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◇ 药物与临床 ◇



长春西汀联合阿加曲班治疗椎基底动脉供血不足性眩晕症

王刚, 王欢欢, 张晓敏, 程怡, 龚珊珊

作者单位: 河北北方学院附属第一医院神经内科, 河北 张家口 075000

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摘要: **目的** 探讨长春西汀、阿加曲班及长春西汀联合阿加曲班在椎-基底动脉供血不足性眩晕症(VBIV) 治疗中的效果。**方法** 选取2018年1月至2019年3月河北北方学院附属第一医院收治的VBIV病人90例, 采用随机数字表法分为观察1、2、3组, 每组各30例, 分别给予长春西汀、阿加曲班及长春西汀联合阿加曲班治疗; 使用彩色多普勒超声(TCD)检查治疗前后椎动脉血流参数的改变; 使用羟胺法检测检测治疗前后三组超氧化物歧化酶(SOD)水平; 使用硫代巴比妥酸法(TBA法)测定丙二醛(MDA)含量变化, 并对比临床疗效, 并对比临床疗效。**结果** 治疗前观察1、2、3组间左椎动脉、右椎动脉及基底动脉血流速度差异无统计学意义, 具有可比性($P > 0.05$), 治疗后上述动脉血流速均较治疗前明显提高($P < 0.05$); 观察1、2组治疗后上述动脉血流速比较差异无统计学意义($P > 0.05$); 观察3组治疗后上述动脉血流速均高于观察1、2组[左椎动脉(38.4 ± 4.6) cm/s 比(31.1 ± 4.1) cm/s、(31.5 ± 4.1) cm/s, 右椎动脉(38.0 ± 4.9) cm/s 比(31.8 ± 4.6) cm/s、(31.3 ± 4.6) cm/s, 基底动脉(38.0 ± 4.0) cm/s 比(32.4 ± 4.7) cm/s、(32.5 ± 4.1) cm/s] ($P < 0.05$); 治疗前三组间SOD、MDA水平差异无统计学意义, 具有可比性($P > 0.05$), 治疗后SOD水平较治疗前明显提高($P < 0.05$), MDA水平较治疗前明显下降($P < 0.05$); 观察1、2组治疗后SOD、MDA水平比较差异无统计学意义($P > 0.05$); 观察3组治疗后SOD[(73.5 ± 12.8) U/mL 比(56.3 ± 10.1) U/mL、(55.1 ± 9.7) U/mL]及MDA[(3.5 ± 1.1) nmol/mL 比(4.9 ± 1.9) nmol/mL、(4.8 ± 1.8) nmol/mL]水平改善优于观察1、2组($P < 0.05$); 观察3组治疗1疗程后总有效率为96.7%, 观察1、2组分别为76.7%及73.3%; 观察3组治疗总有效率高高于观察1、2组($P < 0.05$); 观察1、2组间治疗总有效率比较差异无统计学意义($P > 0.05$)。**结论** 长春西汀联合阿加曲班可迅速缓解VBIV病人临床症状, 改善椎-基底动脉血供, 疗效优于单纯用长春西汀及阿加曲班治疗, 值得临床推广应用。

关键词: 椎底动脉供血不足; 眩晕; 长春西汀; 阿加曲班; 超氧化物歧化酶; 丙二醛

Clinical observation on vinpocetine in combined with argatroban in the treatment of vertebrobasilar insufficiency vertigo

WANG Gang, WANG Huanhuan, ZHANG Xiaomin, CHENG Yi, GONG Shanshan

Author Affiliation: Department of Neurology, The First Affiliated Hospital of Hebei North University, Zhangjiakou, Hebei 075000, China

