为急性感染期、风湿免疫性疾病活动期、肿瘤、恶液质、低白蛋白血症、甲状旁腺切除术后、合并原发性甲状旁腺功能亢进、多发性骨髓瘤等骨代谢异常疾病、严重的心脏疾病(室性心律失常等)、动静脉内瘘流量欠佳。原发病分别为糖尿病肾病32例,高血压肾损害15例,慢性肾小球肾炎28例,多囊肾10例,药物相关性肾损害4例,泌尿系肿瘤3例。本研究已获得医院伦理委员会批准。

1.2 方法

92例患者规律口服碳酸钙400 mg \times 3次/d,骨化三醇0.25 μ g/d(透析过程中未使用影响血钙的药物),按照使用透析液的Ca浓度分为Ca-1.25组和Ca-1.5组,其中Ca-1.25组42例,男20例,女22例,

年龄(60 \pm 15)岁,透析龄(69 \pm 43)个月;Ca-1.5组50例,其中男27例,女23例,年龄(56 \pm 12)岁,透析龄(68 \pm 50)个月,每组再按照透析超滤量分为两个亚组,A组、C组超滤量 < 3 kg,B组、D组超滤量 ≥ 3 kg。

1.3 器材及参数设定

透析机为4008或4008S,由德国Fresenius公司生产;透析器为FX100,聚醚砜膜,透析膜表面积2.2 m²,超滤系数为73 mL/h/mmHg;血流量280~300 mL/min;透析液流量500 mL/min;透析过程中用普通肝素抗凝。

1.4 标本采集及检测

透析前血标本于动静脉内瘘静脉穿刺处采集,透析后血标本于透析管路动脉端采集,采集标本前逐渐降低血泵速至停泵,采集标本时为停泵状态,全血标本提取血清后采用偶氮神Ⅲ法测定血清中总钙浓度(正常值范围2.11~2.52 mmol/L),采用磷钼酸盐法测定血清中磷浓度(正常值范围0.85~1.51 mmol/L),采用化学发光法测定血清中全段甲状旁腺激素(iPTH)浓度(正常值范围12~88 pg/mL)。

1.5 统计学处理

各组数据用均数 \pm 标准差($\bar{x} \pm s$)表示,使用SPSS 19.0软件进行统计学分析,各观察指标比较用配对 t 检验, $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 Ca-1.25 透析液透析前后血钙的比较

各组患者的年龄、性别、透析龄的差异无统计学意义。A组透析前钙与透析后钙相比有差异,透析后钙高于透析前;B组透析前钙与透析后钙

相比,透析后钙高于透析前;A、B两组相比透析前钙无差异,透析后钙有差异,且透析后钙B组(2.29 ± 0.17) mmol/L较A组(2.10 ± 0.09) mmol/L高;A、B两组透析前后血钙变化(透析后钙-透前钙)相比有差异,且B组(0.36 ± 0.16) mmol/L变化较A组(0.18 ± 0.10) mmol/L明显(表1)。

2.2 Ca-1.5 透析液透析前后血钙的比较

C组透前钙与透析后钙相比有差异,透析后钙高于透析前;D组透析前钙与透析后钙相比有差异,透析后钙高于透析前;C、D两组相比透析前钙无差异,透析后钙有差异,且D组透析后钙(2.59 ± 0.14) mmol/L高于C组(2.48 ± 0.15) mmol/L;C、D两组透析前后血钙变化(透析后钙-透前钙)相比有差异,且D组(0.40 ± 0.22) mmol/L变化较C组(0.21 ± 0.16) mmol/L明显(表2)。

2.3 Ca-1.25 与 Ca-1.5 透析液透析前后血钙的比较

Ca-1.25组透析前钙与透析后钙相比有差异,透析后钙高于透析前;Ca-1.5组透析前钙与透析后钙相比有差异,透析后钙高于透析前;Ca-1.25和Ca-1.5两组相比透析前钙有差异,透析后钙差异有统计学意义,且均为Ca-1.5组高于Ca-1.25组,但两组透析前后血钙变化(透析后钙-透析前钙)相比差异无统计学意义(表3)。

2.4 各组透析前后血磷及透析前PTH的比较

A、B两组相比,透析前磷、透析后磷、透析前PTH差异均无统计学意义(表4)。C、D两组相比,透析前磷、透析后磷、透析前PTH差异均无统计学意义(表5)。Ca-1.25和Ca-1.5两组相比,透析前磷、透析后磷及透析前PTH差异均有统计学意义,且均为Ca-1.25组高于Ca-1.5组(表6)。

表1 1.25 mmol/L的Ca²⁺透析液透析前后血钙比较

Table 1 Comparison of serum calcium concentrations with a dialysate calcium concentration of 1.25 mmol/L between pre- and post-hemodialysis

组别	透析前钙/(mmol·L ⁻¹)	透析后钙/(mmol·L ⁻¹)	t	P	透析后钙-透析前钙/(mmol·L ⁻¹)
A组	1.92 ± 0.15	2.10 ± 0.09	-5.477	<0.001	0.18 ± 0.10
B组	1.94 ± 0.14	2.29 ± 0.17	-10.707	<0.001	0.36 ± 0.16
t	-0.380	-3.441			-3.247
P	0.706	0.002			0.003

