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氨氯地平联合阿托伐他汀钙对原发性高血压患者血清 Fractalkine 与内皮功能的影响 *

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摘要 目的：研究氨氯地平联合阿托伐他汀钙对原发性高血压患者血清 Fractalkine 与内皮功能的影响。**方法：**选择 2017 年 2 月至 2018 年 2 月在我院接受治疗的原发性高血压患者 106 例，按照随机数字表随机分为对照组和观察组，对照组使用氨氯地平治疗，观察组以对照组为基础联合阿托伐他汀钙治疗，两组患者均治疗 2 个月。比较两组临床疗效，观察治疗前后两组血压、内皮功能（ET-1、NO、FMO）及血清 Fractalkine 水平变化。**结果：**治疗后，观察组总有效率为 94.33%，明显高于对照组 81.13%（$P<0.05$）；治疗后，观察组收缩压及舒张压水平为（118.43± 15.72）mmHg、（81.32± 6.87）mmHg，明显低于对照组（126.71± 17.38）mmHg、（86.18± 5.29）mmHg（$P<0.05$）；观察组血清 Fractalkine、ET-1 水平为（217.81± 76.62）pg/mL、（53.82± 6.73）ng/L，明显低于对照组（282.17± 83.24）pg/mL、（65.14± 7.92）ng/L（$P<0.05$）；观察组血清 NO、FMO 水平为（21.07± 1.95）μmol/L、（13.94± 0.82）%，均明显高于对照组（18.04± 2.02）μmol/L、（11.28± 1.04）%，比较差异显著（$P<0.05$）。**结论：**氨氯地平联合阿托伐他汀钙治疗原发性高血压可显著提高临床疗效，同时可显著降低血清 FKN 水平，改善其内皮功能。

关键词：氨氯地平；阿托伐他汀钙；原发性高血压

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The Effects on Amlodipine Combine with Atorvastatin on Serum Fractalkine and Endothelial Function in Primary Hypertension Patients*

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ABSTRACT Objective: To study the effect of amlodipine combined with atorvastatin on serum Fractalkine and endothelial function in primary hypertension patients. **Methods:** 106 patients of primary hypertension who received therapy from February 2017 to February 2018 in our hospital were selected as research objects, according to random number table were randomly divided into control group and observation group, the control group was treated with amlodipine, while the observation group was treated with amlodipine combine with atorvastatin, two groups of patients were 2 months treatment. The clinical efficacy, the blood pressure, endothelial function (et-1, NO, FMO) and serum Fractalkine levels of the two groups were observed before and after treatment. **Results:** After treatment, the total effective rate of the observation group was 94.33%, higher than that of the control group was 81.13%($P<0.05$). After treatment, the Systolic and diastolic pressures in Observation group was less than the control group of[(118.43± 15.72)vs(126.71± 17.38) mmHg, (81.32± 6.87)vs (86.18± 5.29) mmHg]($P<0.05$). The serum levels of Fractalkine and et-1 in the observation group was less than the control group of[(217.81± 76.62)vs(282.17± 83.24) pg/mL, (53.82± 6.73)vs(65.14± 7.92) ng/L]($P<0.05$). Serum levels of NO and FMO in Observation group was higher than the control group of[(21.07± 1.95)vs(18.04± 2.02) μmol/L, (13.94± 0.82)vs(11.28± 1.04)%], and the comparison difference was significant ($P<0.05$). **Conclusion:** Amlodipine combine with atorvastatin in the treatment of primary hypertension can significantly improve the clinical efficacy, significantly reduce serum FKN level and improve its endothelial function.

Key words: Amlodipine; Atorvastatin; Primary hypertension

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前言

原发性高血压为临床常见心血管疾病中的一种，主要表现为头晕头痛、乏力、健忘等，部分患者还存在心悸、胸闷等症状，对人们的身体健康具有较为严重的影响[1-3]。由于该疾病比较隐匿，进展也较为缓慢，导致在发病初期难以被发现。氨氯地平为临床常用的降压药物，降压效果也得到临床证实，但有关研究报道，单纯使用降压药物治疗原发性高血压的疗效还有待提升[4,5]。目前降压药物联合他汀类药物应用于高血压的研究逐渐增多，使他汀类药物的应用与高血压的关系受到了广泛的关注，但对其

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治疗效果仍存在一定争议。为近一步了解降压药物与他汀药物联合治疗原发性高血压的治疗效果，本研究旨在观察在氨氯地平联合阿托伐他汀钙对原发性高血压患者血清 Fractalkine 与内皮功能的影响。现报道如下。