Abstract: Objective To explore the effect of vinpocetine in combined with argatroban in the treatment of vertebrobasilar insufficiency vertig (VBIV). **Methods** A total of 90 patients with VBIV who were admitted in the First Affiliated Hospital of Hebei North University from January, 2018 to March, 2019 were included in the study and randomized into observation 1, 2, and 3 groups. The patients in the three groups were given vinpocetine, argatroban, and vinpocetine in combined with argatroban, respectively. The color Doppler ultrasonic diagnosis apparatus was used to detect the blood flow parameters of vertebral artery before and after treatment. The levels of superoxide dismutase (SOD) in the three groups before and after treatment were detected by hydroxylamine method. The changes of malondialdehyde (MDA) content were determined by thiobarbituric acid method (TBA method). The clinical efficacy was compared. **Results** The blood flow rate of the left vertebral artery, right vertebral artery, and basilar artery among the three groups before treatment was comparable ($P > 0.05$), while that of the above arteries after treatment was significantly enhanced ($P < 0.05$). The comparison of the blood flow rate of the above arteries after treatment between observation 1 and 2 groups was not significantly different ($P > 0.05$), while that after treatment in observation 3 group was significantly higher than that in observation 1 and 2 groups [the left vertebral artery (38.4 ± 4.6) cm/s vs. (31.1 ± 4.1) cm/s and (31.5 ± 4.1) cm/s, right vertebral artery (38.0 ± 4.9) cm/s vs. (31.8 ± 4.6) cm/s and (31.3 ± 4.6) cm/s, basilar artery (38.0 ± 4.0) cm/s vs. (32.4 ± 4.7) cm/s and (32.5 ± 4.1) cm/s] ($P < 0.05$). The comparison of SOD and MDA levels before treatment among the three groups was comparable ($P > 0.05$), while SOD level after treatment was significantly elevated ($P < 0.05$), but MDA level was significantly reduced when compared with before treatment ($P < 0.05$). The comparison of SOD and MDA levels before treatment between observation 1 and 2 groups was not significantly different ($P > 0.05$), while the improvement of SOD [(73.5 ± 12.8) U/mL vs. (56.3 ± 10.1) U/mL and (55.1 ± 9.7) U/mL] and MDA [(3.5 ± 1.1) nmol/mL vs. (4.9 ± 1.9) nmol/mL and (4.8 ± 1.8) nmol/mL] levels after treatment in observation 3 groups was significantly superior to that in observation 1 and 2 groups ($P < 0.05$). The total effective rate after one-course treatment in observation 3 groups (96.7%) was significantly higher than that in observation 1 and 2 groups (76.7% and 73.3%, respectively) ($P < 0.05$). The comparison of the total effective rate between observation 1 and 2 groups was not significantly different ($P > 0.05$). **Conclusion** Vinpocetine in combined with argatroban in the treatment of VBIV can rapidly relieve the clinical symptoms, and improve the blood supply of vertebro-basilar artery, with efficacy superior to that pure adoption of vinpocetine and argatroban; therefore, it deserves to be widely recommended in the clinic.

Key words: Vertebrobasilar insufficiency; Vertigo; Vinpocetine; Argatroban; Superoxide dismutase; Malondialdehyde

椎-基底动脉供血不足性眩晕症(vertebrobasilar insufficiency vertig, VBIV)以老年人群高发,是临床常见的脑供血不足性脑血管疾病,主要临床症状为发作性眩晕及恶心、呕吐,严重影响病人日常生活及工作^[1]。VBIV病因主要为椎动脉血管受压、血管狭窄或动脉粥样硬化,造成脑组织缺血、缺氧,进而出现眩晕等系列临床症状,若得不到及时治疗,可发展为脑梗死威胁病人生命^[2]。目前,临床上对于此类疾病的治疗主要以扩张血管、改善微循环为主^[3]。长春西汀及阿加曲班均是临床用于治疗VBIV的常用药,但两药联合应用治疗VBIV,尚未见到相关报道。本研究比较长春西汀、阿加曲班及长春西汀联合阿加曲班治疗VBIV的效果,报告如下。

