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松龄血脉康胶囊联合立普妥对老年高血压患者血清 Fibulin-3、Lp(a)、MCP-1 水平的影响 *

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摘要 目的:研究松龄血脉康胶囊联合立普妥对老年高血压患者血清细胞外基质蛋白-3 (Fibulin-3)、脂蛋白 a (Lipoprotein(a), Lp(a))、单核细胞趋化蛋白-1 (monocyte chemoattractant protein-1, MCP-1) 水平的影响。**方法:**选择 2015 年 04 月至 2017 年 12 月在我院治疗的老年高血压患者 72 例,按照随机数字表法为观察组和对照组,对照组采用立普妥口服治疗,观察组在对照组的基础上联用松龄血脉康胶囊口服治疗,观察和比较两组临床治疗效果,治疗前后血脂、动态血压及 Fibulin-3、Lp(a)、MCP-1 水平的变化情况。**结果:**治疗后,观察组总有效率为 88.89%,明显高于对照组(69.44%, $P < 0.05$);观察组血清血清总胆固醇 (Serum total cholesterol, TC)、低密度脂蛋白胆固醇 (low density lipoprotein cholesterol, LDL-C)、甘油三酯 (triglyceride, TG)、游离脂肪酸 (nonesterified fatty acid, FFA)、Lp(a)、MCP-1 等水平均显著低于对照组 ($P < 0.05$),而血清 HDL-C、Fibulin-3 水平明显高于对照组 ($P < 0.05$);治疗后,观察组动态血压水平降低范围较对照组更明显 ($P < 0.05$);观察组患者生活愉快、心理健康及认知功能等方面评分均显著高于对照组 ($P < 0.05$)。**结论:**松龄血脉康胶囊联合立普妥治疗老年高血压患者的临床疗效显著优于单用立普妥口服治疗,其能更有效维持动态血压的正常水平,且显著改善 Fibulin-3、Lp(a)、MCP-1 水平,降脂效果良好。

关键词:松龄血脉康胶囊;立普妥;老年高血压;细胞外基质蛋白-3、脂蛋白 a、单核细胞趋化蛋白-1

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Effects of Tongling Kumaikang Capsule Combined with Lipitor on the Serum Fibulin-3, Lp (a) and MCP-1 Levels in Elderly Patients with Hypertension*

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ABSTRACT Objective: To study effects of tongling kumaikang capsule combined with lipitor on serum Fibulin-3, Lp(a) and MCP-1 in elderly hypertensive patients. **Methods:** 72 patients of patients with elderly hypertension who received therapy from April 2015 to December 2017 were selected as research objects. According to the random number table method, the observation group and the control group. The control group was treated with Lipitor. The observation group was treated with songling blood capsule on the basis of the control group. The levels of clinical efficacy, blood lipid, ambulatory blood pressure and Fibulin-3, Lp (a) and MCP-1 were observed. **Results:** After treatment, the total effective rate was 88.89% in the observation group, which was higher than that in the control group (69.44%), and the difference was statistically significant ($P < 0.05$). After treatment, the levels of TC, LDL-C, TG and FFA in the observation group were less than those in the control group, and HDL-C was higher than that in the control group ($P < 0.05$). After treatment, the level of ambulatory blood pressure in the observation group was significantly higher than that in the control group ($P < 0.05$). After treatment, the scores of the observation group were significantly higher than those of the control group ($P < 0.05$) in the aspects of happy life, mental health and cognitive function. After treatment, the levels of Lp (a) and MCP-1 in the observation group were significantly lower than those in the control group, and the level of Fibulin-3 in the observation group was significantly higher than that in the control group ($P < 0.05$). **Conclusion:** The clinical efficacy of songling xuemaikang capsule combined with lipitor in the treatment of elderly patients with hypertension is significantly better than that of lipitor alone, which can effectively maintain the normal level of dynamic blood pressure and significantly improve the level of fibulin-3, Lp(a), McP-1, with good lipid lowering effect.

