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盐酸倍他司汀片联合盐酸氟桂利嗪片对椎-基底动脉供血不足性眩晕症患者椎基底动脉血流动力学和生活质量的影响*

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摘要 目的:观察盐酸倍他司汀片联合盐酸氟桂利嗪片对椎-基底动脉供血不足(VBI)性眩晕症患者椎基底动脉血流动力学和生活质量的影响。**方法:**选择2019年5月~2021年2月期间来我院就诊的97例VBI性眩晕症患者,根据乱数表法,入选的患者分为对照组和观察组,分别为48例和49例,对照组接受盐酸倍他司汀片治疗,观察组接受盐酸倍他司汀片联合盐酸氟桂利嗪片治疗,均治疗2周。对比两组疗效、药物不良反应、眩晕症状评分、生活质量、椎基底动脉血流动力学情况。**结果:**观察组的临床总有效率(93.88%)高于对照组(72.92%)($P<0.05$)。治疗2周后,观察组的眩晕评定量表的评分系统(DARS)、眩晕障碍量表(DHI)评分低于对照组($P<0.05$)。治疗2周后,观察组的36项健康调查简表(SF-36)各维度评分均高于对照组($P<0.05$)。治疗2周后,观察组的左侧/右侧椎动脉及基底动脉血流速度较对照组高($P<0.05$)。两组不良反应发生率对比无差异($P>0.05$)。**结论:**盐酸倍他司汀片联合盐酸氟桂利嗪片治疗VBI性眩晕症患者疗效显著,可有效改善其椎基底动脉血流动力学状况,缓解眩晕症状,提高生活质量。

关键词:盐酸倍他司汀片;盐酸氟桂利嗪片;椎-基底动脉供血不足性眩晕症;血流动力学;生活质量

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Effects of Betahistine Hydrochloride Tablet Combined With Flunarizine Hydrochloride Tablet on Vertebrobasilar Hemodynamics and Quality of Life in Patients with Vertebrobasilar Insufficiency Vertigo*

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ABSTRACT Objective: To observe the effects of betahistine hydrochloride tablet combined with flunarizine hydrochloride tablet on vertebrobasilar hemodynamics and quality of life in patients with vertebrobasilar insufficiency (VBI) vertigo. **Methods:** 97 patients with VBI vertigo who came to our hospital from May 2019 to February 2021 were selected. According to the random number table method, the selected patients were divided into control group and observation group, 48 cases and 49 cases respectively. The control group was treated with betahistine hydrochloride tablet, and the observation group was treated with betahistine hydrochloride tablet combined with flunarizine hydrochloride tablet, all patients were treated for 2 weeks. The curative effect, adverse drug reactions, vertigo symptom score, quality of life and vertebrobasilar hemodynamics were compared between the two groups. **Results:** The total clinical effective rate of the observation group (93.88%) was higher than that of the control group (72.92%)($P<0.05$). 2 weeks after treatment, the scores of vertigo Assessment Scale (DARS) and vertigo Disorder Questionnaire (DHI) of the observation group were lower than those of the control group ($P<0.05$). 2 weeks after treatment, the scores of each dimensions of 36-Item Health Survey (SF-36) of the observation group were higher than those of the control group ($P<0.05$). 2 weeks after treatment, the blood flow velocities of left/right vertebral artery and basilar artery of the observation group were higher than those of the control group ($P<0.05$). There was no significant difference in the incidence of adverse reactions between the two groups ($P>0.05$). **Conclusion:** Betahistine hydrochloride tablet combined with flunarizine hydrochloride tablet in the treatment of patients with VBI vertigo has a significant effect, can effectively improve the vertebrobasilar artery blood flow dynamics, relieve vertigo symptoms, improve the quality of life.

