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赖诺普利与贝那普利治疗高血压合并脑卒中的疗效及对血清 ADMA 水平的影响

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摘要 目的:探讨赖诺普利与贝那普利治疗高血压合并脑卒中的疗效及对血清非对称性二甲基精氨酸(ADMA)水平的影响,以期为高血压合并脑卒中的治疗提供指导。**方法:**选取2014年1月-2016年3月在我院确诊并接受治疗的高血压合并脑卒中246例,按随机数字表法将患者随机分为研究组、对照组和常规组,每组各82例。常规组采用基础治疗,研究组采用基础治疗联合赖诺普利治疗,对照组采用基础治疗联合贝那普利治疗。比较3组患者治疗前后血压参数、血清ADMA和Hcy水平、治疗效果和不良反应。**结果:**治疗前三组患者的血压参数(SBP、DBP和PP)、血清ADMA和Hcy水平、mRS评分均无显著差异;治疗后三组患者上述指标水平较治疗前均显著降低($P<0.05$),且研究组患者指标水平明显低于对照组和常规组($P<0.05$)。研究组治疗有效率明显高于对照组和常规组,对照组治疗有效率明显高于常规组,上述差异均具有统计学意义($P<0.05$)。三组患者不良反应率无显著差异($P>0.05$)。**结论:**赖诺普利和贝那普利均能有效降低高血压合并脑卒中患者血压水平,改善血管内皮功能,疗效显著;但赖诺普利的效果要比贝那普利更好,更值得临床推广。

关键词: 赖诺普利; 贝那普利; 高血压合并脑卒中; 疗效; 血清水平

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Effect of Lisinopril and Benner Pury in the Treatment of Hypertensive Stroke and Effect on Serum ADMA Level

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ABSTRACT Objective: To evaluate the clinical efficacy of lisinopril and Benner Pury in the treatment of hypertensive stroke and on serum asymmetric dimethylarginine (ADMA two) levels, in order to provide guidance for the treatment of hypertension and stroke. **Methods:** 246 cases of hypertensive stroke from January 2014 -March 2016 who received treatment in our hospital diagnosed, according to the random number table method were randomly divided into study group compare group and conventional group, 82 cases in each group. The conventional group received basic treatment, study group with basic treatment combined with lisinopril treatment, the control group was treated with combined therapy of Benner Pury treatment. The blood pressure parameters, serum ADMA and Hcy levels, treatment effects and adverse reactions were compared between the 3 groups before and after treatment. **Results:** There were no significant differences in the blood pressure, serum ADMA and Hcy levels and mRS scores of the three groups of patients before treatment (SBP, DBP and PP); the index levels after treatment were significantly lower than before treatment ($P<0.05$), and the index of patients in the study group was significantly lower than the control group and normal group ($P<0.05$). The effective rate of the treatment group was significantly higher than that of the control group and the conventional group, the effective rate of the treatment group was significantly higher than that of the conventional group, the difference was statistically significant ($P<0.05$). There was no significant difference in adverse reaction rate between the three groups ($P>0.05$). **Conclusion:** Lisinopril and Benner Pury can effectively lower blood pressure in hypertensive patients with cerebral stroke, improve endothelial function, with significant effect; but the effect of lisinopril to is better than Benner Pury, more worthy of promotion.

Key words: Lisinopril; Benazepril; Hypertension and stroke; Curative effect; Serum level

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前言

高血压病是诱发心脑血管疾病的重要危险因素之一,高血

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压尤其在老年脑卒中患者中具有较高的比率。临床研究证实控制血压能够有效减少心脑血管疾病的发生^[1]。脑卒中是一种脑组织血液循环障碍性疾病,主要是由于血管阻塞使大脑供血不足或者脑部血管突然破裂造成脑组织损伤,具有高致残率和致死率的特点^[2]。高血压是脑卒中主要的独立危险因素,因此有效控制血压是改善高血压合并脑卒中患者疗效和预后关键环节^[3]。

