

doi: 10.13241/j.cnki.pmb.2020.18.018

银丹心脑血管通软胶囊联合长春西汀治疗缺血性脑卒中患者的疗效*

马 妮 崔小丽 王 妮 高俊卿 张 强

(陕西省人民医院神经内科 陕西 西安 710068)

摘要 目的: 研究银丹心脑血管通软胶囊联合长春西汀治疗缺血性脑卒中患者的疗效。**方法:** 选择 2016 年 1 月~2018 年 12 月我院的 83 例缺血性脑卒中患者,随机分为两组。对照组静脉滴注 30 mg 的长春西汀,每天 1 次。观察组在长春西汀的基础上,口服 4 粒银丹心脑血管通软胶囊,每天 3 次。比较两组的改良爱丁堡-斯堪的那维亚神经功能缺损量表 (Modified Edinburgh Scandinavian neurological deficit scale,MESS)、Barthel 指数、血清白细胞介素 1 β (Interleukin 1 β ,IL-1 β)、单核细胞趋化蛋白-1 (Monocyte chemoattractant protein-1,MCP-1)、血管内皮生长因子 (Vascular endothelial growth factor,VEGF) 水平。**结果:** 观察组的有效率明显高于对照组 ($P<0.05$);治疗后,两组的 MESS 评分明显降低 ($P<0.05$),Barthel 指数明显升高 ($P<0.05$),且观察组的 MESS 评分和 Barthel 指数明显优于对照组 ($P<0.05$);治疗后,两组的血清 IL-1 β 、MCP-1 水平明显降低 ($P<0.05$),血清 VEGF 水平明显升高 ($P<0.05$),且观察组上述指标优于对照组 ($P<0.05$)。**结论:** 银丹心脑血管通软胶囊联合长春西汀能降低缺血性脑卒中患者炎症细胞因子的过度表达,改善脑血流灌注和神经功能,有效控制缺血性脑卒中的进展。

关键词: 银丹心脑血管通软胶囊;长春西汀;缺血性脑卒中;白细胞介素 1 β ;单核细胞趋化蛋白-1;血管内皮生长因子

中图分类号: R743 **文献标识码:** A **文章编号:** 1673-6273(2020)18-3482-04

Effect of Yindanxinnaotong Soft Capsule Combined with Vinpocetine on Patients with Ischemic Stroke*

MA Ni, CUI Xiao-li, WANG Ni, GAO Jun-qing, ZHANG Qiang

(Department of Neurology, Shaanxi Provincial People's Hospital, Xi'an, Shaanxi, 710068, China)

ABSTRACT Objective: To investigate the effect of Yindanxinnaotong soft capsule combined with vinpocetine on patients with ischemic stroke. **Methods:** Selected 83 cases of patients with ischemic stroke who were treated in our hospital from January 2016 to December 2018, divided into two groups randomly. In the control group, 30 mg vinpocetine was given intravenously once a day. On the basis of vinpocetine, the observation group took four Yindanxinnaotong soft capsules three times a day. The modified Edinburgh Scandinavian neurological deficit scale (MESS), Barthel index, interleukin-1 β (IL-1 β), monocyte chemoattractant protein-1 (MCP-1), vascular endothelial growth factor, VEGF) were compared between the two groups. **Results:** The effective rate of the observation group was significantly higher than control group ($P<0.05$). After treatment, the scores of mess and Barthel Index in the two groups were significantly lower ($P<0.05$), and the scores of mess and Barthel Index in the observation group were significantly higher than those in the control group ($P<0.05$). After treatment, the serum levels of IL-1 β and MCP-1 in the two groups were significantly lower ($P<0.05$), the serum VEGF level was significantly higher ($P<0.05$), and the serum levels of IL-1 β and MCP-1 in the observation group were significantly lower than those in the control group ($P<0.05$), and the serum VEGF level was significantly higher than that in the control group ($P<0.05$). **Conclusion:** Yindanxinnaotong soft capsule combined with vinpocetine can reduce the over expression of inflammatory cytokines, improve cerebral blood flow perfusion and nerve function, and effectively control the progress of ischemic stroke.

Key words: Yindanxinnaotongsoft Capsule; Vinpocetine; Ischemic Stroke; Interleukin-1 β ; Monocyte Chemoattractant Protein-1; Vascular Endothelial Growth Factor

Chinese Library Classification(CLC): R743 **Document code:** A

Article ID: 1673-6273(2020)18-3482-04

前言

脑血管疾病是目前造成人类死亡的三大主要疾病之一,以高死亡率、高发病率、高复发率以及高致残率为特点^[1,2]。其中,缺血性脑卒中大约占有脑血管疾病的 75%以上^[3]。缺血性脑卒中患者通常情况下是在脑血栓的基础上发生脑动脉堵塞或

