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苯磺酸左旋氨氯地平片联合厄贝沙坦对老年难治性高血压的临床疗效*

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摘要 目的:探讨苯磺酸左旋氨氯地平片与厄贝沙坦的联合应用对老年难治性高血压患者临床疗效的影响及其可能机制。**方法:**选取我院确诊并治疗的老年难治性高血压患者 72 例作受试者,按随机数字表法分为两组,对照组 36 例予以利尿药联合厄贝沙坦进行血压调控,治疗组 36 例在对照组基础上予联合苯磺酸左旋氨氯地平片 2.5 mg 日一次进行治疗。观察两组患者的临床疗效,监控患者血压情况,比较治疗前后患者血清同型半胱氨酸(Hcy)、TNF- α 及 IL-6 水平的变化。**结果:**对照组总有效率低于治疗组($P<0.05$);与对照组比较,治疗组患者血压控制情况较好,治疗后血清 Hcy、TNF- α 及 IL-6 水平降低,差异具有统计学意义($P<0.05$)。**结论:**苯磺酸左旋氨氯地平片与厄贝沙坦的联合应用可有效控制老年难治性高血压患者的血压、尽早恢复患者血压稳定,可能与其降低血清 Hcy、TNF- α 、IL-6 的水平有关。

关键词:老年难治性高血压;苯磺酸左旋氨氯地平片;厄贝沙坦;同型半胱氨酸(Hcy)

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Effects of Levamlodipine Besylate Tablets Combined with Irbesartan on the Levels of Serum Homocysteine in Elderly Patients with Refractory Hypertension and Its Clinical Efficacy*

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ABSTRACT Objective: To investigate the clinical efficacy of levamlodipine besylate tablets combined with irbesartan on the elderly patients with refractory hypertension and its mechanisms. **Methods:** 72 elderly patients with refractory hypertension who were diagnosed and treated in our hospital were selected and randomly divided into two groups, 36 cases in the control group were treated with diuretic combined with irbesartan for blood pressure control, 36 cases in the experiment group were treated on the base of the control group with levamlodipine besylate tablets 2.5 mg once a day. The clinical efficacy were compared, blood pressure situations were monitored, serum homocysteine (Hcy), TNF- α and IL-6. levels changed situations were compared before and after treatment. **Results:** The total effective rate of control group was lower than that of the experiment group ($P<0.05$); compared with the control group, the blood pressure of the experiment group was better controlled, the serum Hcy, TNF- α and IL-6 levels significantly decreased after treatment ($P<0.05$). **Conclusion:** Levamlodipine besylate tablets combined with irbesartan could reduce the serum Hcy, TNF- α and IL-6 levels, improve the effective control rate of blood pressure in the treatment of elderly patients with refractory hypertension.

Key words: Elderly patients with refractory hypertension; Levamlodipine besylate tablets; Irbesartan; Hcy

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前言

高血压是一种以动脉血压持续增高为特征的慢性心血管疾病,是脑卒中及冠心病等心血管疾病死亡率升高的主要原因^[1]。其病理分型一般为继发性高血压与原发高血压,其中原发性高血压的治疗包括在改善生活方式的基础上合理使用包括利尿剂在内的三种或以上的降压药物三个月,血压控制仍不达标($\geq 140/90$ mmHg)或服用四种或以上降压药物血压才能得到有效控制,称之为难治性高血压^[2]。有研究表明^[3,4]难治性高血压的形成与肥胖、高钠低钾饮食、颈动脉压力反射功能减弱、交感神经及 RAAS 活性增强、继发性高血压、睡眠呼吸暂停、肾脏功能异常等因素有关。同时,血压的异常增高加速了心、脑、肾等

尿剂在内的三种或以上的降压药物三个月,血压控制仍不达标($\geq 140/90$ mmHg)或服用四种或以上降压药物血压才能得到有效控制,称之为难治性高血压^[2]。有研究表明^[3,4]难治性高血压的形成与肥胖、高钠低钾饮食、颈动脉压力反射功能减弱、交感神经及 RAAS 活性增强、继发性高血压、睡眠呼吸暂停、肾脏功能异常等因素有关。同时,血压的异常增高加速了心、脑、肾等

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靶器官的损害,加重心血管损伤,诱发心血管疾病死亡率的增加^[5]。流行病学调查显示^[6]近年来难治性高血压发病率正呈逐年递增,尤其是在老年人群中的发病率增长明显。目前,尚无针对老年难治性高血压的特殊疗法,改善患者不良生活习惯、降压药与利尿药的合理使用、利尿排钠、降低高血容量负荷、缓解精神压力等方法的综合运用是治疗老年难治性高血压的重要手段。厄贝沙坦是一种有效的临床常用的血管紧张素-II受体阻滞剂,其作用机制是通过抑制血管紧张素转换酶的生成,降低机体血管紧张素II的含量缓解全身小动脉平滑肌收缩、降低循环血量及回心血量的增加来实现的^[7]。苯磺酸左旋氨氯地平片是临床常见钙离子阻滞剂,其作用主要是通过舒张血管平滑肌、阻滞钙离子经膜进入心肌及血管平滑肌细胞来实现的^[8]。本实验通过观察治疗前后患者血压变化对比及血清 Hcy、TNF- α 、IL-6 浓度变化,探讨苯磺酸左旋氨氯地平片与厄贝沙坦的联合应用在老年难治性高血压的治疗中控制血压水平的作用。

