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小牛血清去蛋白提取物联合天麻钩藤饮对急性脑梗死患者神经功能及血液流变学的影响 *

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摘要 目的:分析小牛血清去蛋白提取物联合天麻钩藤饮对急性脑梗死患者神经功能及血液流变学的影响。**方法:**选择 2015 年 10 月至 2018 年 10 月在我院治疗的急性脑梗死患者 90 例为研究对象,将其随机均分两组。对照组仅采取小牛血清去蛋白提取物治疗,实验组在对照组基础上联合采用天麻钩藤饮治疗。比较两组治疗的临床总有效率、治疗前和治疗 20 d 后的神经功能缺损评分、日常生活能力评分和血液流变学指标的变化以及治疗期间不良反应的发生情况。**结果:**治疗后,实验组的总有效率为 95.56%,显著高于对照组(77.78%, $P < 0.05$)。两组治疗后的美国国立卫生研究院卒中量表(National Institutes of Health Stroke Scale, NIHSS)和日常生活活动能力量表(Activities of Daily Living, ADL)评分均较治疗前显著升高,且实验组以上指标明显高于对照组($P < 0.05$)。两组治疗后的全血高切黏度、全血低切黏、红细胞比容、血小板聚集率和纤维蛋白原较治疗前均显著降低,且实验组以上指标均显著低于对照组($P < 0.05$)。**结论:**小牛血清去蛋白提取物联合天麻钩藤饮治疗急性脑梗死效果显著优于单用小牛血清去蛋白提取物治疗,其可更有效促进患者神经功能的恢复,提高患者生活质量,改善其血液流变学。

关键词:急性脑梗死;小牛血清去蛋白提取物;天麻钩藤饮;神经功能;血液流变学

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Effect of Bovine Serum Protein Extract Combined with Tianma Gouteng Drink on the Nerve Function and Hemorheology of Patients with Acute Cerebral Infarction*

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ABSTRACT Objective: To analyze the effect of bovine serum protein extract combined with tianma gouteng drink on the nerve function recovery and hemorheology of patients with acute cerebral infarction. **Methods:** Ninety patients with acute cerebral infarction treated in our hospital from October 2015 to October 2018 were selected as the study subjects, they were randomly divided into two groups. The control group was treated with bovine serum protein extract alone, while the experimental group was treated with tianma gouteng drink on the basis of control group. The total effective rate, changes of neurological impairment score, daily living ability score and hemorheology index before and at 20 days after treatment and the occurrence of adverse reactions during treatment were compared between the two groups. **Results:** After treatment, the total effective rate of experimental group was 95.56%, which was significantly higher than that of the control group (77.78%, $P < 0.05$). The scores of National Institutes of Health Stroke Scale (NIHSS) and Activities of Daily Living (ADL) in both groups after treatment were significantly higher than those before treatment, which were significantly higher than those in the control group ($P < 0.05$). After treatment, the whole blood high tangential viscosity, whole blood low tangential viscosity, erythrocyte specific volume, platelet aggregation rate and fibrinogen in both groups were significantly lower than before treatment, and the above indexes in the experimental group were significantly lower than those in the control group ($P < 0.05$). **Conclusion:** Bovine serum protein extract combined with tianma gouteng drink is more effective than bovine serum protein extract alone in the treatment of acute cerebral infarction. It can more effectively promote the recovery of neurological function, improve the hemorheology and quality of life.