目前,高血压的治疗药物主要包括 β -受体阻滞剂、钙离子拮抗剂、血管紧张素转化酶抑制剂(ACEI)、血管紧张素II受体阻断剂等^[4]。然而,临床实践证实目前血压控制有效率较低,同时是对高血压合并脑卒中的治疗及二级预防缺少研究,因此,探索有效控制血压和治疗高血压合并脑卒中的药物对改善高血压合并脑卒中患者生存质量具有重要意义。为此,本研究探讨了ACEI类药物治疗高血压合并脑卒中的疗效及对血清非对称性二甲基精氨酸(ADMA)水平的影响,在高血压合并脑卒中的治疗方面取得了显著效果,以期为高血压合并脑卒中的治疗提供指导,具体报道如下。

1 资料与方法

1.1 一般资料

选择2014年1月至2016年3月在我院确诊并接受治疗的246例高血压合并脑卒中患者为研究对象,纳入标准: \oplus 所有患者均符合世界卫生组织高血压诊断指南中高血压临床诊断标准,收缩压 ≥ 140 mmHg,舒张压 ≥ 90 mmHg^[5]; \ominus 脑卒中诊断标准符合《中国脑血管病防治指南》的诊断标准,且通过CT或者MRI等影像学检查确诊^[6]; \oplus 患者符合ACEI类药物适应症; \ominus 患者及其家属了解研究内容,签署知情同意协议,愿意配合调查研究。排除标准: \oplus 患者存在严重的心功能不全,如急性心肌梗死急性,急性心力衰竭等; \ominus 继发性高血压患者、糖尿病患者; \oplus 患者具有高尿酸血症、高脂血症等病症^[7]。按照按随机数字表法将患者随机分为研究组、对照组、常规组3组,每组各82例。研究组:男性43例,女性39例;年龄41-72岁,平均(58.3±4.9)岁;高血压病程1-10年,平均病程(5.1±3.6)年;脑卒中病程1-14月,平均(11.6±4.6)月。对照组:男性45例,女性37例;年龄40-72岁,平均(58.1±4.8)岁;高血压病程1-9年,平均病程(4.9±3.5)年;脑卒中病程1-13月,平均(11.2±4.3)月。常规组:男性44例,女性38例;年龄41-71岁,平均(58.0±4.7)岁;高血压病程2-9年,平均病程(4.8±3.4)年;脑卒中病程1-15月,平均(11.4±4.9)月。三组患者在性别、年龄、病程等一般资料方面无显著性的差异($P>0.05$),具有可比性。

1.2 治疗方法

所有患者均在入院后经过心肺功能评估、肝肾功能检查等后,评估治疗适应症及潜在风险,采取休息、调节饮食等营养支持治疗。均在治疗前两周采用丁咯地尔输液改善脑循环治疗,治疗两周后口服丁咯地尔片来改善脑循环。常规组采用基础治疗,主要包括阿司匹林抗血小板聚集治疗、钙通道阻滞剂改善心肌耗能治疗、他汀类药物降低血脂稳定斑块治疗。睡前服用阿托伐他汀(辉瑞制药有限公司,国药准字J20120050),20 mg/d,每日一次;早餐后服用阿司匹林(江苏平光制药有限责任公司,国药准字H32025901),100 mg/d,每日一次。研究组采用基础治疗联合赖诺普利治疗。赖诺普利片(晋城海斯制药有限公司,国药准字H20103384),清晨空腹口服,5 mg/d,每日一次;患者服用2周后若血压未达到目标血压适当增加药量,最大不超过10 mg/d,连续治疗12周。对照组采用基础治疗联合贝那普利治疗。盐酸贝那普利片(深圳信立泰药业股份有限公司,国药准字H20043648),口服,10 mg/d,每日一次。连续治疗12周。

