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## 碳酸镧咀嚼片联合依降钙素对血液透析高磷血症患者冠状动脉钙化及血磷水平的影响\*

王 闰<sup>1</sup> 陆春来<sup>2</sup> 王 琦<sup>3</sup> 江 溟<sup>1</sup> 孙建文<sup>4</sup> 孟 慧<sup>1△</sup>

(1 中国人民解放军海军第九〇五医院药剂科 上海 200052; 2.中国人民解放军海军第九〇五医院肾内科 上海 200052;

3 中国人民解放军海军第九〇五医院药剂科静配中心 上海 200052; 4 中国人民解放军海军第九〇五医院检验科 上海 200052)

**摘要目的:** 观察碳酸镧咀嚼片联合依降钙素对血液透析高磷血症患者冠状动脉钙化及血磷水平的影响。**方法:** 选取 2019 年 8 月 ~ 2021 年 3 月我院接收的血液透析高磷血症患者 120 例,采用双色球法,将患者分为对照组(60 例,依降钙素治疗)和观察组(60 例,在对照组基础上结合碳酸镧咀嚼片治疗),对比两组疗效、血磷、血钙、钙磷乘积、全段甲状旁腺激素(iPTH)、成纤维生长因子 23(FGF-23)、冠状动脉钙化积分(CACS),观察两组不良反应发生情况。**结果:** 观察组临床总有效率(91.67%)优于对照组(70.00%)(P<0.05)。两组不良反应发生率组间对比无差异(P>0.05)。观察组治疗结束后血磷、iPTH、血钙、FGF-23、钙磷乘积、CACS 低于对照组(P<0.05)。**结论:** 血液透析高磷血症患者采用碳酸镧咀嚼片联合依降钙素治疗,可延缓冠状动脉钙化,有效降低血磷水平,安全有效。

**关键词:** 碳酸镧咀嚼片; 依降钙素; 血液透析; 高磷血症; 冠状动脉钙化; 血磷

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## Effect of Lanthanum Carbonate Chewable Tablets Combined with Calcitonin on Coronary Artery Calcification and Blood Phosphorus Level in Patients with Hemodialysis Hyperphosphatemia\*

WANG Run<sup>1</sup>, LU Chun-lai<sup>2</sup>, WANG Qi<sup>3</sup>, JIANG Yi<sup>1</sup>, SUN Jian-wen<sup>4</sup>, MENG Hui<sup>1△</sup>

(1 Department of Pharmacy, The 905th Hospital of the PLA Navy, Shanghai, 200052, China;

2 Department of Nephrology, The 905th Hospital of the PLA Navy, Shanghai, 200052, China;

3 Pharmacy Static Distribution Center, The 905th Hospital of the PLA Navy, Shanghai, 200052, China;

4 Department of Clinical Laboratory, The 905th Hospital of the PLA Navy, Shanghai, 200052, China)

**ABSTRACT Objective:** To observe the effect of Lanthanum Carbonate Chewable Tablets Combined with calcitonin on coronary artery calcification and blood phosphorus level in patients with hemodialysis hyperphosphatemia. **Methods:** 120 patients with hemodialysis hyperphosphatemia received by our hospital from August 2019 to March 2021 were selected. The patients were divided into the control group (60 cases, calcitonin treatment) and the observation group (60 cases, Lanthanum Carbonate Chewable Tablets on the basis of the control group treatment) by double color ball method. The curative effects, blood phosphorus, blood calcium, calcium phosphorus product, intact parathyroid hormone (iPTH), fibroblast growth factor 23 (FGF-23) and coronary artery calcification score (CACS) of the two groups were compared, and the adverse reactions of the two groups were observed. **Results:** The total clinical effective rate of the observation group (91.67%) was better than that of the control group (70.00%) (P<0.05). There was no difference in the incidence of adverse reactions in two groups (P>0.05). After treatment, blood phosphorus, iPTH, blood calcium, FGF-23, calcium phosphorus product and CACS in the observation group were lower than those in the control group (P<0.05). **Conclusion:** Lanthanum Carbonate Chewable Tablets combined with calcitonin can delay coronary artery calcification and effectively reduce blood phosphorus level in patients with hemodialysis hyperphosphatemia, which is safe and effective.