1 资料与方法

1.1 一般资料 选取2018年1月至2019年3月河北北方学院附属第一医院收治的VBIV病人90例,采用随机数字表法分为观察1组、观察2组、观察3组,每组各30例。观察1组中男17例,女13例,年龄(43.3 ± 8.2)岁,年龄范围为23~68岁;观察2组中男16例,女14例,年龄(43.5 ± 9.1)岁,年龄范围为24~68岁;观察3组中男18例,女12例,年龄(44.0 ± 7.9)岁,年龄范围为23~69岁;三组病人一般资料比较差异无统计学意义($P > 0.05$),具有可比性。本研究符合《世界医学协会赫尔辛基宣言》相关要求。

1.2 入选标准 (1)VBIB诊断符合《实用神经病学》相关诊断标准;(2)经超声检查确诊为椎-基底动脉供血不足;(3)病人有轻微脑干受损体征;(4)眩晕为发作性,多由体位或头位发生变动而诱发;(5)眩晕发作时可伴有脑干一过性缺血的症状;(6)病人及近亲属知情同意并签字。

1.3 排除标准 (1)小脑、脑干梗死;(2)小脑、脑干出血或肿瘤;(3)眼病、脑外伤、耳疾;(4)重要脏器功能不全;(5)血液系统疾病或近期感染;(6)严重意识障碍;(7)研究治疗药物禁忌证。

1.4 治疗方法 三组病人均给予常规治疗,方案:拜阿司匹林(拜耳医药有限公司,批号J20171021,批次BJ34787) 0.1 g,每日1次;阿托伐他汀(齐鲁制药有限公司,批号H20193144,批次GC2H0448) 20 mg,每天1次;高血压病人予相应降压药物控制血压,糖尿病病人给予降糖药物控制血糖。观察1组在常规治疗的基础上给予长春西汀注射液(河南润弘制药股份有限公司,批号H20041792,批次1311181)静脉点滴,每天1次,每次30 mg;观察2组在常规治疗的基础上给予阿加曲班(天津药物研究院药业有限责任公司,批号H20050918,批次2006079)静脉滴注,每天1次,每次20 mg;观察3组在常规治疗的基础给予长春西汀联合阿加曲班静脉点滴治疗,用法同观察1、2组。各组均以治疗10

d为1个疗程。

1.5 观察项目 使用彩色多普勒超声(TCD)检测治疗前后椎-基底动脉血流参数的改变;使用羟胺法检测治疗前后三组超氧化物歧化酶(SOD)水平;使用硫代巴比妥酸(TBA)法测定丙二醛(MDA)含量变化,并对比临床疗效。疗效标准^[4]:显效:TCD检查显示椎-基底动脉血流正常,临床症状消失;有效:TCD检查显示椎-基底动脉血流明显改善,临床症状明显缓解;无效:TCD检查显示椎-基底动脉血流无变化或恶化,临床症状无缓解。

1.6 统计学方法 采用SPSS 18.0统计软件包处理数据。服从正态分布的计量资料采用 $\bar{x} \pm s$ 表示;治疗前后比较采用配对 t 检验分析;三组间比较采用方差分析,两两比较采用LSD- t 检验。多组间等组资料采用Kruskal-Wallis检验,两两比较采用Wilcoxon检验。以 $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 三组治疗前后椎-基底动脉血流参数比较 治疗前三组间左椎动脉、右椎动脉及基底动脉血流速度差异无统计学意义,具有可比性($F = 0.1025, 0.0372, 0.4488, P > 0.05$),治疗后三组动脉血流速均较治疗前明显提高($P < 0.05$);观察1、2组治疗后两组动脉血流速比较差异无统计学意义($P > 0.05$);观察3组治疗后动脉血流速均高于观察1、2组($P < 0.05$)。见表1。