1.3 观察指标

所有患者治疗前、治疗后均于清晨按照统一标准测量血压,坐位血压测量3次,每次间隔2 min;站起2 min后测量站立位血压1次,观察并比较三组患者治疗前后血压参数SBP(收缩压)、DBP(舒张压)和PP(脉压差)变化情况。治疗前、治疗后抽取所有患者清晨空腹外周静脉血5 mL,离心15 min(3000 r/min),分离血清后,取上清液,-20℃保存。采用高效液相色谱法检测血清ADMA水平,采用循环酶法检测血清Hcy水平。检测所选用试剂盒均由上海酶联生物科技有限公司提供。

1.4 疗效评价

参照高血压合并脑卒中治疗的相关疗效评价标准,分为显效、有效和无效。显效:收缩压保持在(120-140)mmHg,舒张压保持在(80-90)mmHg,患者能够主动配合康复治疗,无视觉、感觉、语言等障碍;有效:患者血压下但有波动,情绪稳定,基本能够配合康复治疗;无效:患者血压波动明显,难以配合康复治疗,出现视觉、感觉、语言等部分障碍^[8]。总有效为显效和有效之和。对患者神经功能的评估采用生活能力评分(mRS),mRS为改良的Rankin修订量表评分,用来衡量患者脑卒中后神经功能恢复情况。评分在0-6分之间,评分越高表示患者神经功能越差^[9]。统计三组患者出现头痛、心悸、胸闷等不良反应事件的例数^[10]。

1.5 统计学方法

本次研究采用SPSS 20.0统计学软件对患者的数据资料进行统计分析。计量型资料采用“平均数±标准差”进行统计学描述,选用t或方差检验进行比较;计数型资料采用百分数表示,选用卡方检验进行比较。检验水准 $\alpha=0.05$,当 $P<0.05$ 时,表示差异具有统计学意义,当 $P>0.05$ 时,表示差异不具有统计学意义。

2 结果

2.1 三组患者治疗前后血压参数比较

根据表1可知,治疗前三组患者的SBP、DBP、PP水平相近,经方差检验,差异均无统计学意义($P>0.05$)。治疗后三组患者上述指标水平较治疗前均显著降低,且研究组患者指标水平明显低于对照组和常规组,经方差检验比较,差异具有统计学意义($P<0.05$)。

2.2 三组患者治疗前后血清ADMA、Hcy和mRS评分比较

根据表2可知,治疗前三组患者的血清ADMA、Hcy水平和mRS评分相近,差异均无统计学意义($P>0.05$);治疗后三组患者上述血清指标水平和mRS评分较治疗前均显著降低,且研究组患者指标水平明显低于对照组和常规组,对照组患者指标水平明显高于常规组,分别经t检验比较,差异均有统计学意义($P<0.05$)。

2.3 三组患者治疗效果比较

根据表3可知,研究组治疗有效率明显高于对照组和常规组,对照组治疗有效率明显高于常规组,经卡方检验,上述差异均具有统计学意义($P<0.05$)。

2.4 三组患者不良反应比较

根据表4可知,三组患者治疗后不良反应发生率均较低,且三组间并无显著差异,经卡方检验,上述差异均无统计学意义($P>0.05$)。

表 1 三组患者治疗前后血压参数比较

Table 1 Comparison of blood pressure parameters before and after treatment in three groups

Groups	SBP(mmHg)		DBP(mmHg)		PP(mmHg)	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Research group	153.73± 7.35	132.31± 5.37 ^{ab}	92.04± 6.83	84.15± 5.42 ^{ab}	61.71± 8.52	52.87± 5.31 ^{ab}
Control group	153.69± 7.31	135.81± 5.95 ^{ac}	91.96± 6.67	86.59± 6.14 ^{ac}	61.73± 8.56	54.67± 5.82 ^{ac}
Routine group	153.65± 7.33	138.64± 6.07 ^a	91.93± 6.75 ^a	88.32± 6.21 ^a	61.56± 8.36 ^a	56.85± 5.69 ^a
F	0.475	13.465	2.371	14.273	1.274	14.723
P	>0.05	<0.05	>0.05	<0.05	>0.05	<0.05

Note: Three groups of patients after treatment compared with before treatment group, ^aP<0.05; Patients in the study group compared with the control group, the conventional group, ^{ab}P<0.05; The control group after treatment compared with the conventional group, ^{ac}P<0.05.