Key words: Songling blood clon capsules; Lipitor; Elderly hypertension; Ambulatory blood pressure; Fibulin-3, Lp(a), MCP-1

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前言

目前,临床对于老年高血压的发病起因还未有完全成熟的定义^[1]。多篇文献报道认为老年高血压主要因为随着年龄的增大导致主动脉壁内膜增厚、结缔组织增加、动脉管腔狭窄等原因造成,且由于老年人多数出现动脉硬化等症状,该症状是导致收缩压及舒张压大幅度上升的关键因素^[2-3]。我国老年高血压患者主要多发于 60 岁以上人群,过去临床认为高血压是因年龄增大产生的自然生理现象,并没有深入研究该病的起因及改善方法,随着人口老龄化的日趋严重,老年高血压的发病率居高不下,严重影响老年人的生活质量以及威胁老年人的身体健康,主要临床症状表现为血压波动较大、味觉灵敏度下降及易引发其他心血管疾病,致死率及致残率高^[4-6]。

立普妥又名阿托伐他汀,是我国用于治疗老年高血压的一线汀类药物,该药具有降脂及降压等作用,但单药治疗疗程长、见效慢等局限性使其难以适应临床的需要^[7]。Fibulin-3 是一种细胞外基质蛋白,参与了形成和稳定基膜、弹性纤维、疏松结缔组织等,在高血压的发生发展中起了一定作用。在对人和实验动物高血压病的众多研究中,均发现 Lp(a)与 MCP-1 与高血压有密切的关系。据相关文献报道松龄血脉康胶囊同样适用于治

疗老年高血压患者,且通过与立普妥的联合使用可显著提升临床治疗效果^[8]。为进一步了解二者联合用药对高血压的临床疗效,本研究旨在探讨松龄血脉康胶囊联合立普妥对老年高血压患者动态血压及血清 Fibulin-3、Lp(a)、MCP-1 的影响,结果报道如下。

1 资料与方法

1.1 一般资料

选择 2015 年 4 月至 2016 年 12 月在我院进行治疗的老年高血压患者 72 例。纳入标准^[9]:(1)符合相关高血压诊断标准;(2)伴有一项以上心脑血管类疾病;(3)未出现对研究药物出现过过敏反应者。排除标准:(1)其他肾脏疾病患者;(2)拒绝配合治疗患者;(3)近期出现感染类患者。将所有患者随机分为观察组及对照组,观察组 36 例患者,年龄 47-75 岁,平均年龄(57.33±8.68)岁,体质指数为(27.38±4.01) kg/m²,其中早发心血管疾病 18 例,血脂异常 28 例,心肌梗死史 4 例;对照组 36 例患者,年龄在 50-78 岁,平均年龄(56.81±8.23)岁,体质指数为(27.92±4.22) kg/m²,其中早发心血管疾病 20 例,血脂异常 29 例,心肌梗死史 4 例,详见表 1。

表 1 两组患者一般临床资料的比较($\bar{x} \pm s, n$)

Table 1 Comparison of the general information between two groups of patients($\bar{x} \pm s, n$)

Groups	n	m/w	age	Body mass index (kg/m ²)	Total cholesterol (mmol/L)	Early onset of cardiovascular disease (例)	Dyslipidemia (n)	History of myocardial infarction (n)
Observation group	36	9/27a	57.33±8.68 ^a	27.38±4.01 ^a	5.56±1.25 ^a	18(50.00) ^a	28(77.78) ^a	4(11.11) ^a
Control group	36	20/16	56.81±8.23	27.92±4.22	5.82±1.51	20(55.55)	29(80.55)	4(11.11)

Note: compared with the control group *P>0.05.

1.2 治疗方法

所有研究者均行常规调节饮食、控制烟酒、运动基础治疗并于治疗前后进行血常规、尿常规及血脂等检测。对照组患者采用立普妥(国药准字 H314689986,美国辉瑞制药有限公司,10 mg/片)10 mg 口服治疗,一日 1 次持续治疗三个月。观察组在对照组的治療基础上联用松龄血脉康胶囊(国药准字 H20103244,成都康弘制药有限公司,0.5 g/粒)3 粒口服治疗,一日三次持续治疗两个月。

1.3 观察指标

① 所有患者治疗前后于清晨抽取 8 h 静脉空腹血 6-8 mL,放置于肝素管内,并采用全自动化分析仪(济南格利特科技有限公司生产)检测胆固醇(TC)、低密度脂蛋白胆固醇(LDL-C)、三酰甘油(TG)、游离脂肪酸(FFA)水平。② 采用动态血压检测仪(深圳市东仪通电子仪器有限公司生产),观察 24 h 平均收缩压(24hSBP)、24 h 平均舒张压(24hDBP)、白昼平均舒张压(dDBP)、白昼平均收缩压(dSBP)、夜间平均收缩压(nSBP)、夜间平均舒张压(nDBP)等变化情况;③ 采用酶联免疫吸附法检测治疗后 Fibulin-3、Lp(a)、MCP-1 水平,试剂盒均为(北京信和翔科技有限责任公司生产)并观察其变化情况;④ 两组患者临床疗效变化。

