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脑血康胶囊联合巴曲酶对急性脑梗死患者血清 MBP、NSE 水平的影响*

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摘要 目的:研究脑血康胶囊联合巴曲酶对急性脑梗死患者血清髓鞘碱性蛋白(myelin basic protein, MBP)、神经元特异性烯醇化酶(neuron-specific enolase, NSE)水平的影响。**方法:**选择 2018 年 3 月~2019 年 3 月我院收治的 161 例急性脑梗死患者,将其随机分为两组。对照组静脉滴注巴曲酶,首次给予 10 BU,隔日给予 5 BU,每两天给药 1 次;观察组在巴曲酶的基础上联合口服脑血康胶囊,每天 3 次,每次 3 粒。观察和比较两组治疗总有效率、治疗前后血清 MBP、NSE、全血黏度(whole blood viscosity, WBV)、红细胞压积(hematocrit, HCT)、血浆黏度(plasma viscosity, PV)和纤维蛋白原(fibrinogen, FIB)水平及 NHSS 和 BI 评分的变化。**结果:**治疗后,观察组的有效率为 91.25%,明显高于对照组(64.2%, $P<0.05$);两组血清 MBP、NSE、WBV、HCT、PV 和 FIB 水平均较治疗前明显降低($P<0.05$),且观察组的以上指标明显低于对照组($P<0.05$);两组的 BI 评分明显升高($P<0.05$),NHSS 评分明显降低($P<0.05$),观察组 BI 评分明显高于对照组,而 NHSS 评分明显低于对照组($P<0.05$)。**结论:**脑血康胶囊联合巴曲酶对急性脑梗死有显著的疗效,能明显降低患者血清 MBP、NSE 水平,促进神经功能的恢复。

关键词:脑血康胶囊;巴曲酶;急性脑梗死;髓鞘碱性蛋白;神经元特异性烯醇化酶

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Effect of Naoxuekang Capsule Combined with Batroxobin on the Serum MBP and NSE Levels of Patients with Acute Cerebral Infarction*

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ABSTRACT Objective: To investigate the effect of Naoxuekang capsule combined with batroxobin on serum MBP and NSE levels in patients with acute cerebral infarction. **Methods:** Selected 161 cases of patients with acute cerebral infarction who were treated in our hospital from March 2018 to March 2019, divided into two groups randomly. In the control group, batroxobin was given intravenously, 10 BU for the first time, 5 BU for the next day, once every two days; in the observation group, Naoxuekang capsule was taken orally on the basis of batroxobin, three times a day, three capsules each time. Observe and compare the total treatment efficiency, serum MBP, NSE, whole blood viscosity (WBV), hematocrit (HCT), plasma viscosity (PV) and fibrinogen before and after treatment fibrinogen (FIB) levels and changes in NHSS and BI scores. **Results:** After treatment, the effective rate of the observation group was 91.25%, which was significantly higher than that of the control group (64.2%, $P<0.05$). Serum MBP, NSE, WBV, HCT, PV and FIB levels in the two groups were significantly lower than before treatment ($P<0.05$), and the above indicators in the observation group were significantly lower than those in the control group ($P<0.05$). The BI score of the two groups was significantly increased ($P<0.05$), the NHSS score was significantly decreased ($P<0.05$), the BI score of the observation group was significantly higher than that of the control group, and the NHSS score was significantly lower than that of the control group ($P<0.05$). **Conclusion:** Naoxuekang capsule combined with batroxobin had a significant effect on acute cerebral infarction, could significantly reduce the level of serum MBP, NSE, and promote the recovery of nerve function.

Key words: Naoxuekang Capsule; Batroxobin; Acute Cerebral Infarction; Myelin Basic Protein; Neuron Specific Enolase

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前言

急性脑梗死的病因极为复杂,主要包括血液系统的病变、血管本身的异常、血流动力学的异常等^[1-3]。脑梗死发病后,患者

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机体能量代谢出现障碍,产生大量的氧自由基,损伤血管内皮细胞、血小板黏附,细胞膜通透性增加,导致患者出现颅内高压和脑水肿,威胁患者的生命^[4-6]。目前,临床治疗急性脑梗死主要采取改善脑缺血、缺氧状态,降低颅内压,建立侧支循环以及挽救缺血半暗带^[7]。