2.2 三组治疗前后超氧化物歧化酶(SOD)、丙二醛(MDA)水平比较 治疗前三组间SOD、MDA水平差异无统计学意义,具有可比性($P > 0.05$),治疗后SOD水平较治疗前明显提高($P < 0.05$),MDA水平较治疗前明显下降($P < 0.05$);观察1、2组治疗后SOD、MDA水平比较差异无统计学意义($P > 0.05$);观察3组治疗后SOD及MDA水平改善程度优于观察1、2组($P < 0.05$)。见表2。

2.3 三组疗效对比 观察3组治疗1疗程后总有效率为96.7%,观察1、2组分别为76.7%及73.3%;观察3组治疗总有效率高于观察1、2组($\chi^2 = 14.5343, P < 0.001$);观察1、2组间治疗总有效率比较差异无统计学意义($P > 0.05$)。见表3。

3 讨论

VBIV是临床常见的缺血性脑血管疾病,主要病因为椎动脉血管受压、动脉粥样硬化及血管狭窄等,复发率高,若得不到及时干预治疗,可诱发脑缺血损伤甚至脑梗死,严重影响病人生活质量^[5-6]。

目前,临床对此类疾病的治疗主要以增强缺血脑组织的供血、供氧,改善和恢复脑细胞功能,解除动脉痉挛为主^[7-8]。有研究表明^[9-11],脑缺血损伤过程中能量代谢、炎症反应及氧化应激均是重要环节,其中以氧化应激尤为重要。当脑组织缺血损伤时可生成大量氧自由基,且会使自由基清除酶活性降低,而脑组织抗氧化作用较弱,易受到自由基侵害^[12-13]。SOD是重要的氧自由基清除剂,MDA则是氧自由基反应的代谢产物,毒性较强;MDA及SOD在正常人体中处于平衡状态,当脑组织缺血时,MDA水平明显上升,其水平超出SOD的清除能力时,即可发生脑损伤^[14-16]。因此,本研究将此指标列入评价疗效观察项目,以观察治疗效果。长春西汀是治疗VBIV的常用药物,能改善缺血性脑血管病人血流速度,改善脑代谢^[12]。阿加曲班是直接凝血酶抑制剂,能够直接灭活凝血酶,能抑制与血凝块结合的凝血酶及游离的凝血酶,并对收缩的血管有舒张作用^[13]。本研究中,观察3组采用长春西汀联合阿加曲班治疗,治疗后左椎动脉、右椎动脉及基底动脉血流速度均高于观察1、2组($P < 0.05$),且观察3组治疗后SOD及MDA水平改善程度优于观察1、2组($P < 0.05$);表明长春西汀、阿加曲班联合用药能更为有效的改善椎-基底动脉血流,促进氧自

表1 椎-基底动脉供血不足性眩晕症90例长春西汀与阿加曲班分别及联合治疗前后椎-基底动脉血流参数比较/(cm/s, $\bar{x} \pm s$)

组别	例数	左椎动脉		右椎动脉		基底动脉	
		治疗前	治疗后	治疗前	治疗后	治疗前	治疗后
观察1组	30	19.5±4.1	31.1±4.1 ^①	20.2±4.1	31.8±4.6 ^③	20.6±4.3	32.4±4.7 ^⑤
观察2组	30	20.0±4.2	31.5±4.1 ^①	19.9±4.3	31.3±4.6 ^③	21.1±4.5	32.5±4.1 ^⑤
观察3组	30	19.7±4.6	38.4±4.6 ^{①②}	20.0±4.6	38.0±4.9 ^{③④}	20.0±4.7	38.0±4.0 ^{⑤⑥}
F值		0.102 5	27.672 5	0.037 2	18.900 0	0.448 8	16.836 1
P值		0.902 7	0.000 0	0.963 5	0.000 0	0.633 9	0.000 0