**Key words:** Lanthanum Carbonate Chewable Tablets; Calcitonin; Hemodialysis; Hyperphosphatemia; Coronary Artery Calcification; Blood phosphorus

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作者简介:王闰(1977-),女,本科,主管药师,研究方向:药事管理与临床药学,E-mail: wangr0801@163.com

△ 通讯作者:孟慧(1970-),女,本科,主任药师,研究方向:药事管理与临床药学,E-mail: mengh1970@163.com

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## 前言

高磷血症是血液透析患者常见的并发症,可导致软组织及血管钙化<sup>[1]</sup>。有研究显示<sup>[2]</sup>,在血液透析患者中,持续的高磷血症与患者的病死率呈正相关。因此,积极控制血液透析患者的高磷血症发生对于改善其预后有积极的意义。依降钙素的作用主要是治疗骨质疏松,但其同时也具有降低机体血磷、血钙水平的作用,故也常用于高磷血症的治疗<sup>[3]</sup>。现有的研究发现<sup>[4]</sup>,含钙的磷结合剂可导致高钙血症,提高转移性钙化的发生风险。碳酸镧咀嚼片是一种新型磷结合剂,主要特点是不含铝和钙,其中的镧离子可在酸性环境中从碳酸盐中释放出来,与磷结合后生成磷酸镧,随粪便排出,进而降低血磷水平<sup>[5,6]</sup>。本次研究以血液透析高磷血症患者作为研究对象,观察碳酸镧咀嚼片联合依降钙素对冠状动脉钙化及血磷水平的影响。

## 1 资料与方法

### 1.1 一般资料

选取2019年8月~2021年3月我院接收的血液透析高磷血症患者120例,本次研究已经通过我院伦理学委员会批准进行。其中女性51例,男性69例,透析时间范围3~17月,平均透析时间(10.29±1.38)月;年龄范围42~74岁,平均年龄(59.68±4.52)岁;原发疾病:高血压肾小动脉硬化17例,慢性肾小球肾炎35例,糖尿病肾病43例,慢性肾盂肾炎18例,其他7例。采用双色球法,分为对照组(n=60)和观察组(n=60),其中对照组女性26例,男性34例,透析时间范围3~17月,平均透析时间(10.42±2.69)月;年龄范围42~74岁,平均年龄(59.82±4.37)岁;原发疾病:高血压肾小动脉硬化9例,慢性肾盂肾炎8例,糖尿病肾病22例,慢性肾小球肾炎18例,其他3例。观察组女性25例,男性35例,透析时间范围4~15月,平均透析时间(10.16±3.24)月;年龄范围44~73岁,平均年龄(59.53±4.26)岁;原发疾病:高血压肾小动脉硬化8例,慢性肾小球肾炎17例,糖尿病肾病21例,慢性肾盂肾炎10例,其他4例。两组一般资料对比无差异( $P>0.05$ ),具有可比性。纳入标准:(1)行血液透析的肾脏病患者,每周3次,透析时间在3个月及以上;(2)血磷水平≥1.78 mmol/L, 血钙水平正常为2.1~2.64 mmol/L;(3)均为年龄≥18周岁的成年患者;(4)入组前未使用过磷结合剂或其他影响磷结合剂的药物者;(5)患者对本研究知情且签署同意书。排除标准:(1)严重肺、肝功能不全者;(2)合并甲状腺功能亢进者;(3)合并胃肠功能异常者;(4)合并心功能不全、

脑出血等心脑血管疾病者;(5)对本次研究药物具有过敏症者。

### 1.2 治疗方法

两组患者均进行常规血液透析治疗,使用磷酸氢盐透析液,透析血流量为250 mL/min,透析液钙浓度为1.25 mmol/L,低分子肝素抗凝,每次4 h,每周3次。治疗期间,对照组维持优质低蛋白饮食、低磷饮食,尽量将磷的摄入量控制在800~1000 mg/d。在此基础上,对照组患者接受依降钙素注射液(山东绿叶制药有限公司,国药准字H20040338,规格:1 mL:10单位)治疗,静脉注射,1 mL/次,1次/周。观察组患者在对照组基础上结合碳酸镧咀嚼片(英国Hamol Limited,国药准字HJ20171351,规格:500 mg)治疗,与食物同服或餐后立即服用,本品的起效剂量为0.75 g/d,随后视患者情况逐渐加量,最大剂量可达3.75 g/d。两组均连续治疗3个月。