疗效判定标准^[10]:显著好转: TG 降低程度大于或等于 40%、TC 及 LDL-C 降低程度大于或等于 20%、HDL-C 上升程

度大于或等于 0.26 mmol/L;好转: TG、TC、LDL-C 降低程度在 10%-20%之间,且 HDL-C 上升程度在 0.10-0.26 mmol/L 之间;无变化:治疗后, TG、TC、LDL-C、HDL-C 无任何变化。

1.4 统计学分析

选择 SPSS18.0 进行数据统计,计量资料的比较采用 t 检验,计数资料的比较采用 χ^2 检验,当 P<0.05 时表示其差异具有统计学意义。

2 结果

2.1 两组临床疗效比较

治疗后,观察组总有效率为 88.89%,明显高于对照组(69.44%),两组差异具有统计学意义(P<0.05),详见表 2。

2.2 两组患者治疗前后血脂水平对比

治疗后,观察组血清胆固醇(TC)、低密度脂蛋白胆固醇(LDL-C)、三酰甘油(TG)、游离脂肪酸(FFA)水平显著低于对照组水平,但血清 HDL-C 明显高于对照组水平,两组差异具有统计学意义(P<0.05),详见表 3。

2.3 两组患者治疗前后动态血压水平对比

治疗前,两组动态血压水平无明显差异(P>0.05);治疗后,两组患者的动态血压水平均明显降低,但观察组动态血压水平明显低于对照组,两组差异具有统计学意义(P<0.05),详见表 4。

表 2 两组临床疗效比较[n(%)]

Table 2 Comparison of the efficacy between two groups after treatment[n(%)]

Groups	n	Significant improvement	improve	No change	Total improvement
Observation group	36	21(58.33) ^b	11(30.50) ^b	4(11.11) ^b	32(88.89) ^b
Control group	36	10(27.77)	15(41.66)	11(30.55)	25(69.44)

Note: Compared with the control group ^bP<0.05.

表 3 两组患者治疗前后血脂水平对比分析($\bar{x} \pm s$)

Table 3 Comparison of the blood lipid levels between two groups before and after treatment($\bar{x} \pm s$)

Groups	n	TC(mmol/L)	HDL-C(mmol/L)	LDL-C(mmol/L)	TG(mmol/L)	FFA(mmol/L)
Observation group	36	4.31± 0.68 ^b	1.10± 0.16 ^b	2.42± 0.30 ^b	1.70± 0.21 ^b	0.71± 0.07 ^b
Control group	36	7.15± 1.24	0.62± 0.10	3.56± 0.55	2.66± 0.44	1.69± 0.28

Note: Compared with the control group ^bP<0.05.

表 4 两组患者治疗前后动态血压水平对比($\bar{x} \pm s$)

Table 4 Comparison of the ambulatory blood pressure levels before and after treatment between two groups($\bar{x} \pm s$)

Groups		24hSBP	24hDBP	dSBP	dDBP	nSBP	nDBP
Observation group	Before treatment	133.20± 21.08 ^a	82.64± 12.05 ^a	133.82± 20.29 ^a	82.66± 12.11 ^a	128.55± 20.17 ^a	78.18± 10.32 ^a
	After treatment	120.14± 18.34 ^b	75.12± 9.92 ^b	120.48± 18.14 ^b	78.34± 10.63 ^b	110.58± 18.36 ^b	70.28± 10.67 ^b
Control group	Before treatment	131.83± 20.54	83.02± 12.30	134.24± 20.57	83.54± 12.25	129.72± 20.19	79.64± 11.04
	After treatment	125.20± 19.68	80.64± 11.44	124.22± 19.03	80.51± 11.02	114.10± 19.33	73.42± 11.22

Note: Compared with the control group after treatment ^bP<0.05; Compared with the control group before treatment ^aP>0.05.

