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## 活血化瘀中药复方治疗急性脑出血的疗效及对相关血清指标的影响\*

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**摘要 目的:**探讨活血化瘀中药复方治疗急性脑出血的疗效及对星形胶质源性蛋白(S100 $\beta$ )、N-末端脑钠素原(NT-proBNT)、血清超敏C反应蛋白(hs-CRP)及白细胞介素-6(IL-6)水平的影响。**方法:**选择2015年3月到2016年7月84例在我院接受治疗的急性脑出血患者,随机分为对照组(n=42)和试验组(n=42)。对照组患者给予抗血小板、降脂、营养神经、抗凝、自由基清除、降低颅内压、静脉滴注依达拉奉等常规治疗,试验组在此基础上给予活血化瘀中药复方,疗程均为14d。观察并比较两组患者临床疗效、不良反应及治疗前后脑血肿体积、欧洲脑卒中评分(ESS)。检测并比较两组患者治疗前后血清S100 $\beta$ 、NT-proBNT、hs-CRP及IL-6水平。**结果:**两组患者不良反应发生率比较差异无统计学意义(P>0.05)。试验组总有效例数37例,对照组总有效例数28例,总有效率高于对照组,有统计学差异(P<0.05)。两组患者治疗后ESS评分高于治疗前,脑血肿体积小于治疗前,并且试验组患者ESS评分高于对照组,脑血肿体积小于对照组,差异具有统计学意义(P<0.05)。两组患者治疗后血清S100 $\beta$ 、NT-proBNT、hs-CRP及IL-6水平低于治疗前,试验组上述指标为(1.02 $\pm$  0.21)ng/mL、(120.26 $\pm$  19.47)pmol/L、(8.33 $\pm$  1.45)mg/L、(11.25 $\pm$  2.71)pg/mL,低于对照组的(1.45 $\pm$  0.24)ng/mL、(219.68 $\pm$  22.51)pmol/L、(16.92 $\pm$  2.70)mg/L、(20.07 $\pm$  4.62)pg/mL,有统计学差异(P<0.05)。**结论:**对于急性脑出血患者,采用活血化瘀中药复方治疗其临床疗效确切,降低炎症反应,改善血清S100 $\beta$ 、NT-proBNT水平,安全性较好,值得临床推广应用。

**关键词:**活血化瘀中药复方;急性;脑出血;超敏C反应蛋白;白细胞介素-6;疗效

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## Effect of Chinese Herbal Medicine for Activating Blood Stasis on Acute Cerebral Hemorrhage and its Influence on Related Serum Indexes\*

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**ABSTRACT Objective:** To study the effect of Chinese herbal medicine for activating blood stasis on acute cerebral hemorrhage and the influence of stellate source sex protein (S100 $\beta$ ), N-terminal proBNP (NT-proBNT), serum hypersensitive C-reactive protein (hs-CRP), interleukin-6 (IL-6). **Methods:** 84 patients with acute cerebral hemorrhage treated in our hospital from March 2015 to July 2016 were selected. The patients were randomly divided into control group (n=42) and experimental group (n=42). The control group was given antiplatelet, lipid-lowering, nutritional nerve, anticoagulant, free radical scavenging, intracranial pressure reduction, intravenous drip of Edaravone and other conventional treatment. The experimental group were treated with Chinese herbal medicine for activating blood stasis on the basis of the control group. The two groups were treated for 14 days. The clinical efficacy, adverse reactions, cerebral hematoma volume, the European stroke score (ESS) before and after treatment were observed and compared between the two groups. The serum levels of S100 $\beta$ , NT-proBNT, hs-CRP, IL-6 between the two groups before and after treatment were compared. **Results:** There was no significant difference in the incidence of adverse reactions between the two groups (P>0.05). The total effective cases were 37, and the control group were 28, the total effective rate was higher than that in the control group, the difference was statistically significant (P<0.05). The ESS scores of the two groups after treatment were higher than before treatment, the cerebral hematoma volume was less than before treatment, and the ESS scores of the experimental group were higher than that of the control group, the cerebral hematoma volume was less than that of the control group, the differences were statistically significant (P<0.05). After treatment, serum S100, NT-proBNT, hs-CRP and IL-6 levels in the two groups were lower than before treatment. The indexes of the experimental group were (1.02 $\pm$  0.21)ng/mL, (120.26 $\pm$  19.47)pmol/L, (8.33 $\pm$  1.45)mg/L, (11.25 $\pm$  2.71)pg/mL, lower than (1.45 $\pm$  0.24)ng/mL, (219.68 $\pm$  22.51) pmol/L, (16.92 $\pm$  2.70)mg/L, (20.07 $\pm$  4.62)pg/mL in the control group, the differences were statistically significant (P<0.05). **Conclusion:** For patients with acute cerebral hemorrhage, Chinese herbal medicine for activating blood stasis have good clinical efficacy, can reduce inflammation and improve serum S100 $\beta$ , NT-proBNT levels, it is safety and worthy of clinical application.