巴曲酶是一种强力的降纤药物,可以降低血液的粘度和血小板聚集,使红细胞变形的能力大大增强,进而减轻血管的阻力,增加血流量,保护机体的神经功能,减少氧自由基,有效修复内皮的损伤^[8]。脑血康胶囊具有破瘀散结和活血化瘀的功效,主要适用于半身不遂、血瘀中风和脑血栓等证候者。脑血康胶囊的药理作用为降低血液的粘度,加快纤维蛋白的溶解速度,有效改善微循环,降低血压,改善脑部的缺氧情况,促进神经功能的恢复。目前尚未将脑血康胶囊和巴曲酶联用的报道。因此,本研究分析了脑血康胶囊联合巴曲酶对急性脑梗死患者的疗效,并探讨其对血清 MBP、NSE 水平的影响。

1 资料与方法

1.1 一般资料

选择 2018 年 3 月~2019 年 3 月我院收治的 161 例急性脑梗死患者,纳入标准:符合脑梗死的诊断标准^[9],首次发病,或既往虽然有脑卒中病史但没有遗留神经功能缺损,病程均<72 h,均知情同意。排除标准:(1)对脑血康胶囊和巴曲酶过敏者;(2)伴有重症糖尿病、造血系统疾病、颅内肿瘤、免疫系统疾病、重症高血压和亚急性细菌性心内膜炎的患者;(3)有出血性疾病的患者;(4)伴有心室中隔穿孔、多器官功能衰竭和心源性休克的患者;(5)伴有精神障碍者。用抽签法随机分为两组。观察组 80 例,男 43 例,女 37 例;年龄 34~78 岁,平均(51.69±7.28)岁;发病时间 11~45 h,平均(17.34±1.29)h;梗死部位:小脑梗死患者 11 例、基底节区梗死患者 59 例、多发梗死患者 10 例。对照组 81 例,男 43 例,女 38 例;年龄 34~78 岁,平均(52.25±8.34)岁;发病时间 11~45 h,平均(16.54±1.33)h;梗死部位:小脑梗死患者 11 例、基底节区梗死患者 60 例、多发梗死患者 10 例。两组

的基线资料比较差异无统计学意义($P>0.05$),具有可比性。

1.2 治疗方法

两组均采取吸氧、改善循环、控制血压和营养脑神经等治疗。对照组静脉滴注巴曲酶(北京托毕西药业,国药准字 H20030295),首次给予 10 BU,隔日给予 5 BU,每两天给药 1 次;观察组在巴曲酶的基础上联合口服脑血康胶囊(山东昊福药业,国药准字 Z10960009),每天 3 次,每次 3 粒。均治疗 14 d。

1.3 观察指标

疗效标准^[9]:(1)基本治愈:急性脑梗死患者的病残程度降低为 0 级,功能缺损评分减少 91%~100%;(2)显效:急性脑梗死患者的病残程度降低为 1~3 级,功能缺损评分降低 46%~90%;(3)有效:急性脑梗死患者的功能缺损评分降低 18%~45%;(4)无效:急性脑梗死患者的功能缺损评分降低<17%;(5)恶化:急性脑梗死患者的功能缺损评分升高。

治疗前后,用 NIHSS 量表和 BI 指数进行评估。BI 指数的内容包括进食、如厕、修饰、转移、大小便管理、穿衣、上楼梯、步行和洗澡等项目,分数越高,即日常的生活能力越好。NIHSS 量表包括凝视、意识水平、视野、上肢运动、面瘫、下肢运动、感觉、共济失调、语言、忽视症以及构音障碍等项目,其中评分 0~15 分表示轻型,评分 16~30 分表示中型,评分 31~45 分表示重型。

治疗前后,空腹采集 3 mL 静脉血,用 ELISA 法检测血清 MBP、NSE 水平,试剂盒均购自国药集团化学试剂有限公司;采取 DV-S 型黏度计检测两组的 WBV、HCT、PV 和 FIB 水平。

1.4 统计学分析

采用 SPSS 21.0 软件对数据进行统计学分析,两组间计量资料用($\bar{x} \pm s$)表示,组间对比用 t 检验,计数资料用%表示,组间对比用 χ^2 检验,以 $P<0.05$ 为差异有统计学意义。

2 结果

2.1 两组治疗后临床疗效对比

治疗后,观察组治疗的有效率为 91.25%,明显高于对照组(64.20%),差异有统计意义($P<0.05$),见表 1。

表 1 两组临床疗效比较[例(%)]

Table 1 Comparison of the clinical effect between two groups [n(%)]

Groups	n	Basic cure	Effective	Valid	Invalid	Deteriorate	The total effect rate
Control group	81	16(19.75)	26(32.10)	10(12.34)	15(18.52)	4(4.94)	52(64.20)
Observation group	80	23(28.75)	31(38.75)	19(23.75)	6(7.50)	1(1.25)	73(91.25)*

Note: Compared with the control group, * $P<0.05$.