Key words: Betahistine hydrochloride tablet; Flunarizine hydrochloride tablet; Vertebrobasilar insufficiency vertigo; Hemodynamic monitoring; Quality of life

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前言

椎-基底动脉供血不足(VBI)性眩晕是中老年群体的常见疾病,主要是指椎-基底动脉供血出现障碍而产生眩晕、头痛等症状,具有一过性或间接性发作的特点,对患者的生活质量及身体健康造成严重影响^[1-3]。目前,临床针对 VBI 性眩晕症的治疗通常以扩张血管,改善脑部血流为主。盐酸倍他司汀片为组胺类药物,因其具有扩张血管作用而成为治疗 VBI 性眩晕症的一线药物^[4,5],但长期应用不良反应发生风险增加,患者依从性较差。盐酸氟桂利嗪片为选择性钙拮抗剂,具有缓解血管痉挛、改善脑微循环及神经原代谢等作用^[6,7]。本研究就盐酸倍他司汀片联合盐酸氟桂利嗪片对 VBI 性眩晕症患者椎基底动脉血流动力学和生活质量的影响进行分析,以期为临床治疗提供参考。

1 资料与方法

1.1 临床资料

纳入标准:(1)参考《中国后循环缺血专家共识》^[8],经颅彩色多普勒超声检查确诊为 VBI,有典型的眩晕症状;(2)均为初次就诊者,签署治疗承诺书;(3)患者生命体征平稳,且对本次研究用药无禁忌症者。排除标准:(1)伴有严重肝肾功能异常者;(2)颅脑手术史及颅内肿瘤患者;(3)合并精神疾病患者;(4)占位性病变、脑外伤等其他疾病引发的眩晕者;(5)合并造血系统疾病者;(6)合并自身免疫性疾病者。选择 2019 年 5 月~2021 年 2 月间来我院就诊的 97 例 VBI 性眩晕症患者,根据乱数表法,入选的患者分为对照组(盐酸倍他司汀片治疗)和观察组(盐酸倍他司汀片联合盐酸氟桂利嗪片治疗)两组,分别为 48 例和 49 例,对照组男性 31 例,女性 17 例,平均病程(2.48 ± 0.64)年;平均年龄(53.92 ± 5.38)岁;有饮酒史者 29 例,有吸烟史者 23 例;合并基础性疾病:高血压、糖尿病、高血脂各 9 例、6 例、7 例。观察组男性 33 例,女性 16 例,平均病程(2.54 ± 0.71)年;平均年龄(54.38 ± 6.27)岁;有饮酒史者 30 例,有吸烟史者 25 例;合并基础性疾病:高血压、糖尿病、高血脂各 11 例、7 例、5 例。两组一般资料比较无差异($P>0.05$),本次研究内容已获得我院伦理学委员会批准进行。

1.2 方法

入院后积极控制原发疾病、指导其营养饮食、适当运动、保持充足的休息,均禁烟、禁酒。对照组口服盐酸倍他司汀片(厂

家:上海上药信谊药厂有限公司,规格:4 mg,国药准字 H31022080)治疗,2 片/次,3 次/d。观察组在对照组盐酸倍他司汀片用药的基础上结合盐酸氟桂利嗪片[厂家:国药集团容生制药有限公司,国药准字 H19993527,规格:5 mg (按 $C_{26}H_{26}F_2N_2$ 计)]治疗,口服,2 片/次,1 次/d,睡前服用。两组均治疗 2 周。

1.3 疗效判定标准^[9]

眩晕或位置性眼震完全消失,经颅彩色多普勒超声检查血流指标恢复正常视为痊愈。眩晕或位置性眼震完全消失,经颅彩色多普勒超声检查血流指标有所改善视为显效。眩晕或位置性眼震部分消失或缓解,经颅彩色多普勒超声检查血流指标有所改善为有效。眩晕或位置性眼震无改善甚至加重视为无效。总有效率=有效率+显效率+痊愈率。

1.4 评价指标

(1)使用眩晕评定量表的评分系统(DARS)^[10]、眩晕障碍量表(DHI)^[11]观察两组治疗前、治疗 2 周后的眩晕症状改善情况。DARS 包括 6 条目,每个条目评分 0~6 分,依次为:无症状、很轻、轻度、轻到中度、中度、中到重度、重度。DHI 包括 10 条目,每个条目评分 0、2、4 分,依次为:否、有时、经常。两种量表均评分越高,眩晕症状越严重。(2)治疗前、治疗 2 周后患者的生活质量采用 36 项健康调查简表(SF-36)^[12]进行评价。SF-36 包括总体/精神健康、生理/社会功能、躯体疼痛、精力、情感/生理职能 8 个维度,每个维度各为 100 分,分数越高,生活质量越好。(3)治疗前、治疗 2 周后采用 DC-N3S 经颅彩色多普勒超声系统检测基底动脉、左/右椎动脉的平均血流速度,仪器来源于南京贝登医疗股份有限公司。(4)关注并记录两组治疗期间的不良反应。