1 材料与方法

1.1 一般资料

于 2018 年 12 月至 2019 年 2 月期间选择在我院治疗的原发性高血压患者 82 例，纳入标准：(1)检测符合《中国高血压防治指南》[6]中有关原发性高血压的诊断标准；(2)患者自行停用降压药 2 周以上；(3)对本研究知情并同意，同时按要求复诊。排除标准：(1)各种继发性高血压患者；(2)伴有心绞痛、充血性心力衰竭者；(3)患有明显肝肾功能障碍者；(4)合并糖尿病、内分泌疾病、恶性肿瘤、神经障碍患者；(5)入院前一个月内未使用过他汀类药物治疗。按照随机数字表法分为观察组和对照组，观察组 42 例，其中男 22 例，女 20 例，年龄 48~74 岁，平均年龄(54.83± 6.43)岁。对照组 40 例，其中男 23 例，女 17 例，年龄 43~80 岁，平均年龄(58.12± 10.52)岁。两组患者基线资料比较存在可比性。

1.2 方法

入院后所有患者均给予基础治疗。对照组在口服苯磺酸氨氯地平片(辉瑞制药有限公司，5 mg/ 片)5 mg，口服，一天一次。观察组以对照组为基础加用阿托伐他汀钙（辉瑞制药有限公司，20 mg/ 片)20 mg，口服，一天一次。两组治疗周期均为 2 个月。

1.3 观察指标

观察两组疗效；比较治疗前后两组血压、内皮功能(ET-1、NO FMO)及血清 Fractalkine 水平变化。于治疗前后收集静脉血 5 mL，离心处理后取上清液待检，使用半自动血凝仪检测血清 ET-1 水平，使用硝酸还原酶比色法检测血清 NO 水平，使用彩色多普勒超声探头检测 FMD；使用酶联免疫吸附法测定血清 Fractalkine 水平。

疗效判断标准参照相关文献进行[6]，具体为：显效：治疗后，患者 DBP 下降幅度≥ 10 mmHg 并降至正常水平，或 SBP 下降幅度≥ 20 mmHg；有效：治疗后，患者 DBP 下降幅度＜10 mmHg，但降至正常水平，或 10 mmHg＜SBP 下降幅度＜19 mmHg；无效：治疗后，患者 DBP 或 SBP 未达到以上标准。

1.4 统计学分析

本研究数据选择 SOSS18.0 进行统计，计量资料比较使用 t 检验，计数资料比较使用 x^2 检验，等级资料使用秩合检验，当 $P<0.05$ 时表示差异显著。

2 结果

2.1 疗效分析

观察组总有效率为 94.33%，明显高于对照组($P<0.05$)，详见表 1。

表 1 两组临床疗效比较

Table 1 Comparison of clinical efficacy in two groups[(n)%]

Groups	n	Excellent	Effective	Invalid	Total effective rate
Observation group	42	38(71.70)	12(22.64)	3(5.67)	50(94.33)[a]
Control group	40	30(56.60)	13(24.53)	10(18.87)	43(81.13)

Note: Compared with the control group, [a]$P<0.05$.

2.2 血压分析

治疗前，两组患者血压比较均无显著差异($P>0.05$)；治疗后，两组血压均明显降低，且观察组降低幅度更大，两组比较差异显著($P<0.05$)。详见表 2。

表 2 两组治疗前后血压水平比较

Table 2 Comparison the blood pressure level in two groups before and after treatment ($\bar{x}\pm s$，mmHg)

Groups	n	Time	SPB	DBP
Observation group	42	Before treatment	145.21± 20.14	103.21± 12.43
		After treatment	118.43± 15.72[ab]	81.32± 6.87[ab]
Control group	40	Before treatment	148.53± 18.32	101.76± 10.52
		After treatment	126.71± 17.38[b]	86.18± 5.29[b]

Note: Compared with the control group, [a]$P<0.05$; Compared with before the operation, [b]$P<0.05$.