脑梗死,从而出现意识障碍以及偏瘫^[4,5]。在脑卒中的急性期会发生比较严重的脑损伤以及脑水肿,患者的死亡率最高,对社会、家庭和国家造成严重的精神损失以及经济方面的负担^[6,7]。我国的脑卒中死亡率高达美国、日本、法国的 4~6 倍^[8]。中医学治疗缺血性脑卒中有非常悠久的历史。近年来的研究显示,银丹心脑血管通软胶囊能通过抗炎以及降血脂等机制,对早期动脉粥

* 基金项目:陕西省科技厅基金项目(2017SF-264)

作者简介:马妮(1979-),女,本科,主治医师,研究方向:神经系统疾病诊疗,电话:13909180848,E-mail:mnshanxi1228@126.com

(收稿日期:2019-12-08 接受日期:2019-12-31)

样硬化发挥较好的防治效果^[9]。该药可以从多种机制及途径抗动脉硬化、改善动脉循环、降血脂、抗炎和稳定斑块等,以促使神经功能的恢复^[10]。但关于其治疗缺血性脑卒中的具体机制方面的研究比较少见。本研究在长春西汀的基础上,联用银丹心脑通软胶囊,分析其对缺血性脑卒中的疗效和可能的机制。

1 资料与方法

1.1 一般资料

选择2016年1月~2018年12月我院收治的83例缺血性脑卒中患者,均符合相关的诊断标准,既往无短暂性脑缺血发作病史或脑卒中病史,均知情同意。排除标准:(1)经影像学或者腰穿检查疑为出血性梗死的患者;(2)伴有意识障碍或者卒中病中脏腑的患者;(3)有精神智能障碍或者重要脏器功能不全的患者;(4)生命体征不稳定的患者;(5)合并患有消化道出血者的患者;(6)不能耐受银丹心脑通软胶囊以及长春西汀的患者;(7)未按照规定服用银丹心脑通软胶囊以及长春西汀的患者;(8)有糖尿病病史的患者。用抽签法随机分为两组。观察组42例,男30例,女12例;年龄43~79岁,平均(61.73±14.22)岁;病程1~10个月,平均(2.97±1.46)个月。对照组41例,男29例,女12例;年龄43~79岁,平均(62.35±13.78)岁;病程1~10个月,平均(2.83±1.54)个月。两组的基线资料具有可比性($P>0.05$)。

1.2 方法

两组入院后均采取改善循环治疗(疏血通)、抗血小板聚集治疗(阿司匹林)以及脑细胞活化剂治疗(脑蛋白水解物)等。对照组:静脉滴注30 mg的长春西汀(匈牙利吉瑞大药厂,H20130774),每天1次。观察组:在长春西汀的基础上,口服4粒银丹心脑通软胶囊(贵州百灵制药公司,国药准字Z20027144),每天3次。两组均总计治疗1个月。

1.3 观察指标

疗效标准:①痊愈:患者治疗后的神经功能得到了明显的改善,身体状态全部恢复正常,生活基本上能自理;②有效:患者治疗后的神经功能有所改善,身体状态全部得到缓解,生活上经过患者家属的简单帮助,可以自理;③无效:患者治疗后的身体状态、神经功能没有改善,生活上仍然不能自理。

治疗前后,用MESS量表判断神经功能缺损程度,Barthel指数判断日常生活能力;并抽取3 mL静脉血,用ELISA法检测血清IL-1 β 、MCP-1、VEGF水平,试剂盒购自武汉赛培生物公司。

1.4 统计学分析

采用SPSS21.0,计量资料用t检验,计数资料用 χ^2 检验,以 $P<0.05$ 有统计学意义。

2 结果

2.1 疗效比较

观察组的有效率明显高于对照组($P<0.05$),见表1。

表1 疗效比较[例(%)]

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

Groups	n	Recovery	Valid	Invalid	The total effect rate
Control group	41	10(24.39)	17(41.46)	14(34.15)	27(65.85)
Observation group	42	11(26.19)	26(61.90)	5(11.90)	37(88.09)*

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

2.2 MESS评分和Barthel指数比较

治疗后,两组的MESS评分明显降低($P<0.05$),Barthel指

数明显升高($P<0.05$),且观察组的MESS评分和Barthel指数明显优于对照组($P<0.05$),见表2。

表2 治疗前后的MESS评分和Barthel指数比较($\bar{x}\pm s$,分)

Table 2 Comparison of mess score and Barthel index between the two groups before and after treatment ($\bar{x}\pm s$, Score)

Groups	n		MESS score	Barthel index
Control group	41	Before treatment	20.73±4.26	51.72±10.43
		After treatment	11.32±2.54 [#]	63.82±11.45 [#]
Observation group	42	Before treatment	19.45±5.62	52.43±10.59
		After treatment	6.53±1.42* [#]	72.36±12.85* [#]

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

2.3 血清IL-1 β 、MCP-1、VEGF水平比较

治疗后,两组的血清IL-1 β 、MCP-1水平明显降低($P<0.05$),血清VEGF水平明显升高($P<0.05$),且观察组上述指标优于对照组($P<0.05$),见表3。