3 讨论

老年高血压是老年群体中常见的心脑血管类疾病,且国际上对于老年高血压的发病机制还未有全面的了解。我国已步入人口老龄化社会,伴随着老年人口数量的急剧上升,老年高血压患者的数量日益扩大,严重影响患者的生活质量^[11,12]。相关研究表明高血压患者的血脂含量普遍较高,可引起血液黏稠度上升,且进一步促使血压升高,临床主要症状表现为动脉血压持续升高、脂质代谢紊乱、头晕及气虚等,高血压、高血脂及高血液黏稠度是导致老年心脑血管类疾病的关键因素^[13,14]。Mitsniefes MM 等^[15]认为老年患者的脂质代谢出现异常及胆固醇升高是导致机体血管内皮损伤的导火线,且粥样动脉硬化是引起血管内壁狭窄、血流速度变慢及血液黏稠度上升的原因之一,临床研究表明高血压患者颈部斑块的形成可导致血栓的发生,因此通过改善动脉粥样硬化及降压、降脂等一系列措施可显著控制老年高血压的病情。但该病较难治愈,临床上常通过药物干预达到降血脂、血压的目的。过去临床常应用丁类药物(立普妥)治疗心脑血管类疾病,但单药治疗疗程长且见效慢,联合用药已成为临床干预老年高血压的重要手段。松龄血脉康胶囊是由鲜松叶、葛根等组成的纯中药制剂,其降压效果已被临床证实^[16,17],但有关联合立普妥对高血压患者动态血压、及血清 Fibulin-3、Lp(a)、MCP-1 水平影响的报道较罕见。

立普妥(Lipitor)是一种他汀类降脂、降压药,主要应用于临床治疗高胆固醇、冠心病、血脂异常类患者,已被一百多个国家临床使用近二十年,其疗效已被广泛认可。相关文献表明立普妥可显著降低机体内低密度脂蛋白胆固醇(LDL-C)含量,且可明显降低冠心病、糖尿病及高血压等心脑血管类疾病的发生率^[18]。松龄血脉康胶囊内含多种有效成分,如粗蛋白、脂肪酸及氨基酸等成分具有降压降脂及抗炎症等作用,且其含有的钙类微

量元素可维持神经肌肉兴奋。Karpov YA 等^[19]认为松龄血脉康可调节脂肪代谢、维持血管弹性及扩张动脉血管等作用,并通过降压、降脂及将低血液粘稠度改善老年高血压患者的动态血压 SBP、DBP 水平。随着年龄的增大机体内主动脉壁内膜增厚、结缔组织增加、动脉管腔变得狭窄,收缩压及舒张压大幅度上升引起动脉血压异常,导致老年患者出现动脉硬化。本研究中,采用两种方法治疗的老年高血压患者动态血压 SBP、DBP 及血脂 TC、LDL-C、TG、FFA 等水平均有明显降低,但松龄血脉康胶囊联合立普妥治疗患者的动态血压及血脂水平均明显低于单药立普妥治疗的患者,提示联合用药降压降脂效果更好,可明显控制老年高血压患者动态血压及血脂持续上升的情况。

细胞外基质蛋白-3(Fibulin-3)参与细胞外基质结构的合成及稳定。目前我国对 Fibulin-3 的研究主要集中在肿瘤和盆腔支持组织间质中细胞外基质结构的聚集和稳定过程^[20]。Kaya H 等^[21]发现 Fibulin-3 在小于 5 年病程的高血压患者中水平明显偏低,并提出 Fibulin-3 水平的高低变化可作为观察高血压早期血管重构的标志物之一。脂蛋白 a(Lipoprotein(a), Lp(a))主要分布于机体的肝脏部位,其阻止血管内血块溶解并促进动脉粥样硬化形成,脂蛋白水平持续升高与心脑血管类疾病密切相关,是脑卒中和冠心病的独立危险因素。单核细胞趋化蛋白-1(monocyte chemoattractant protein-1, MCP-1)又称单核细胞趋化和激活因子,属于 C-C 亚族(β 亚族)成员。当患者出现高胆固醇时,动脉内侧平滑肌细胞产生高水平 MCP-1,单核细胞粘附于血管壁并浸润动脉壁;当患者出现高血脂时,LDL 与肾小球细胞结合,刺激其产生 MCP-1,趋化单核细胞在局部浸润。本研究中,联合用药治疗患者的血清 Lp(a)、MCP-1 水平较单药治疗患者明显降低,且 Fibulin-3 水平及生活质量水平较单药治疗患者上升更明显,表明联合用药治疗的患者其高胆固醇及高血脂得到有效的控制,并明显提升了老年高血压患者的生活质量,效

果较单一用药更突出。

综上所述,松龄血脉康胶囊联合立普妥治疗老年高血压患者疗效显著,不仅能维持动态血压的正常水平,且能显著改善 Fibulin-3、Lp(a)、MCP-1 水平,且降脂效果良好。

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