1 资料与方法

1.1 临床资料

回顾性选取于 2014 年 6 月~2015 年 6 月入住我院的符合 2010 年我国高血压指南诊断标准的难治性高血压患者 72 例,即选取曾服用包括利尿剂在内的三种或以上降血压药物进行治疗,血压控制效果仍不理想者,作为本次试验对象,患者年龄不低于 65 岁。排除患有心肌梗塞等器质性心脏疾病、心率失常、心绞痛、严重肝肾功能异常及意识障碍合并患有其他重大疾病的患者,排除继发性高血压患者,排除血压测量不标准、患者依从性差、白大衣性高血压等原因所致血压异常的患者,经患者及家属确认无异议后,自主签署知情同意书,并积极配合此次研究。本次研究对象为 2、3 级高血压患者,且研究对象 BMI 水平差别不明显,无吸烟史或已戒烟三年以上。

按照随机数字表法进行分组,对照组 36 例予以氢氯噻嗪联合厄贝沙坦进行治疗,其中男性 14 例,女 22 例;年龄为 65-82 岁,平均年龄为(74.38 $\pm$ 2.86)岁;治疗组 36 例在对照组基础上予以苯磺酸左旋氨氯地平片联合治疗,其中男性 20 例,女 16 例;年龄为 65-82 岁,平均年龄为(75.29 $\pm$ 2.91)岁;两组未有脱落,且 2 组间平均年龄、性别、病情发展状况等基本资料选

择无偏倚性($P>0.05$)。本次研究获得批准,并在我市伦理委员会的追踪监督下完成。

1.2 治疗方法

入院后,所有患者进行血常规、尿常规、血糖及血压等一般检查,评估患者一般身体状态,采取改善生活习惯一般治疗,戒烟忌酒、适度锻炼、控制体重,进行限盐高纤维低脂饮食。对照组:本次采用氢氯噻嗪片 50 mg 日二次联合厄贝沙坦 150 mg 日一次进行降血压治疗。治疗组:在对照组的基础上,给予苯磺酸左旋氨氯地平片 2.5 mg/次,1 次/d 口服治疗。两组患者连续治疗 12 周。

1.3 观察指标及检测方法

1.3.1 血压变化 患者进行入院常规检查,并对患者血压进行 24 小时动态监测,记录治疗前后血压变化。

1.3.2 血清 Hcy、TNF- α 及 IL-6 水平 血清 Hcy 水平通过美国雅培公司 AXSYM 仪器的全自动荧光偏振免疫技术检测;采用酶联免疫吸附试验法测定血清 TNF- α 、IL-6 水平。

1.4 疗效评价标准

参照 2008 年美国心脏协会关于难治性高血压诊断标准及 2010 年发布的《我国高血压指南诊断标准》,记录所有患者血压水平变化状况,综合评定治疗效果。显效:治疗后血压下降明显至正常范围,即血压 $\leq$ 140 / 90 mmHg,且血压水平稳定,波动较小。有效:患者治疗后血压(舒张压或收缩压)下降至正常水平或下降 20 mmHg 以上,接近正常范围,患者血压水平趋近稳定。无效:患者血压变化不明显,用药后血压下降水平不足 10 mmHg。总有效率 = [(显效例数 + 有效例数) / 本组患者例数] $\times$ 100%。

1.5 统计学分析

采用 spss17.0 软件将研究数据进行统计学分析,计量资料以均数 $\pm$ 标准差($\bar{x} \pm s$)表示,采用 t 检验,计数资料以率(%)表示,采用 χ^2 检验,等级资料以率(%)表示,以 $P<0.05$ 作为差异具有统计学意义的标准。

2 结果

2.1 两组患者临床疗效的比较

治疗后,治疗组患者 94.44%(34/36)的临床有效率明显高于对照组 77.78%(28/36),差异具有统计学意义($P<0.05$)。(表 1)

表 1 两组临床疗效的比较[例(%)]

Table 1 Comparison of the clinical curative effect between two groups[n(%)]

Groups	n	excellence	effective	invalid	Total effective rate
Control group	36	19(52.78)	9(25.00)	8(22.22)	28(77.78)
Experiment group	36	21(58.33)	13(36.11)	2(5.56)	34(94.44)*

Note: Compared with the control group, * $P<0.05$.