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## 前言

脑出血是临床常见的一种脑血管疾病,是指脑实质内非外伤性血管破裂导致的出血,从而引发脑组织、脑细胞、脑神经等发生病理生理学改变,严重时会导致患者死亡<sup>[1-3]</sup>。急性脑出血发病急、病情不稳定、病死率高,如抢救不及时很可能危及到患者的生命安全<sup>[4,5]</sup>。目前,急性脑出血在我国的发病率为 60-80/10 万,病死率为 30%-40%,其发病率较高,对患者的身体和精神造成压力,增加家庭经济负担<sup>[6,7]</sup>。急性脑出血的发病原因主要与脑血管病变、硬化有关,其中高血压是引起脑出血的主要原因,因此,目前临床上主要采用降低颅内压、减轻脑水肿的治疗措施<sup>[8,9]</sup>。近年来,随着中医药的快速发展,活血化瘀法在治疗急性脑出血中具有较好的效果<sup>[10]</sup>。本研究探讨应用活血化瘀中药复方对急性脑出血患者血清星形胶质源性蛋白(stellate source sex protein, S100 $\beta$ )及 N-末端脑钠素原(N-terminal proBNP, NT-proBNT)、超敏 C 反应蛋白(hypersensitive C-reactive protein, hs-CRP)及白细胞介素-6(interleukin-6, IL-6)水平的影响,旨在为临床提供治疗方案。

## 1 资料与方法

### 1.1 一般资料

选择 2015 年 3 月到 2016 年 7 月 84 例在我院接受治疗的急性脑出血患者,纳入标准:(1)符合第四届全国脑血管疾病会议制定的急性脑出血诊断标准<sup>[11]</sup>中相关规定;(2)经颅脑 CT 或 MRI 检查确诊为脑出血者;(3)知情同意并签署知情同意书者;(4)首次发病者且发病到入院时间 <48 h。排除标准:(1)脑肿瘤、脑卒中等器质性病变者;(2)凝血功能障碍者;(3)合并心、肝、肾功能障碍者。随机分为对照组(n=42)和试验组(n=42),其中对照组男 24 例,女 18 例;年龄 31-75 岁,平均(55.73 $\pm$ 13.30)岁;体重 45-71 kg,平均(56.19 $\pm$ 10.31)kg;丘脑出血者 13 例、脑叶出血者 8 例、基底节出血者 16 例、小脑出血者 5 例;发病到入院时间 1-48 h,平均(17.54 $\pm$ 4.39)h。试验组男 23 例,女 19 例;年龄 30-74 岁,平均(54.88 $\pm$ 14.16)岁;体重 44-72 kg,平均(55.91 $\pm$ 13.38)kg;丘脑出血者 12 例、脑叶出血者 9 例、基底节出血者 14 例、小脑出血者 7 例;发病到入院时间

1-47 h,平均(16.58 $\pm$ 5.72)h。患者一般资料比较差别无统计学意义(P>0.05),可进行组间比较。研究经医院伦理委员会批准通过。

### 1.2 方法

给予患者抗血小板、降脂、营养神经、抗凝、自由基清除、降低颅内压等常规治疗,采用依达拉奉注射液(南京先声东元制药有限公司,国药准字:H20050280,规格:20 mL:30 mg)静脉滴注,30 mg/次,2 次/d。试验组患者在此基础上给予活血化瘀中药复方治疗,方剂为丹参 30 g、茯苓 30 g、泽泻 15 g、党参 20 g、怀山药 20 g、白术 15 g、赤芍 30 g、黄芪 30 g、决明子 20 g、生山楂 20 g,煎服,300 mL/剂,1 剂/d,早晚两次温服。两组患者疗程均为 14 d。