表2 1.5 mmol/L的Ca²⁺透析液透析前后血钙比较

Table 2 Comparison of serum calcium concentrations with a dialysate calcium concentration of 1.5 mmol/L between pre- and post-hemodialysis

组别	透析前钙/(mmol·L ⁻¹)	透析后钙/(mmol·L ⁻¹)	t	P	透析后钙-透析前钙/(mmol·L ⁻¹)
C组	2.28 ± 0.19	2.48 ± 0.15	-6.235	<0.001	0.21 ± 0.16
D组	2.19 ± 0.21	2.59 ± 0.14	-10.669	<0.001	0.40 ± 0.22
t	1.775	-3.367			-4.476
P	0.081	0.001			<0.001

表3 1.25与1.5 mmol/L的Ca²⁺透析液透析前后血钙比较

Table 3 Comparison of serum calcium concentrations with dialysate calcium concentrations of 1.25 and 1.5 mmol/L between pre- and post-hemodialysis

组别	透析前钙/(mmol·L ⁻¹)	透析后钙/(mmol·L ⁻¹)	t	P	透析后钙-透析前钙/(mmol·L ⁻¹)
Ca-1.25组	1.93 ± 0.14	2.23 ± 0.18	-10.480	<0.001	0.30 ± 0.17
Ca-1.5组	2.25 ± 0.21	2.53 ± 0.15	-9.906	<0.001	0.29 ± 0.24
t	-7.762	-8.784			0.334
P	<0.001	<0.001			0.739

表4 1.25 mmol/L的Ca²⁺透析液透析前后血磷及透析前PTH比较

Table 4 Comparison of serum phosphate and PTH concentrations with a dialysate calcium concentration of 1.25 mmol/L in pre- and post-hemodialysis

组别	透析前磷/(mmol·L ⁻¹)	透析后磷/(mmol·L ⁻¹)	透析前PTH/(pg·mL ⁻¹)
A组	2.26 ± 0.69	0.77 ± 0.20	523.54 ± 160.68
B组	1.87 ± 0.54	0.79 ± 0.20	450.65 ± 241.03
<i>t</i>	1.735	-0.329	0.872
<i>P</i>	0.089	0.744	0.39

表5 1.5 mmol/L的Ca²⁺透析液透析前后血磷及透析前PTH比较

Table 5 Comparison of serum phosphate and PTH concentrations with a dialysate calcium concentration of 1.5 mmol/L in pre- and post-hemodialysis

组别	透析前磷/(mmol·L ⁻¹)	透析后磷/(mmol·L ⁻¹)	透析前PTH/(pg·mL ⁻¹)
C组	1.61 ± 0.62	0.64 ± 0.16	278.48 ± 276.44
D组	1.83 ± 0.57	0.66 ± 0.20	309.65 ± 259.12
<i>t</i>	-1.451	-0.338	-0.469
<i>P</i>	0.152	0.737	0.641

表6 1.25与1.5 mmol/L的Ca²⁺透析液透析前后血磷及透析前PTH比较

Table 6 Comparison of serum phosphate and PTH concentrations with dialysate calcium concentrations of 1.25 and 1.5 mmol/L in pre- and post-hemodialysis

组别	透析前磷/(mmol·L ⁻¹)	透析后磷/(mmol·L ⁻¹)	透析前PTH/(pg·mL ⁻¹)
Ca-1.25组	1.99 ± 0.61	0.78 ± 0.20	472.74 ± 219.91
Ca-1.5组	1.73 ± 0.60	0.65 ± 0.18	294.30 ± 266.15
<i>t</i>	2.023	3.291	3.317
<i>P</i>	0.046	0.001	0.001

3 讨论

在MHD患者中, 因为肾功能不全导致了肾脏1- α -羟化酶活性下降, 同时血清成纤维生长因子23增多, 其进一步抑制1- α -羟化酶活性, 导致了1,25二羟维生素D活性被抑制, 从而发生低钙血症^[3]。为了纠正这一病理过程, 临床上多予补充钙剂及活性维生素D治疗, 同时调整透析液中钙离子浓度^[4-5]。

钙离子是血清的重要成分, 参与机体多项生理过程, 其浓度应维持在一个稳定的生理范围内, 因此在选择透析液钙离子浓度时, 既要考虑血钙浓度的稳定, 又要兼顾不增加机体钙流失及钙负荷^[6], 即达到一个“钙平衡”状态。美国肾脏病与透析病人生存治疗指南(Kidney Disease Outcomes Quality Initiative, KDOQI)建议: 血液透

析过程中常规使用钙离子浓度为1.25~1.5 mmol/L的透析液。在血液透析过程中, 钙离子的转运主要依靠患者透析前血钙与透析液钙的浓度差, 即钙离子的弥散^[7-8], 但随着高通量透析器使用的日益增多, 观察钙转运时也应考虑对流的作用^[8-11], 不超滤或超滤量较小时, 对流的劣势不能充分发挥, 使得溶质交换效率亦降低^[12]。