2.3 血清 FKN 及内皮功能分析

治疗前，两组患者血清 FKN 水平及内皮功能比较均无显著差异($P>0.05$)；治疗后，观察组血清 FKN 水平、ET 水平明显低于对照组，NO 及 FMO 水平均高于对照组，两组比较差异显著($P<0.05$)。详见表 3。

2.4 不良反应分析

两组治疗期间均未发生严重的不良反应。

3 讨论

原发性高血压是影响中老年人健康的危险因素之一，目前临床对于其发病机制尚未明确，但相关报道认为血管内皮功能紊乱与其发病有较为密切的关系[7,8]。血管内皮具有一定的分泌

表 3 两组治疗前后血清 FKN 及内皮功能的变化比较($\bar{x}\pm s$)

Table 3 Comparison the Serum Fractalkine level and in two Endothelial function in two groups before and after treatment($\bar{x}\pm s$)

Groups	n	Time	Fractalkine(pg/ml)	ET-1(ng/L)	NO(μmol/L)	FMO(%)
Observation group	42	Before treatment	408.43± 85.71	89.07± 9.32	14.63± 2.11	9.17± 1.12
		After treatment	217.81± 76.62[ab]	53.82± 6.73[ab]	21.07± 1.95[ab]	13.94± 0.82[ab]
Control group	40	Before treatment	398.12± 90.23	86.43± 10.26	15.07± 1.73	9.43± 1.07
		After treatment	282.17± 83.24[b]	65.14± 7.92[b]	18.04± 2.02[b]	11.28± 1.04[b]

Note: Compared with the control group, [a]$P<0.05$; Compared with before the operation, [b]$P<0.05$.

功能,因此能够分泌多种因子,其代谢较为活跃,可参与机体的免疫反应、炎症反应等。据研究显示,当内皮细胞受损时极易导致急性心机梗死[9,10]。NO 为血管内皮释放的重要内源性输血管物质,其舒张作用较强但较为短暂,能够抑制白细胞的黏附与平滑肌细胞的繁殖作用,从而抗粥样硬化[11,12]。因此当血清 NO 水平下降时会导致内皮依赖性血管舒张功能出现障碍,从而诱发血压升高[13]。ET-1 是由血管内皮分泌的一种因子,具有强效持久的收缩血管的作用,同时能够促进冠状动脉粥样硬化的形成,可反应出血管内皮损伤[14]。有文献报道[15-17],血清 NO 水平提高,而 ET-1 水平下降则表示患者病情变化严重,二者的平衡可维持血管张力且组织正常的灌溉作用,而内皮功能受损者会导致患者血管张力调节功能受损,最终出现血压升高。另有研究报道,原发性高血压患者血管内皮功能受损可降低 FMD[18,19]。本研究结果也显示,患者在治疗前 FMD 水平均低于正常值。从而近一步说明血管内皮细胞功能受损在高血压的发生发展过程中具有重要的作用。

对于原发性高血压的治疗临床以控制血压为目的。氨氯地平是一种新型氢吡啶类钙拮抗剂, 兼有 L 型钙通道阻滞作用,且具有较高的生物利用度作用持久,是临床较为常见的降压药物[20]。氨氯地平通过阻止钙离子内流,从而阻止血管平滑肌收缩,最终达到降低血压的目的;同时具有保护血管内皮细胞,缓解血管内皮细胞受到损伤[21,22]。阿托伐他汀钙是血脂调节药物,但有研究发现阿托伐他汀钙还需要抗炎、调节免疫功能的作用,同时能够减轻血管炎症反应,抑制白细胞黏附聚集,促进了内皮组织细胞的分化,使受损的内皮功能得到修复[23-25]。本研究结果显示, 患者在使用西尼地平联合阿托伐他汀钙治疗后,其血压水平显著降低,且血清 ET 水平明显降低,血清 NO 水平及 FMO 水平明显增高, 提示氨氯地平联合阿托伐他汀钙治疗原发性高血压具有协同作用。

此外,有文献报道[26,27],高血压会促进血清 FKN 的分泌,导致其水平升高, 而血清 FKN 水平的增加又可导致内皮细胞的紊乱使病情加重。从本结果可见,患者在行联合治疗后,其血清 FKN 水平显著降低,同时患者的内皮功能得到了明显的改善,由此可见, 血清 FKN 水平的降低与高血压患者内皮功能改善具有密切联系。我们认为,氨氯地平联合阿托伐他汀钙通过降低了患者血压,阻止了血清 FKN 过度分泌,从而调节了内皮细胞的紊乱,但因本研究的研究样本过少等原因,对氨氯地平联合阿托伐他汀钙降低血清 FKN 水平的具体病理机制未进一步明确,有待更深入的探讨。

综上所述,氨氯地平联合阿托伐他汀钙治疗原发性高血压可显著提高临床疗效,同时可显著降低血清 FKN 水平,改善其内皮功能。

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