1.5 统计学方法

数据处理选择 SPSS20.0 软件。计数资料以%表示,接受卡方检验。经检验符合正态分布的计量资料使用($\bar{x} \pm s$)表示,组内、组间比较分别接受配对样本或成组 t 检验。检验水准为 $\alpha=0.05$ 。

2 结果

2.1 疗效对比

观察组临床总有效率(93.88%)高于对照组(72.92%),差异有统计学意义($P<0.05$),如表 1 所示。

表 1 疗效对比 [例(%)]

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

Groups	Recovery	Remarkable effect	Effective	Invalid	Total effective rate
Control group (n=48)	4 (8.33)	16 (33.33)	15 (31.25)	13 (27.08)	35 (72.92)
Observation group (n=49)	9 (18.37)	25 (51.02)	12 (24.49)	3 (6.12)	46 (93.88)
χ^2					7.734
P					0.005

2.2 DARS、DHI 评分对比

治疗前,对照组、观察组 DARS、DHI 评分组间对比无统计

学差异($P>0.05$)。治疗 2 周后,对照组、观察组 DARS、DHI 评分均下降,且观察组的 DARS、DHI 评分低于对照组($P<0.05$),

如表 2 所示。

2.3 SF-36 各维度评分对比

治疗前,对照组、观察组 SF-36 各维度评分组间对比无差

异($P>0.05$)。治疗 2 周后,对照组、观察组 SF-36 各维度评分均升高,且观察组的 SF-36 各维度评分均高于对照组($P<0.05$),如表 3 所示。

表 2 DARS、DHI 评分对比($\bar{x}\pm s$,分)
Table 2 Comparison of DARS and DHI scores($\bar{x}\pm s$, scores)

Groups	DARS		DHI	
	Before treatment	2 weeks after treatment	Before treatment	2 weeks after treatment
Control group(n=48)	21.93± 2.23	14.59± 2.06*	27.78± 3.12	16.98± 2.82*
Observation group(n=49)	21.67± 3.09	8.18± 1.53*	27.36± 4.23	11.72± 1.96*
t	0.474	17.422	0.556	10.686
P	0.636	0.000	0.580	0.000

Note: * compared with before treatment, $P<0.05$.

表 3 SF-36 各维度评分对比($\bar{x}\pm s$,分)
Table 3 Comparison of scores of SF-36 each dimensions($\bar{x}\pm s$, scores)

Groups	Time points	Physical pain	Social function	Mental health	Physiologic energy	Physiologic function	Emotional function	Overall health	Energy
Control group (n=48)	Before treatment	51.32± 6.92	53.38± 6.09	52.83± 5.73	53.74± 6.28	52.43± 7.12	59.01± 6.83	57.32± 7.12	58.43± 6.32
	2 weeks after treatment	64.94± 7.22*	70.29± 8.02*	69.37± 6.34*	68.12± 6.98*	68.98± 6.27*	71.59± 7.02*	73.12± 8.44*	72.38± 6.47*
Observation group (n=49)	Before treatment	51.85± 6.26	69.15± 7.63	52.28± 6.39	52.97± 7.31	52.18± 6.32	59.69± 7.34	57.89± 9.15	58.12± 7.06
	2 weeks after treatment	80.46± 6.41* [@]	83.76± 5.34* [@]	82.26± 6.41* [@]	81.39± 7.22* [@]	85.17± 6.35* [@]	86.08± 7.51* [@]	88.31± 7.14* [@]	90.39± 6.79* [@]

Note: *compared with that before treatment, $P<0.05$. [@]Compared with the control group, $P<0.05$.

2.4 椎 - 基底动脉的血流速度对比

治疗前,两组左侧 / 右侧椎动脉、基底动脉血流速度组间对比无统计学差异($P>0.05$)。治疗 2 周后,对照组、观察组左侧

/ 右侧椎动脉、基底动脉的血流速度均升高,且观察组高于对照组($P<0.05$),如表 4 所示。

表 4 椎 - 基底动脉的血流速度对比($\bar{x}\pm s$,cm/s)
Table 4 Comparison of blood flow velocity between vertebrobasilar artery($\bar{x}\pm s$, cm/s)

Groups	Left vertebral artery		Right vertebral artery		Basilar artery	
	Before treatment	2 weeks after treatment	Before treatment	2 weeks after treatment	Before treatment	2 weeks after treatment
Control group (n=48)	37.38± 3.43	40.43± 4.12*	38.33± 4.29	41.71± 3.09*	39.48± 3.27	42.80± 3.68*
Observation group (n=49)	37.69± 3.68	44.08± 4.58*	38.02± 3.25	43.99± 3.14*	39.82± 3.36	45.72± 2.97*
t	-0.429	-4.124	0.402	-3.604	-0.505	-4.305
P	0.669	0.000	0.689	0.001	0.615	0.000

Note: * compared with before treatment, $P<0.05$.