表 2 三组患者治疗前后血清 ADMA、Hcy 和 mRS 评分比较

Table 2 Comparison of serum ADMA, Hcy and mRS score between three groups before and after treatment

Groups	ADMA(μmol/L)		Hcy(μmol/L)		mRS	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Research group	0.992± 0.136	0.713± 0.117 ^{ab}	20.37± 6.53	11.62± 3.51 ^{ab}	4.35± 0.32	1.91± 0.19 ^{ab}
Control group	0.989± 0.132	0.796± 0.124 ^{ab}	20.31± 6.39	13.07± 4.18 ^{ac}	4.32± 0.33	2.36± 0.28 ^{ab}
Routine group	0.991± 0.133	0.854± 0.126 ^a	20.35± 6.45 ^a	14.78± 4.38 ^a	4.33± 0.31	2.93± 0.27 ^{ab}
F	0.325	12.431	1.643	13.863	2.133	12.453
P	>0.05	<0.05	>0.05	<0.05	>0.05	<0.05

Note: Three groups of patients after treatment compared with before treatment group, ^aP<0.05; Patients in the study group compared with the control group, the conventional group, ^{ab}P<0.05; The control group after treatment compared with the conventional group, ^{ac}P<0.05.

表 3 三组患者治疗效果比较[n(%)]

Table 3 Comparison of therapeutic effects between the three groups[n(%)]

Groups	N	Significantly effective	Effective	Invalid	Total effective
Research group	82	41(50.00)	37(45.12)	4(4.88)	78(95.12) ^a
Control group	82	32(39.02)	38(46.34)	12(14.63)	70(85.37) ^b
Routine group	82	26(31.71)	32(39.02)	24(29.27)	58(70.73)

Note: Patients in the study group were compared with those in the control group and the control group, ^aP<0.05; Control group compared with the conventional group, ^bP<0.05.

表 4 三组患者不良反应比较[n(%)]

Table 4 Comparison of adverse reactions between the three groups[n(%)]

Groups	N	Headache	Palpitation	Chest tightness	Adverse reaction rate
Research group	82	1(1.22)	1(1.22)	2(2.44)	4(4.88)
Control group	82	2(2.44)	1(1.22)	2(2.44)	5(6.10)
Routine group	82	1(1.22)	0(0.00)	1(1.22)	2(2.44)

3 讨论

高血压是由多种病因引发的心血管疾病综合征,是影响人类健康的常见疾病之一。血压长期偏高会改变损害心脏、脑等重要器官的功能与结构,诱发脑卒中、冠心病等心血管疾病^[1]。脑卒中是一种急性脑血管疾病,是由于血管阻塞使大脑供血不足或者脑部血管突然破裂造成脑组织损伤的疾病。临床表现为神经功能损伤、肢体麻木、语言障碍或偏瘫等,具有高致残率和高致死率的特点^[12]。高血压是脑卒中的重要危险因素之一,对于高血压合并脑卒中患者能够有效控制血压,保证脑组织灌注和供血有助于减轻神经功能损伤,改善血管内皮功能,提高治疗效果,减轻脑卒中引发的生理病害^[13]。