### 1.3 观察指标

观察两组患者临床疗效和不良反应,临床疗效分为 4 个等级:① 基本治愈:意识清楚,行动方便,生活自理;② 显效:言语相对清楚,临床症状明显改善,有基本的生活自理能力;③ 有效:语言转清,能够借助工具行走,部分简单生活能够自理;④ 无效:临床特征和临床症状无任何改善,甚至更加严重。总有效率为基本治愈率、显效率、有效率之和。检测并比较两组患者治疗前后脑血肿体积。采用欧洲脑卒中评分(ESS)评价并比较两组患者治疗前后神经功能缺损程度<sup>[12]</sup>。于治疗前后空腹抽取患者肘静脉血 5 mL,低温离心 15 min,离心速度为 3000 r/min,吸取上清液即得血清,采用酶联免疫吸附法(ELISA)检测 S100 $\beta$  及 NT-proBNT、hs-CRP 及 IL-6 水平,试剂盒购自上海西唐生物科技有限公司,相关操作参照说明书。

### 1.4 统计学方法

采用 SPSS19.0 进行统计分析,脑血肿体积、S100 $\beta$  水平等计量资料以( $\bar{x} \pm s$ )表示,选择双侧 t 检验,计数资料以率(%)表示,选择  $\chi^2$  检验,检验标准设置为  $\alpha=0.05$ 。

## 2 结果

### 2.1 两组患者临床疗效比较

试验组患者总有效例数 37 例,对照组总有效例数 28 例,总有效率高于对照组,有统计学差异(P<0.05)。见表 1。

表 1 两组患者临床疗效比较[n(%)]

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

Groups	n	Basic cure	Markedly effective	Effective	Invalid	Total effective rate
Experimental group	42	6(14.29)	13(30.95)	18(42.86)	5(11.90)	37(88.10)
Control group	42	3(7.14)	8(19.05)	17(40.48)	14(33.33)	28(66.67)
$\chi^2$						5.509
P						0.019

### 2.2 两组患者治疗前后脑血肿体积、ESS 评分比较

两组患者治疗后 ESS 评分高于治疗前,脑血肿体积小于

治疗前,并且试验组患者 ESS 评分高于对照组,脑血肿体积小于对照组,有统计学差异(P<0.05)。见表 2。

表 2 两组患者治疗前后脑血肿体积、ESS 评分比较( $\bar{x} \pm s$ )

Table 2 Comparison of ESS scores and cerebral hematoma volume before and after treatment between the two groups( $\bar{x} \pm s$ )

Groups	n	Times	ESS scores (scores)	Cerebral hematoma volume(mL)
Control group	42	Before treatment	41.12± 20.05	22.17± 4.35
		After treatment	50.71± 20.42*	15.34± 3.11*
Experimental group	42	Before treatment	40.96± 19.65	22.52± 4.14
		After treatment	62.82± 21.26**	10.05± 2.86**

Note: Compared with before treatment, \*P<0.05; Compared with control group, \*\*P<0.05.

2.3 两组患者血清 S100β、NT-proBNT、hs-CRP 及 IL-6 水平比较  
 治疗前, 两组患者血清 S100β、NT-proBNT、hs-CRP 及 IL-6 水平无统计学差异 (P>0.05); 两组患者治疗后血清 S100β、

NT-proBNT、hs-CRP 及 IL-6 水平低于治疗前, 且试验组低于对照组, 有统计学差异(P<0.05)。见表 3。

表 3 两组患者血清 S100β、NT-proBNT、hs-CRP 及 IL-6 水平比较( $\bar{x} \pm s$ )

Table 3 Comparison of serum S100β, NT-proBNT, hs-CRP, IL-6 levels between the two groups( $\bar{x} \pm s$ )

Groups	n	Times	hs-CRP (mg/L)	IL-6 (pg/mL)	S100β (ng/mL)	NT-proBNT (pmol/L)
Control group	42	Before treatment	37.80± 5.69	39.89± 6.14	1.83± 0.39	371.18± 50.04
		After treatment	16.92± 2.70*	20.07± 4.62*	1.45± 0.24*	219.68± 22.51*
Experimental group	42	Before treatment	37.26± 5.82	40.17± 6.48	1.89± 0.40	369.75± 48.35
		After treatment	8.33± 1.45**	11.25± 2.71**	1.02± 0.21**	120.26± 19.47**

Note: Compared with before treatment, \*P<0.05; Compared with control group, \*\*P<0.05.