2.2 两组患者治疗前后血压的变化

治疗后,两组患者血压均有所降低,差异具有统计学意义($P<0.05$);与对照组相比,治疗组患者血压水平更接近理想状态,差异具有统计学意义($P<0.05$)。(表 2)。

2.3 两组患者治疗前后血清 Hcy、TNF- α 及 IL-6 水平的比较

治疗后,两组患者血清 Hcy、TNF- α 、IL-6 水平均较治疗前明显降低,差异具有统计学意义($P<0.05$);与对照组相比,治疗组患者血清 Hcy、TNF- α 、IL-6 水平更低,差异具有统计学意义

($P<0.05$)。(表 3)。

3 讨论

目前,临床关于难治性高血压的治疗主要是通过降低交感神经系统活性、减少肾性水钠潴留、阻止 RAAS 异常兴奋、保持细胞膜离子转运正常来完成的^[13]。厄贝沙坦是临床常用的血管紧张素 II 受体阻滞剂,其对血压的抑制作用主要是通过特异性地拮抗血管紧张素转换酶 1 受体,选择性地阻断其与 Ang II 的

结合,抑制血管收缩和醛固酮的释放实现^[14]。同时,厄贝沙坦的使用能有效抵消由利尿剂诱发的代偿机制,加强降压效果^[15]。苯磺酸左旋氨氯地平作为常用的钙离子通道阻滞剂其对血压的降低作用主要是通过舒张平滑肌、扩张外周小动脉、减少后

负荷,扩张冠状动脉及冠状小动脉实现^[16]。本研究结果显示治疗组患者血压控制有效率高于对照组,表明老年难治性高血压治疗效率的提升与苯磺酸左旋氨氯地平片和厄贝沙坦的联合应用有直接关系。

表 2 两组患者治疗前后血压变化情况的比较

Table 2 Comparison of the change of blood pressure between two groups before and after treatment

Groups		Diastolic pressure (mmHg)	Systolic pressure (mmHg)
Control group	Before treatment	116.5± 9.4	192.6± 15.8
	After treatment	92.7± 5.2*	152.3± 10.9*
Experiment group	Before treatment	115.7± 10.0	195.1± 13.2
	After treatment	86.6± 5.1**	142.6± 9.5**

Note: Compared with before treatment, *P<0.05. Compared with the control group, **P<0.05.

表 3 两组患者治疗前后血清 Hcy、TNF-α 及 IL-6 水平的比较

Table 3 Comparison of the serum Hcy, TNF-α and IL-6 levels between two groups before and after treatment

Groups		Hcy(μmol/L)	TNF-α(mg/L)	IL-6(μg/L)
Control group(n=36)	Before treatment	21.67± 4.72	49.67± 6.72	137.53± 61.03
	After treatment	17.31± 3.52*	23.31± 4.52*	119.32± 51.97*
Experiment group(n=36)	Before treatment	22.01± 4.87	51.51± 5.87	138.53± 58.84
	After treatment	12.83± 2.74**	15.83± 3.74**	105.37± 41.03**

Note: Compared with before treatment, *P<0.05; Compared with the control group, **P<0.05.

血清同型半胱氨酸(Hcy)是一种含硫氨基酸,可参与机体氧化还原及氧化应激反应,通过促进过氧化物及超氧化物的生成,损伤血管内皮细胞,改变凝血因子功能,增加血栓倾向^[17]。有研究显示^[18]高浓度的 Hcy 可损伤阻力血管和容量血管的内皮细胞功能,减少血管舒张因子生成引起血压升高及血管重构。由巨噬细胞分泌的肿瘤坏死因子-α(TNF-α)及白细胞介素-6(IL-6)参与免疫和炎症反应,与血管阻力的增加、血管内皮细胞损伤及粥样斑块的形成密切相关^[19]。有研究表明^[20]高血压患者血清 TNF-α、IL-6 水平明显增高且其浓度与高血压严重呈正相关。本组结果显示对照组患者血清 Hcy、TNF-α、IL-6 的水平较高,提示苯磺酸左旋氨氯地平片和厄贝沙坦的联合应用有效改善难治性高血压老年患者血压异常可能与降低血清 Hcy、TNF-α、IL-6 的水平有关。

综上所述,苯磺酸左旋氨氯地平片与厄贝沙坦的联合应用在有效控制老年难治性高血压患者的血压、尽早恢复患者血压稳定等方面效果显著,可能与其降低血清 Hcy、TNF-α、IL-6 的水平有关。然而,本次研究样本数、例数限制,关于苯磺酸左旋氨氯地平片与厄贝沙坦的联合应用对难治性高血压老年患者的有效性需要循证医学证据进一步证实。

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腹腔路径的腹腔镜肾癌根治术,取得良好疗效。

综上所述,腹腔镜肾癌根治术治疗肾癌较开放性肾癌根治术有疗效佳、安全性好、术后恢复快及并发症少的优势,值得临床推广。

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