注:①与治疗前左椎动脉比较,观察1组 $t = 20.4216, P < 0.001$,观察2组 $t = 18.2531, P < 0.001$,观察3组 $t = 24.6891, P < 0.001$ 。②与观察1组左椎动脉治疗后比较, $t = 6.5801, P = 0.002$;与观察2组左椎动脉治疗后比较, $t = 6.2538, P = 0.003$ 。③与治疗前右椎动脉比较,观察1组 $t = 14.3879, P < 0.001$,观察2组 $t = 16.3495, P < 0.001$,观察3组 $t = 22.5914, P < 0.001$ 。④与观察1组右椎动脉治疗后比较, $t = 5.1067, P = 0.005$;与观察2组右椎动脉治疗后比较, $t = 5.5186, P = 0.004$ 。⑤与治疗前基底动脉比较,观察1组 $t = 18.7356, P < 0.001$,观察2组 $t = 20.1687, P < 0.001$,观察3组 $t = 25.3184, P < 0.001$ 。⑥与观察1组基底动脉治疗后比较, $t = 5.0710, P = 0.013$;与观察2组基底动脉治疗后比较, $t = 4.9795, P = 0.016$ 。

表2 椎-基底动脉供血不足性眩晕症90例长春西汀与阿加曲班分别及联合治疗前后超氧化物歧化酶(SOD)、丙二醛(MDA)水平比较/ $\bar{x} \pm s$

组别	例数	SOD/(U/mL)		MDA/(nmol/mL)	
		治疗前	治疗后	治疗前	治疗后
观察1组	30	44.1±4.9	56.3±10.1 ^①	6.9±2.7	4.9±1.9 ^③
观察2组	30	44.0±4.7	55.1±9.7 ^①	6.9±2.7	4.8±1.8 ^③
观察3组	30	43.7±4.6	73.5±12.8 ^{①②}	6.9±2.6	3.5±1.1 ^{③④}
F值		0.058 0	26.497 7	0.000 0	6.811 4
P值		0.943 7	0.000 0	1.000 0	0.001 8

注:①与治疗前SOD比较,观察1组 $t = 12.568\ 1, P < 0.001$,观察2组 $t = 13.627\ 8, P < 0.001$,观察3组 $t = 32.048\ 9, P < 0.001$ 。②与观察1组SOD治疗后比较, $t = 6.081\ 6, P < 0.01$;与观察2组SOD治疗后比较, $t = 6.505\ 9, P < 0.01$ 。③与治疗前MDA比较,观察1组 $t = 9.436\ 5, P = 0.005$,观察2组 $t = 8.648\ 7, P = 0.006$,观察3组 $t = 15.246\ 1, P < 0.001$ 。④与观察1组MDA治疗后比较, $t = 3.308\ 0, P = 0.001$;与观察2组MDA治疗后比较, $t = 3.071\ 7, P = 0.003$ 。

表3 椎-基底动脉供血不足性眩晕症90例长春西汀与阿加曲班分别及联合治疗后疗效对比/例(%)

组别	例数	显效	有效	无效	总有效率
观察1组	30	11(36.7)	12(40.0)	7(23.3)	23(76.7)
观察2组	30	10(33.3)	12(40.0)	8(26.7)	22(73.3)
观察3组	30	20(66.7)	9(30.0)	1(3.3)	29(96.7)

注:观察1组与观察2组疗效比较, $Z = -0.554, P = 0.579$;观察1组与观察3组疗效比较, $Z = -3.241, P = 0.001$;观察2组与观察3组疗效比较, $Z = -3.377, P = 0.001$ 。

由基清除,进而达到缓解VBIV病人临床症状的治疗目的。另外,观察3组治疗总有效率高于观察1、2组($P < 0.05$),亦证实长春西汀、阿加曲班联合用药可提高VBIV疗效,治疗优势明显。

综上,长春西汀联合阿加曲班可提高VBIV病人椎基底动脉血流速度,促进氧自由基清除,提高疗效,使病人受益临床。

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