2.4 两组患者不良反应比较

试验组患者出现腹泻 1 例、恶心 2 例, 不良反应发生率为 7.14%(3/42), 对照组患者出现腹泻 2 例、恶心 2 例, 不良反应发生率为 9.52%(4/42), 两组患者不良反应发生率比较差异无统计学意义( $\chi^2=0.156, P=0.693$ )。

使用依达拉奉的基础上联合给予活血化瘀中药复方治疗, 中西医结合发挥活血化瘀、降低脑组织水肿的作用。本研究结果显示两组患者治疗后 ESS 评分高于治疗前, 脑血肿体积小于治疗前, 并且试验组患者 ESS 评分高于对照组, 脑血肿体积小于对照组(P<0.05)。说明采用活血化瘀中药复方能够促进脑部血肿吸收和损伤组织的修复, 从而改善脑部神经功能, 患者在治疗后头痛缓解、神智转清、语言及肢体功能逐渐恢复<sup>[24-26]</sup>。本研究结果显示两组患者治疗后血清 S100β、NT-proBNT、hs-CRP 及 IL-6 水平低于治疗前, 且试验组低于对照组(P<0.05), 说明对照组的处理方法可降低急性脑出血患者血清 hs-CRP、IL-6、S100β 及 NT-proBNT 水平, S100β 是一种酸性钙离子结合蛋白, 在神经胶质细胞中大量存在, 患者脑部受损后迅速释放进入血液, 其在血液中的水平能够反应出急性脑出血脑部受损情况。NT-proBNT 是脑钠素的一种裂解产物, 其在血清中的水平与脑梗死有一定相关性, 脑部损伤越严重, NT-proBNT 的血清含量越高<sup>[27,28]</sup>。hs-CRP 和 IL-6 都是炎症反应中的重要因子, 其水平越高, 代表炎症反应严重。活血化瘀中药复方能够明显改善急性脑出血患者脑部损伤情况, 从而显著降低 hs-CRP、IL-6、S100β 及 NT-proBNT 在血清中的水平<sup>[29,30]</sup>。另外本研究结果显示, 治疗期间, 两组患者不良反应发生率比较差异无统计学意义( $\chi^2=0.156, P=0.693$ )。提示活血化瘀中药复方治疗急性脑出血的不良反应发生率较低, 安全性较好。患者在治疗期间的不良反应均为恶心、腹泻等较轻的症状, 在给予相应的治疗后均不影响患者的治疗。

3 讨论

急性脑出血的发病机制是高血压、动脉粥样硬化等因素导致脑血管破裂, 引发脑血管内外溢血, 形成局部血肿<sup>[13-15]</sup>。因此, 西医治疗急性脑出血以控制高血压、降低颅内压及减轻脑水肿为主要目的, 而这会引起患者血容量的降低和血液黏稠度增加, 导致常规的西医治疗未取得满意的疗效。中医认为急性脑出血属 " 卒中 "、" 中风 " 范畴, 主要是由于脏腑功能失调, 气血逆行, 血溢脉外, 淤阻不行, 淤积化热所致, 故以活血化瘀为治疗原则<sup>[16-18]</sup>。活血化瘀中药复方是由丹参、茯苓、泽泻、党参、怀山药、白术、赤芍、黄芪、决明子及生山楂等多味中药制成的复方制剂, 其中丹参具有活血化瘀、养心安神的作用, 茯苓是益气活血的良药, 党参和怀山药都可以起到祛风止痛、活血行气的作用, 白术具有活淤散结之功效, 赤芍、决明子、生山楂主要功效为开窍醒神、养血安神<sup>[19,20]</sup>。另外, 有临床前实验表明<sup>[21]</sup>, 丹参还具有清除自由基、抑制血小板聚集、降低血液黏稠度、改善微循环的作用, 黄芪还具有加强机体免疫力、保护脑细胞、清除自由基的作用。

本研究中试验组患者的总有效率高于对照组, 有统计学差异(P<0.05)。提示活血化瘀中药复方治疗急性脑出血的临床疗效显著。两组患者在基础治疗后给予依达拉奉, 依达拉奉是一种新型的自由基清除剂, 能够降低脑内自由基水平, 从而抑制白三烯合成, 降低脑水肿和对脑组织的损伤<sup>[22,23]</sup>。试验组患者在

综上所述, 活血化瘀中药复方治疗急性脑出血的临床疗效显著, 能够明显降低血清 S100β、NT-proBNT、hs-CRP 及 IL-6 水平, 不良反应少, 值得在临床上推广应用。

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