2.2 两组治疗前后的血清 MBP 和 NSE 水平对比

治疗前,两组的血清 MBP 和 NSE 水平无明显差异($P>0.05$),治疗后,两组的血清 MBP 和 NSE 水平明显降低($P<0.05$),且观察组的血清 MBP 和 NSE 水平明显低于对照组($P<0.05$),见表 2。

2.3 两组治疗前后的 WBV、HCT、PV 和 FIB 水平对比

治疗前,两组的 WBV、HCT、PV 和 FIB 水平无明显差异($P>0.05$);治疗后,两组的 WBV、HCT、PV 和 FIB 水平较治疗前

明显降低($P<0.05$),且观察组的 WBV、HCT、PV 和 FIB 水平明显低于对照组($P<0.05$),见表 3。

2.4 两组治疗前后的 NIHSS 评分和 BI 评分对比

治疗前,两组的血清 NIHSS 和 BI 评分比较无明显统计学差异($P>0.05$),治疗后,两组的 BI 评分均较治疗前明显升高($P<0.05$),NIHSS 评分均较治疗前明显降低($P<0.05$),观察组 BI 评分明显高于对照组,NIHSS 评分显著低于对照组($P<0.05$),见表 4。

表 2 两组治疗前后的血清 MBP 和 NSE 水平对比($\bar{x} \pm s, \text{ng} \cdot \text{mL}^{-1}$)Table 2 Comparison of the serum MBP and NSE levels between the two groups before and after treatment ($\bar{x} \pm s, \text{ng} \cdot \text{mL}^{-1}$)

Groups	n		MBP	NSE
Control group	81	Before treatment	5.39 $\pm$ 1.27	38.27 $\pm$ 4.49
		After treatment	4.57 $\pm$ 0.92 [#]	28.13 $\pm$ 3.65 [#]
Observation group	80	Before treatment	5.36 $\pm$ 1.14	38.62 $\pm$ 4.71
		After treatment	3.69 $\pm$ 0.84 ^{*#}	22.36 $\pm$ 1.54 ^{*#}

Note: Compared with the control group, ^{*} $P < 0.05$; compared with before treatment, [#] $P < 0.05$.

表 3 两组治疗前后的 WBV、HCT、PV 和 FIB 水平对比($\bar{x} \pm s$)Table 3 Comparison of the WBV, HCT, PV and FIB levels between the two groups before and after treatment ($\bar{x} \pm s$)

Group	n		WBV/(m Pa·s)	HCT/%	PV/(m Pa·s)	FIB/(m Pa·s)
Control group	81	Before treatment	7.69 $\pm$ 1.34	55.39 $\pm$ 10.27	5.84 $\pm$ 1.23	9.86 $\pm$ 1.32
		After treatment	4.27 $\pm$ 1.16 [#]	42.29 $\pm$ 7.38 [#]	3.62 $\pm$ 1.07 [#]	5.74 $\pm$ 1.24 [#]
Observation group	80	Before treatment	7.63 $\pm$ 1.54	56.17 $\pm$ 11.32	5.89 $\pm$ 1.36	9.83 $\pm$ 1.25
		After treatment	2.13 $\pm$ 0.84 ^{*#}	31.64 $\pm$ 5.17 ^{*#}	1.19 $\pm$ 0.34 ^{*#}	3.04 $\pm$ 0.78 ^{*#}

Note: Compared with the control group, ^{*} $P < 0.05$; compared with before treatment, [#] $P < 0.05$.