### 1.3 观察指标

(1)疗效评价<sup>[7]</sup>:无效:血磷水平上升或血磷水平降低≤25%。有效:治疗后血磷水平降低>25%,但仍>1.78 mmol/L。显效:治疗结束后,血磷水平≤1.78 mmol/L。总有效率=显效率+有效率。(2)治疗前、治疗结束后采集患者静脉血4 mL,经转速3300 r/min,离心时间12 min,离心半径8 cm,分离取上清液待检测。采用HITACHI 7600-020全自动生化分析仪(日本株式会社日立高新技术)检测血磷、血钙水平,计算钙磷乘积。采用酶联免疫吸附试验(试剂盒购自南京赛泓瑞生物科技有限公司)检测成纤维生长因子23(FGF-23)水平,采用BECKMAN COULTER DXI 800全自动化学发光免疫分析仪(美国贝克曼库尔特股份有限公司)检测血清全段甲状旁腺激素(iPTH)水平。(3)治疗前、治疗结束后使用东芝Aquilion16排螺旋CT对两组患者的冠状动脉钙化积分(CACS)进行评价,每个断层图像需独立分析,测量钙化灶峰值×发生钙化病变的面积,所有断层钙化分数之和即为CACS。分数越高提示脑血管疾病风险越高。(4)观察不良反应(恶心呕吐、腹泻、皮疹等)发生情况。

### 1.4 统计学方法

采用SPSS 25.0软件处理数据。计量资料如CACS、iPTH、血磷水平等组间比较采用t检验,以 $(\bar{x}\pm s)$ 表示。计数资料如不良反应、疗效等采用 $\chi^2$ 检验,以率表示。检验水准为 $\alpha=0.05$ 。

## 2 结果

### 2.1 疗效对比

与对照组(70.00%)相比,观察组的临床总有效率(91.67%)明显更高( $P<0.05$ )。见表1。

表1 疗效对比【例(%)]

Table 1 Comparison of curative effects[n(%)]

Groups	Remarkable effect	Valid	Invalid	Total effective rate
Control group(n=60)	13(21.67)	29(48.33)	18(30.00)	42(70.00)
Observation group(n=60)	19(31.67)	36(60.00)	5(8.33)	55(91.67)
$\chi^2$				9.090
P				0.003

### 2.2 钙磷乘积指标变化

治疗结束后两组血钙、血磷、钙磷乘积均较治疗前明显降

低( $P<0.05$ )。观察组治疗结束后血磷、血钙、钙磷乘积低于对照组( $P<0.05$ )。见表2。

表 2 钙磷乘积指标变化( $\bar{x} \pm s$ )  
Table 2 Changes of calcium phosphorus product indexes( $\bar{x} \pm s$ )

Groups	Time	Blood phosphorus(mg/dl)	Blood calcium(mg/dl)	Calcium-phosphorus product(mg/dl)
Control group(n=60)	Before treatment	11.33±2.38	1.28±0.27	74.72±8.57
	After treatment	7.96±1.29	0.86±0.15	52.21±7.49
	t	9.643	10.533	15.319
	P	0.000	0.000	0.000
Observation group(n=60)	Before treatment	11.28±2.42	1.26±0.21	74.18±9.68
	After treatment	5.54±1.31 <sup>a</sup>	0.67±0.16 <sup>a</sup>	38.17±7.36 <sup>a</sup>
	t	16.157	17.311	22.938
	P	0.000	0.000	0.000

Note: Comparison between groups, <sup>a</sup>P<0.05.

### 2.3 FGF-23、iPTH、CACS 对比

两组治疗结束后 FGF-23、iPTH、CACS 均较治疗前明显降

低(P<0.05)。观察组治疗结束后 FGF-23、iPTH、CACS 低于对照组(P<0.05)。见表 3。

表 3 FGF-23、iPTH、CACS 对比( $\bar{x} \pm s$ )  
Table 3 Comparison of FGF-23, iPTH and CACS ( $\bar{x} \pm s$ )

Groups	Time	FGF-23(ng/L)	iPTH(ng/L)	CACS
Control group(n=60)	Before treatment	568.39±73.36	473.54±82.84	257.53±49.67
	After treatment	475.68±64.27	382.17±76.73	163.46±32.59
	t	7.363	6.268	12.266
	P	0.000	0.000	0.000
Observation group(n=60)	Before treatment	567.52±90.44	472.16±74.69	256.47±38.62
	After treatment	329.52±67.39 <sup>a</sup>	296.58±72.64 <sup>a</sup>	128.34±27.63 <sup>a</sup>
	t	16.345	13.054	20.901
	P	0.000	0.000	0.000

Note: Comparison between groups, <sup>a</sup>P<0.05.