Key words: Acute cerebral infarction; Bovine serum protein extract; Tianma gouteng drink; Neurologic function; Hemorheology

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前言

脑血管疾病是一种严重危害公众身体健康和生命的常见病之一,发病率逐年增高,已成为了我国居民死亡的主要原因之一^[1,2]。供应脑部血液的动脉出现粥样硬化,形成血栓使得管腔狭窄或者闭塞,导致局灶性脑供血不足,引起脑组织坏死^[3,4]。异常物体沿血液循环进入脑动脉或颈动脉,也可能造成血流中断或流量减少,产生相应支配区域的脑组织软化、坏死。脑梗死患者的临床表现主要为头痛、眩晕、半身不遂、吞咽困难、言语不清等,严重者会昏迷不醒^[5,6]。脑梗死分为脑血栓形成、脑梗死和腔隙性脑梗死,对急性脑梗死患者采取及时、有效的治疗,对降低致残率、改善患者的生活质量和预后意义重大^[7]。

目前,对于急性脑梗死的治疗有抗凝疗法、溶栓疗法、降纤疗法、血液稀释疗法等^[8]。急性脑梗死在中医中属于“中风病”范畴,病机为气血逆乱、脏腑失调。已有多项研究结果表明中西医结合治疗急性脑梗死效果显著^[9]。小牛血清去蛋白提取物对大脑循环和营养方面的障碍(缺血性疾病发作、颅脑外伤)、外周血流(动、静脉)障碍以及由这些障碍引起的动脉血管病等效果

显著,且在治疗急性脑梗死方面具有一定的效果。天麻钩藤饮是平熄内风的方剂,临床上常用于治疗高血压病、急性脑血管病、内耳性眩晕等属于肝阳上亢,肝风上扰者,但是二者联合用药在急性脑梗死治疗中尚未见报道。本研究主要分析了小牛血清去蛋白提取物联合天麻钩藤饮对急性脑梗死的治疗效果,现将研究结果报道如下。

1 资料与方法

1.1 研究资料

将我院收治的 90 名急性脑梗死患者作为研究对象,所有患者临床症状符合相关诊断标准,均经头颅 CT 或 MRI 确诊。纳入标准:(1)首次发病、发病 24 小时内入院;(2)意识清醒能配合完成研究;(3)对本研究知情同意;(4)无严重的心、肺、肾功能不全等合并症。排除标准:(1)恶性肿瘤者;(2)颅内肿瘤、感染及血液系统疾病者;(3)近期手术、服用抗炎药物等影响检验指标者。所有患者随机均分为两组,其一般资料见表 1,具有可比性($P>0.05$)。

表 1 两组一般资料比较

Table 1 Comparison of the general data between the two groups

Groups	n	Male/Female	Mean age	Site of lesion Basal ganglia/Cerebellum/temporal lobe/Occipital lobe/multiple sites	Major concomitant diseases Hypertension/Diabetes Mellitus
Research group	45	28/17	62.34± 9.24	18/10/4/3/10	26/19
Control group	45	30/15	61.89± 10.12	17/11/4/5/8	24/21
χ^2/t		0.194	0.22	0.567	0.979
P		0.66	0.826	0.336	0.323

1.2 治疗方法

所有患者均给予控制血糖、降血压、脱水降颅压、神经康复等基础治疗,在此基础上对照组:采用小牛血清去蛋白提取物治疗,将 0.8 g 小牛血清去蛋白提取物溶于 250 mL 0.9%氯化钠注射液或 5%葡萄糖注射液中静脉滴注,1 次/日,连续治疗 20 d。观察组在对照组治疗的基础上加用天麻钩藤饮,组方:天麻 10 g,栀子 10 g,钩藤 12 g,黄芩 9 g,益母草 15 g,杜仲 10 g,夜交藤 15 g,桑寄生 10 g,牛膝 12 g,石决明 30 g。言语不利者,加石菖蒲 10 g,郁金 12 g,远志 10 g。头痛严重者,加水牛角 15 g,夏枯草 10 g,水煎服,1 剂/d,分两次饭后服用,连续治疗 20 d。

1.3 评价指标

(1)临床疗效评价:治疗 20 d 后进行效果评价,按照第四届脑血管病学术会议制定的脑卒中评价标准^[10],痊愈:神经缺损评分减少 91%-100%,0 级病残;显效:神经缺损评分减少 90%-46%,1-3 级病残;有效:神经损伤评分减少 18%-45%;无效:神经缺损评分未降低甚至增加。