高血压的治疗药物主要包括β-受体阻滞剂、钙离子拮抗剂、血管紧张素转化酶抑制剂(ACEI)、血管紧张素Ⅱ受体阻断剂等^[14]。ACEI类药物能够抑制全身和血管局部的血管紧张素转换酶,减少血管紧张素Ⅱ的生成,在降低血压的同时,能够有效改善内皮功能,减轻管壁肥厚,从增强动脉顺应性^[15]。ACEI类药物治疗高血压具有以下优点:^① 不直接作用影响神经系统及中枢神经,亦不波及交感神经作用,由此对患者麻醉、运动以及出血等无影响,也对患者性功能无降低作用;^② 区别于扩血管药物,不会发生扩血管药物治疗高血压时心动过速的应激反应;辅助加用利尿剂,可起到保持血钾水平平衡的作用,在与利尿剂合用时,可有效预防高醛固酮血症的发生;^③ 对患者机体代谢不产生影响,保证血钾水平平衡,对心血管事件无影响或

者起到改善作用,甚至对糖尿病并发患者有有效改善胰岛素水平的作用。赖诺普利和贝那普利均属于ACEI类药物,是一类血管紧张素转化酶抑制剂,能够对血管紧张素转换酶进行抑制,更好地舒张全身小动脉和血管,减少血液流动压力,有效的改善高血压的症状、调节肾脏血流量、降低尿蛋白的水平,同时可以扩张冠脉血管、增加心肌供氧量^[16]。

临床研究表明,降压治疗能够有效预防脑卒中的发生和复发,监测动态血压指标能更好反映血压与心血管病危险、靶器官损害之间的关系^[17]。血管内皮功能失调对血压变化、脑卒中发生发展过程具有重要影响,而ADMA(非对称性二甲基精氨酸)是血管内皮功能失调的重要危险因子,血清ADMA水平升高会诱发严重的心血管事件^[18]。ADMA通过抑制内皮细胞一氧化氮形成,能够使内皮细胞功能发生紊乱,造成血管内皮功能失调,对颅内血液循环产生不利影响,进而促进脑卒中的发生^[19]。陈东骊等^[19],在高血压合并缺血性脑卒中患者血浆ADMA水平变化及厄贝沙坦干预研中,也证实血浆ADMA水平与高血压脑出血有显著相关性,并可能是其治疗高血压合并脑卒中有益的作用机制之一。临床研究证实,高Hcy(同型半胱氨酸)是诱发脑血管事件的重要危险因子,其水平变化与脑卒中发生发展具有密切关系。当高血压伴随高Hcy同时存在时,能够发挥对脑血管病发生的协同作用,使脑卒中发生率进一步提高^[20]。因此,降低Hcy水平能够显著减少高血压患者脑血管事件的发生。本研究结果显示,治疗前三组患者的血压参数(SBP、DBP和PP)和血清ADMA、Hcy水平均处于较高水平,且三组患者无显著差异,治疗后三组患者的血压参数(SBP、DBP和PP)和血清ADMA、Hcy水平均显著下降,且研究组患者上述指标水平明显低于对照组和常规组,而对照组患者上述指标水平明显高于常规组,结果表明ACEI类药物用于治疗高血压合并脑卒中能够更有效控制患者血压,改善患者内皮功能,更好地舒张全身小动脉和血管,减少血液流动压力,保证脑组织灌注和供血。而ACEI类药物中赖诺普利对血压控制和血清ADMA、Hcy水平调节要优于贝那普利。三组患者治疗后疗效评价结果显示研究组患者治疗有效率和mRS评分要明显优于对照组和常规组,对照组患者治疗有效率和mRS评分要明显优于常规组,结果表明ACEI类药物治疗高血压合并脑卒中能够更有效改善患者神经功能损伤,提高患者生存质量,疗效更好,这也是与ACEI类药物对血压控制、血清ADMA、Hcy水平调节更有效相一致的,而ACEI类药物中赖诺普利的治疗效果要优于贝那普利。对三组患者治疗后的不良反应统计显示,三组患者不良反应发生率较低,且组间无显著差异,结果揭示联合用药不良反应发生少,安全可靠。

综上所述,在高血压合并脑卒中的治疗中采用赖诺普利和贝那普利均能有效降低高血压合并脑卒中患者血压水平,改善血管内皮功能,疗效显著;但赖诺普利的效果要比贝那普利更好,更值得临床推广。

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