2.5 对比不良反应

治疗期间,对照组有 2 例患者出现口干、1 例患者出现食欲不振、1 例患者出现皮肤瘙痒,观察组有 3 例患者出现口干、1 例患者出现胃部不适、1 例患者出现皮肤瘙痒,对照组(8.33%)与观察组(10.20%)间不良反应发生率比较无差异($\chi^2=0.101$, $P=0.751$)。

3 讨论

椎基底动脉是指脑的重要供血动脉,其中椎动脉左右各一支,左右两支椎动脉穿行于颈椎两侧的横突孔,向上进入颅后窝,在脑内合为一支,称为基底动脉^[13-15]。现代解剖医学发现,椎基底动脉可向大脑半球五分之一的区域、脑干、小脑、内耳及高

位颈髓进行供血,具有较广的供血范围^[10]。故而当椎基底动脉受到动脉粥样硬化、血液流变学异常、血管痉挛、血流动力学异常等因素的影响后,可导致管腔狭窄、痉挛,血流速度下降,脑组织区域供血不足,进而出现以眩晕为主的临床症状。VBI性眩晕症早期虽然不易形成脑梗死,但因其常常反复发作,若不及时治疗,可导致脑干、小脑及枕叶梗死,进而出现神经功能障碍,影响患者日常生活工作,降低生活质量^[17]。

盐酸倍他司汀片是一种组胺类药物,其作用机制主要体现在:可松弛内耳的毛细血管前括约肌,从而消除内耳性眩晕;促进下丘脑结节乳头体核内的组胺合成,扩张脑血管、心血管,增加血流量;对抗儿茶酚胺的缩血管作用及降低动脉压,抑制血小板凝集,改善机体微循环^[18-20]。但近年来的研究证实^[21-23],联合用药会比单用盐酸倍他司汀片治疗取得更好的治疗效果。如孙英等^[24]学者认为舒血宁注射液联合盐酸倍他司汀片治疗可有效改善 VBI 性眩晕症患者的临床症状及血液流变学。郑石洲等^[25]学者认为血塞通联合盐酸倍他司汀片治疗后循环缺血性眩晕,可改善患者血流动力学。盐酸氟桂利嗪片可选择性阻断激活的钙离子过多的进入细胞,从而防止脑血管痉挛,改善椎动脉供血^[26,27]。本研究结果显示,相比于单用盐酸倍他司汀片治疗,联合药物治疗的患者其眩晕症状改善更为明显,近期疗效进一步提高,同时还利于其生活质量的提升。可能是因为盐酸氟桂利嗪片可作用于脑血管平滑肌上的电压依赖性钙通道上的特异性位点,使细胞膜去极化,减少细胞损伤,提高细胞的耐缺氧、缺血能力,联合盐酸倍他司汀片治疗可进一步扩张脑血管、改善脑代谢,进而解除由供血不足带来的眩晕症状,随着患者眩晕症状的缓解,患者正常的工作及生活受到疾病困扰的程度减轻,逐渐改善其生活质量^[28-30]。通过观察实验室指标发现,盐酸倍他司汀片联合盐酸氟桂利嗪片可进一步改善左侧椎动脉、右侧椎动脉、基底动脉的血流速度,可能与本研究中的两种药物均具有疏通微循环,提高脑组织灌注作用有关,可产生协同增效作用。关于药物安全性方面,该联合治疗方案安全有效,不会增加不良反应发生率。

综上所述,盐酸倍他司汀片联合盐酸氟桂利嗪片可促进 VBI 性眩晕症患者症状改善,同时还可提高患者生活质量,近期疗效显著,可能与改善其椎基底动脉血流动力学有关。本次研究的不足之处在于纳入样本量较少,后续将进一步扩大样本量、多中心研究报道。

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