(2)NISHH 评分和 ADL 评分:治疗前和治疗 20d 后对所有患者进行神经功能缺损和日常生活能力评价,分别采用美国国立卫生研究院卒中量表(NISHH)^[11]和,日常生活活动能力量表(ADL)^[12]。

(3)血液流变学指标检测:所有患者在治疗前和治疗 20d 后

采集患者清晨空腹静脉血,检测全血高切黏度(HSV)、全血低切黏度(LSV)、红细胞比容(HCT)、血小板聚集率(PAG)、纤维蛋白原(Fbg)。

(4)不良反应:记录两组患者治疗期间出现的低血压休克、皮肤过敏等现象。

1.4 统计学分析

采用 SPSS21.0 软件分析数据,计量资料和计数资料分别用 $\bar{x} \pm s$ 和 % 表示,组间比较分别行 t 检验和 χ^2 检验,以 $P<0.05$ 为差异具有统计学意义。

2 结果

2.1 两组临床疗效的比较

治疗后,实验组临床总有效率为 95.56%,对照组为 77.78%,试验组显著高于对照组($P<0.05$),见表 2。

2.2 两组治疗前后神经功能缺损评分和日常生活能力评分的比较

治疗前,两组的 NISHH 和 ADL 评分比较差异无统计学意义($P>0.05$);治疗 20d 后,两组 NISHH 和 ADL 评分均较治疗前显著升高,且实验组以上指标均显著高于对照组($P<0.05$),见表 3。

2.3 两组治疗前后血液流变学指标的比较

治疗前,两组的全血高切黏度、全血低切黏、红细胞比容、血小板聚集率和纤维蛋白原比较差异均无统计学意义;治疗后,两组的上述各项指标均较治疗前显著降低,且实验组以上指标均显著低于对照组($P<0.05$),见表4。

表2 两组治疗后临床疗效比较[例(%)]

Table 2 Comparison of the clinical effect between two groups [n(%)]

Groups	n	Cure	Effective	Valid	Invalid	The total effect rate
Research group	45	39	3	1	2	43(95.56)
Control group	45	25	6	4	10	35(77.78)
χ^2						6.154
P						0.013

表3 两组治疗前后神经功能缺损评分和日常生活能力评分的比较($\bar{x}\pm s$,分)Table 3 Comparison of the NISHH and ADL scores between two groups before and after treatment($\bar{x}\pm s$, points)

Groups	n	NISHH		ADL	
		Before treatment	After treatment	Before treatment	After treatment
Research group	45	24.45 $\pm$ 5.72	69.67 $\pm$ 10.63*	17.53 $\pm$ 1.23	78.56 $\pm$ 12.73*
Control group	45	24.94 $\pm$ 5.35	61.34 $\pm$ 9.74*	17.82 $\pm$ 1.45	61.21 $\pm$ 8.52*
t	/	0.42	3.876	1.023	7.598
P	/	0.675	<0.001	0.309	<0.001

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

表4 两组治疗前后血液流变学指标的比较($\bar{x}\pm s$)Table 4 Comparison of the hemorheology indexes between the two groups before and after treatment ($\bar{x}\pm s$)

Groups	HSV(mPa·s)		LSV(mPa·s)		HCT(%)		PAG(%)		Fbg(g/L)	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Research group	7.45 $\pm$ 1.23	5.12 $\pm$ 0.89*	8.34 $\pm$ 1.67	6.56 $\pm$ 1.21*	46.59 $\pm$ 9.21	35.35 $\pm$ 7.54*	0.87 $\pm$ 0.22	0.54 $\pm$ 0.13*	4.24 $\pm$ 1.23	2.36 $\pm$ 0.98*
Control group	7.26 $\pm$ 1.34	6.23 $\pm$ 0.92*	8.53 $\pm$ 1.45	7.34 $\pm$ 1.52*	47.54 $\pm$ 9.89	40.23 $\pm$ 8.78*	0.85 $\pm$ 0.24	0.67 $\pm$ 0.21*	4.45 $\pm$ 1.24	3.58 $\pm$ 1.02*
t	0.701	5.817	0.576	2.693	0.472	2.829	0.412	3.531	0.807	5.786
P	0.485	<0.001	0.566	0.008	0.638	0.006	0.681	0.001	0.422	<0.001