表 4 两组治疗前后的 NIHSS 评分和 BI 评分对比($\bar{x} \pm s$, 分)Table 4 Comparison of NIHSS and BI score before and after treatment between the two groups ($\bar{x} \pm s$, score)

Groups	n		NIHSS score	BI score
Control group	81	Before treatment	16.27 $\pm$ 2.24	42.27 $\pm$ 10.14
		After treatment	7.15 $\pm$ 1.34 [#]	59.73 $\pm$ 11.62 [#]
Observation group	80	Before treatment	15.97 $\pm$ 2.13	43.86 $\pm$ 10.45
		After treatment	4.29 $\pm$ 1.03 ^{*#}	67.31 $\pm$ 14.25 ^{*#}

Note: Compared with the control group, ^{*} $P < 0.05$; compared with before treatment, [#] $P < 0.05$.

3 讨论

目前,脑血管疾病已成为一种对人类的生命健康安全造成严重威胁的恶性疾病,患者病死率明显高于恶性肿瘤^[10]。脑梗死指因机体脑部缺血、血液供应障碍和缺氧而导致局限性脑软化或者脑组织缺血性坏死,血管内膜受到损伤,脑动脉的管腔狭窄,促进局部血栓的形成,使动脉完全闭塞或者加重狭窄程度,造成脑缺血,而引发一种神经功能障碍性脑血管疾病^[11-15]。急性脑梗死的起病较为急骤,患者的特征为局灶性神经功能缺损,且伴有不同程度的言语、运动、认知、感觉等功能障碍^[16-18]。因神经系统具有不可再生性,脑梗死患者的运动功能、神经功能及日常活动能力均会受到很大的影响^[19-21]。目前,针对脑梗死患者最有效的治疗手段为溶栓疗法,但其受时间窗的影响比较大,使其应用受到极大的限制。

中医认为脑梗死是由于饮食油腻,长期饮酒,体质虚弱和心情郁结导致,其治疗主要是活血化瘀,调节气血,疏通经络,以尽最大程度地对缺血受到损伤的脑细胞进行保护。脑血康胶囊的药效组分主要是水蛭,能破血散结、活血祛瘀。药理研究显示脑血康胶囊可以有效阻止凝血酶对纤维蛋白发挥作用,加快纤维蛋白的溶解速度,阻碍血液凝固,促进脑部肿块的融化以及吸收,促进脑细胞代谢,改善脑部的缺氧症状以及脑部的微循环,加快神经功能恢复^[22,23]。本研究中,观察组 WBV、HCT、PV 和 FIB 水平明显低于对照组,NIHSS 和 BI 评分明显优于对照组,提示在巴曲酶的基础上联用脑血康胶囊能更明显的改善

血液流变学、提高日常生活能力,改善神经功能。其原因为脑血康胶囊能降低脑血管的阻力,改善血液流变性,促进血液循环,抑制血栓的形成,促进纤溶酶活性,改善血液循环,同时也能消除瘀血,通过抗凝血、降血脂、抗血栓作用,改善脑部缺氧状态和微循环^[24]。何育教等^[25]对 43 例高血压脑出血患者在脑苷肌肽的基础上联用脑血康胶囊,患者的 NIHSS 评分及生活能力评分明显改善,与本研究结果相一致。

MBP 是一种临床上评估神经损伤程度的新型标志物,主要参与了神经胶质细胞的形成过程,脑组织受损后会导致神经胶质细胞的骨架受到破坏,使得 MBP 被大量释放进入到血液循环中^[26-28]。NSE 主要存在于脑组织中,能调控神经细胞的能量代谢情况,当机体的血脑屏障受损后,大量的 NSE 会进入血液中,导致血清 NSE 含量的增高^[29-31]。本研究结果显示观察组的血清 MBP 和 NSE 水平明显低于对照组,提示脑血康胶囊联合巴曲酶能使患者神经功能受损的程度明显减轻。分析其原因为脑血康胶囊治疗急性脑梗死后,其药理作用能够促进脑部肿块的融化以及吸收,促进脑细胞代谢,使患者神经细胞得以再生与修复,从而阻止 MBP 和 NSE 从受损神经细胞的放出,经过已破坏的血脑屏障释放进入外周血液,导致血清 MBP 和 NSE 水平明显降低。因此 MBP 和 NSE 降低是评价神经功能恢复的重要标志物^[32]。

综上所述,脑血康胶囊联合巴曲酶对急性脑梗死有显著的疗效,能明显降低血清 MBP、NSE 水平,促进神经功能的恢复。

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