2.4 不良反应

两组均未检测发现凝血功能异常、肾功能异常及肝功能异常等不良反应。

3 讨论

缺血性脑卒中是一种多种病因导致的极易反复多次发作的慢性脑血管疾病^[11]。该病的发病机制主要是由于机体的脑组织出现了动脉粥样硬化,造成血管的管腔痉挛以及狭窄,从而使得血液的凝聚性升高、血流动力学发生变化或血液的黏稠度增加等,导致患者机体脑内局部的动脉出现供血不足,脑组织

表 3 血清 IL-1 β 、MCP-1、VEGF 水平比较($\bar{x}\pm s$)
Table 3 Comparison of serum levels of IL-1 β , MCP-1 and VEGF ($\bar{x}\pm s$)

Groups	n		IL-1 β (ng/L)	MCP-1(mg/L)	VEGF(ng/L)
Control group	41	Before treatment	6.39 $\pm$ 1.24	122.73 $\pm$ 45.63	403.75 $\pm$ 104.21
		After treatment	4.23 $\pm$ 0.75 [#]	76.21 $\pm$ 34.18 [#]	493.24 $\pm$ 117.25 [#]
Observation group	42	Before treatment	6.41 $\pm$ 1.17	123.65 $\pm$ 43.29	402.53 $\pm$ 103.28
		After treatment	2.15 $\pm$ 0.64 ^{*#}	51.34 $\pm$ 29.76 ^{*#}	591.73 $\pm$ 124.65 ^{*#}

出现急性的缺氧、缺血,甚至坏死,最终使其全身表现出一系列的临床症状^[12-15]。临床上推荐在早期控制水肿、降低血液黏度、抑制脑组织细胞过氧化以及改善微循环,促进受损神经细胞恢复^[16-18]。长春西汀可以加速脑局部缺血部位的血供,保护缺血神经元细胞^[19]。但单用的效果不佳。

现代药理学研究发现,中医的治疗缺血性脑卒中的方法有的是通过保护缺血脑损伤,有的是通过增加缺血脑组织的血流量,有的是通过保护缺血再灌注损伤等^[20]。银丹心脑通软胶囊的中药成分包括丹参、银杏叶、灯盏细辛、山楂、绞股蓝、大蒜、冰片以及三七等,主要用于气滞血瘀导致的胸痹,症见胸闷、胸痛、心悸和气短等,以及中风后遗症、中风、心绞痛、冠心病、脑动脉硬化、高脂血症等多种疾病^[21-24]。其中,三七可以抑制基质金属蛋白酶的表达和扩张血管,有效稳定血管中的粥样斑块。银杏叶可以清除机体中的氧自由基,抑制血小板激活因子,改善机体的血液供应。丹参可以抑制巨噬细胞引发的脂质过氧化反应,明显升高粥样硬化斑块的一氧化氮含量,降低血浆内皮素水平,有效消退粥样斑块。灯盏细辛可以增加冠脉血流,抑制血小板聚集,降低外周血管的阻力,有效降低血液的黏稠度。大蒜可以在一定程度上增强机体的抵抗力。山楂以及绞股蓝可以与血液内的胆固醇发生结合,有效阻断肝肠循环,降低机体吸收胆固醇的量,还可以升高高密度脂蛋白,改善消化功能。观察组的 MESS 评分和 Barthel 指数明显优于对照组。表明银丹心脑通软胶囊联合长春西汀可以通过各种机制以及途径降低血液黏稠度,改善动脉粥样硬化,从而改善神经功能,提高生活能力。

IL-1 β 的大量释放能促进血管内皮细胞进一步表达黏附因子,促进浸润,造成其释放大量的氧自由基以及炎症因子^[25,26]。在损伤、缺氧、感染、血流动力学改变以及免疫反应等情况下,脑组织会大量分泌和释放 MCP-1,造成炎症细胞在受损脑组织局部发生活化以及聚集,且通过炎症细胞的作用使脑损伤进一步加重^[27,28]。VEGF 能保护神经元,促进脑部的毛细血管发生增生,可以特异性的作用于内皮细胞分裂、侧支循环的建立以及血管的生长,在脑卒中患者体内,VEGF 能促进脑组织内皮细胞的大量表达,使其完整性得到重塑^[29,30]。观察组的血清 IL-1 β 、MCP-1 水平明显低于对照组,血清 VEGF 水平明显高于对照组($P<0.05$)。表明银丹心脑通软胶囊可以降低炎症细胞表达,减少对脑组织的破坏作用,发挥减轻缺血脑组织再灌注损伤以及稳定动脉粥样斑块的效果。对缺血性脑卒中患者炎症浸润的减少、神经细胞和血管内皮细胞的修护具有重要的意义。

综上所述,银丹心脑通软胶囊联合长春西汀能降低缺血性脑卒中患者炎症细胞因子的过度表达,改善脑血流灌注和神经

功能,有效控制缺血性脑卒中的进展。

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