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

2.4 两组不良反应发生情况的比较

两组患者在治疗过程中未出现皮肤过敏、发热、低血压休克等不良反应。

3 讨论

急性脑梗死是因动脉粥样硬化、血小板功能异常等使得脑部局部血液循环障碍,当大脑出现缺血缺氧或者循环受阻时,会引起机体能量耗竭及酸中毒^[13,14],在这种情况下,氧自由基及兴奋性氨基酸会大量的聚集,对神经元细胞膜造成损伤,导致细胞内的钙离子大量聚集,最终神经元会在炎性细胞因子受损下死亡^[15,16]。脑梗死灶周围会产生一个缺血损伤区,该区域细胞的正常功能会因为脑血流减缓而发生障碍,当血流循环正常、体内积聚的氧自由基减少、钙离子进入细胞受阻,可有效改善脑细胞代谢、补充神经修复所需物质和能量,即可促进脑细胞功能的恢复^[17-19]。中医认为脑梗死是由于年老体衰、肾精不足、

肝肾阴虚、阴不制阳、肝阳上亢、阳亢化风,经脉瘀阻发生中风的,其形成与脏腑功能失调有关,因此治疗原则应以平肝熄风、补益肝肾、清热活血为主^[20,21]。

天麻钩藤饮出自胡光慈的《杂病论治新义》,是平肝降逆的经典组方,该组方中的药物主要具有活血通络、平肝潜阳等功效^[22,23]。天麻具有治风神药的称号,常用于眩晕的治疗,与钩藤和石决明共奏平肝潜阳的功效,为君药。栀子与黄芩具有清热泻火的作用,为臣药^[24],杜仲、桑寄生补肝益肾,川牛膝引血下行,夜交藤安神定志,益母草活血化瘀^[25]。诸药合用具有潜阳熄风、补肝益肾的功效,肝平风熄、经脉通畅即可达到病征消失。小牛血清去蛋白提取物是以出生28 d的小牛血清为原料,制成的分子量<5000U的注射液^[26,27],其主要成分有:核酸衍生物、低分子肽、氨基酸和糖脂类等^[28]。该药的主要作用成分为小分子激活肽和磷酸肌醇寡糖(IPOS),神经元蛋白质的合成主要成分是小分子激活肽,其能恢复细胞激活酶活性,使神经元获

得再生和修复^[29]。除此之外,IPOS 具有纠正能量代谢障碍、减缓酸中毒的作用,因此能降低炎症细胞因子对神经元的损害^[30]。

本研究结果表明联合用药治疗急性脑梗死效果显著,能有效改善患者的神经损伤情况提高患者的生活质量,且血液流变学指标的改善情况明显优于仅采取小牛血清去蛋白提取物治疗。分析原因为心脑血管疾病的发作、发展多于情绪激动、暴怒伤肝,肝气郁结、气郁化火,火灼阴伤导致肝肾阴虚,肝阳偏亢,肝阳化风,肝风上扰发病。现代药理表明,天麻钩藤饮具有改善血管收缩和舒张失衡状态,且该药具有改善微循环和脑组织供血供氧,有利于脑神经功能恢复。小牛血清去蛋白提取物具有纠正缺血神经细胞酸中毒、增强脑代谢的储备能力,延长细胞生存时间的作用。二者联合用药具有协同作用,对改善急性脑梗死症状效果显著。

综上所述,小牛血清去蛋白提取物联合天麻钩藤饮治疗急性脑梗死效果显著优于单用小牛血清去蛋白提取物治疗,其可更有效促进患者神经功能的恢复,提高患者生活质量,改善其血液流变学。

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(上接第 4718 页)

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