### 2.4 不良反应发生率对比

对照组不良反应发生率 6.67%(4/60) 与观察组的 10.00%

表 4 不良反应发生率对比【例(%)】  
Table 4 Comparison of adverse reaction rates[n(%)]

Groups	Nausea and vomiting	Rash	Diarrhea	Total incidence
Control group(n=60)	2(3.33)	1(1.67)	1(1.67)	4(6.67)
Observation group(n=60)	3(5.00)	2(3.33)	1(1.67)	6(10.00)
$\chi^2$				0.436
P				0.509

## 3 讨论

目前全球范围内,各种原因导致的慢性肾脏病的发病率和死亡率逐年上升,严重威胁人类健康。血液透析可明显提升患者的临床生存率,但长期维持性血液透析的患者也存在较多的并发症,其中又以高磷血症较为常见<sup>[8-10]</sup>。高磷血症将导致机体钙磷代谢异常、增加心血管类疾病发生风险、肾性骨病、促使继发性甲状旁腺功能亢进等一系列问题<sup>[11-13]</sup>。以往的报道

显示<sup>[14]</sup>,我国高磷血症的发病率远高于西方发达国家,约有半数以上的血液透析患者其血磷值>1.78 mmol/L。美国肾脏病基金会指南指出<sup>[7]</sup>,有效控制血液透析患者的血磷水平,可明显降低死亡风险。

现临床有关血液透析高磷血症患者的治疗主要有以下几种,包括充分透析、磷结合剂的应用、低磷饮食。但充分透析亦无法清除体内多余的血磷含量,因人体每天摄入的磷大约在1000~1400 mg,每次透析仅能将约 800 mg 的磷清除,无法满

足降磷需求<sup>[15]</sup>。而低磷饮食虽可一定程度上减少血磷水平,但因磷的摄入与蛋白的摄入相平行,低磷饮食会导致人体摄入低蛋白饮食,可能造成营养不良<sup>[16,17]</sup>。故不少患者选择使用磷结合剂来降低血磷水平。依降钙素注射液既往常用于治疗骨质疏松,对机体钙平衡和骨转换有调节作用<sup>[18]</sup>。近年来不少研究证实<sup>[19,20]</sup>,依降钙素注射液可通过抑制破骨细胞活性来降低血钙、血磷水平。但也有的学者研究认为<sup>[21-23]</sup>,含钙磷结合剂可导致血管、软组织钙化。故仍需进一步优化治疗方案。碳酸镧咀嚼片作为非铝非钙类磷结合剂,有口服方便、药效高等优点,可有效降低血磷水平,减轻血管钙化程度,是目前较安全、有效的磷结合剂<sup>[24,25]</sup>。本次观察结果表明,与单纯的依降钙素治疗相比,血液透析高磷血症采用碳酸镧咀嚼片辅助治疗,血钙、血磷、钙磷乘积水平可有效控制,疗效显著。

iPTH是一种碱性单链多肽类激素,由甲状旁腺主细胞分泌,主要功能是调节钙和磷的代谢<sup>[26]</sup>。血液透析高磷血症患者可促进iPTH分泌,从而引发或加重继发性甲状旁腺功能亢进<sup>[27]</sup>。FGF-23也是一种循环磷调节因子,可维持维生素D及磷酸盐代谢。血液透析高磷血症患者的肾小球滤过率降低,致使磷滞留,而过量的磷负荷可促进FGF-23大量生成,导致维生素D分泌异常,进一步影响血钙水平<sup>[28,29]</sup>。CACS是对冠状动脉钙化的一个评估方法,研究证实<sup>[30]</sup>,CACS与患者后期脑部血管疾病的发生率呈正相关。而高磷血症又会提高心血管类疾病发生风险,因此CACS可能可作为高磷血症患者预后指标之一。本研究中,观察组治疗结束后FGF-23、iPTH、CACS低于对照组。表明碳酸镧咀嚼片联合依降钙素治疗可延缓冠状动脉钙化,阻止高磷血症的疾病进展。而两组不良反应发生率对比无差异,分析主要是因为碳酸镧咀嚼片不易被胃肠道吸收,可经粪便排出体外,不良反应轻微。

综上所述,碳酸镧咀嚼片联合依降钙素治疗血液透析高磷血症,疗效显著,可有效控制血磷水平,延缓冠状动脉钙化,安全可靠。

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