在本研究所采用的高通量透析过程中, 可以看到Ca-1.25组中, A, B两亚组的各组内比较, 透析后钙均较透析前钙升高, 差异具有统计学意义($P < 0.01$)。在Ca-1.5组中也观察到同样的结果, C, D两亚组的各组内比较, 透析后钙均较透析前钙升高, 差异具有统计学意义($P < 0.01$)。本研究中所测血钙为血液中总钙浓度, 其约为离子钙浓度的2倍^[11], 可推断出在Ca-1.25组透析前血中离子钙浓度低于透析液, 因此透析液中的钙离子进入血

液中, 透析后血钙升高, 这与张东亮等^[11]研究结果一致, 且其在检测透析前后透析液钙离子浓度时发现: 透析后废液中钙离子浓度较透析前新鲜透析液减少, 由此进一步证明在透析过程中存在钙向体内转运。在A, B两亚组组间比较可见透析前钙两亚组相比无差异, 透析后钙B组明显高于A组, 透析前后血钙变化(透析后钙-透析前钙)B组明显大于A组($P < 0.01$)。在C, D两亚组组间比较可见相同结果, 透析前钙两亚组相比无差异, 透析后钙D组明显高于C组, 透析前后血钙变化(透析后钙-透析前钙)D组明显大于C组($P < 0.01$)。由此可证实在使用Ca-1.25和Ca-1.5透析液的高通量透析患者中, 超滤量影响着钙转运, 其与血钙变化成正相关, 超滤量越大则有更多的钙进入到血液中。在Ca-1.25和Ca-1.5两组比较中, 各组内比较可见透析后钙均高于透析前钙($P < 0.01$), 组间比较可见两组透析前钙有差异, 为Ca-1.5组高于Ca-1.25组, 更接近血钙的正常值范围, 透析后钙比较结果与透析前钙一致, 但两组透析前后血钙变化(透析后钙-透析前钙)相比无差异, 由此说明透析前后血钙变化与透析液钙浓度无关, 但是使用Ca-1.5 mmol/L的透析液更有利于帮助患者达到正常的血钙水平。Basile等^[7-8]研究认为在透析治疗过程中, 透析液钙离子浓度升高, 可以促进血钙浓度升高, 达到一个钙离子轻度升高的钙平衡, 以利于维持血钙在正常范围, 与本研究结果一致。

在A, B两亚组组间比较及在C, D两亚组组间比较可见超滤量对透析前、透析后血磷及透析前PTH均没有影响($P > 0.05$)。但在Ca-1.25和Ca-1.5两组相比透析前、透析后血磷及透析前PTH均为Ca-1.25组高于Ca-1.5组($P < 0.05$), 与Ca-1.25组中透析前血钙较Ca-1.5组低相符合。因磷主要由肾排泄, 而在MHD患者中肾小球滤过率下降, 尿排磷减少, 加上磷结合剂不足或使用不当, 透析不充分等原因造成血磷升高, 蓄积的磷与钙结合形成磷酸钙沉积于软组织, 使血钙进一步下降, 低钙高磷血症可反馈刺激甲状旁腺分泌PTH, 出现提高血钙、降低血磷的慢性代偿的临床表现, 即继发性甲状旁腺功能亢进症(secondary hyperparathyroidism, SHPT)^[1-2]。唐利等^[13]研究认为在长期使用钙离子浓度为1.25 mmol/L的低钙透析液的MHD患者中, 血钙浓度明显下降, 同时PTH升高, 加重SHPT。Spasovski等^[14]研究证实在长期使用低钙透析液的治疗中易并发SHPT。Basile等^[8]认为在使用Ca-1.5 mmol/L透析液时, 可使血钙更接近正常水平, 不刺激PTH分泌。因此在长期使用低钙透析

液的MHD患者应定期监测血钙及PTH, 及时调整治疗方案。本研究为单中心、单次血液透析前后血清总钙变化的临床研究, 而血清总钙仅占人体中钙含量的0.025%^[15], 不能准确反映MHD患者体内总钙含量的状况, 且影响钙平衡的因素很多^[16]。目前缺乏一个简单易操作的方式来确定钙量是流失了还是被骨吸收利用, 也很难给临床工作提供一个精确的钙平衡的控制点^[4], 因此对于透析过程中钙的变化有待进一步深入研究。

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本文引用: 郑美洁, 林小洁, 黄坤, 王铠. 超滤量及透析液钙浓度对透析前后血钙的影响[J]. *临床与病理杂志*, 2017, 37(3): 516-521. doi: 10.3978/j.issn.2095-6959.2017.03.012

Cite this article as: ZHENG Meijie, LIN Xiaojie, HUANG Kun, WANG Kai. Effect of ultrafiltration volume and dialysate calcium concentration on serum calcium in pre- and post-hemodialysis[J]. *Journal of Clinical and Pathological Research*, 2017, 37(3): 516-521. doi: 10.3978/j.issn.2095-6959.2017.03.012