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针灸联合奥拉西坦治疗脑出血的疗效及对患者神经功能和炎性因子的影响 *

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摘要 目的:探讨脑出血患者经针灸联合奥拉西坦治疗后的临床疗效。**方法:**选取 2015 年 2 月 2018 年 7 月期间我院收治的 90 例脑出血患者,根据随机数字表法将患者分为对照组($n=45$)和研究组($n=45$),对照组给予奥拉西坦治疗,研究组在对照组的基础上联合针灸治疗,比较两组临床疗效、血肿体积、脑水肿体积、神经功能及炎性因子水平,记录两组治疗期间不良反应情况。**结果:**研究组治疗 2 个疗程后的临床总有效率为 91.11%(41/45),高于对照组的 71.11%(32/45)($P<0.05$)。治疗 2 个疗程后,两组患者的简易精神状态量表(MMSE)评分升高,且研究组高于对照组($P<0.05$);两组患者美国国立卫生院卒中量表(NIHSS)评分降低,且研究组低于对照组($P<0.05$);两组白介素-8(IL-8)、肿瘤坏死因子- α (TNF- α)、超敏 C 反应蛋白(hs-CRP)均下降,且研究组低于对照组($P<0.05$)。两组不良反应发生率对比无差异($P>0.05$)。与治疗第 1 d 相比,两组治疗第 7 d、治疗第 28 d 血肿体积呈先增大后缩小趋势($P<0.05$),脑水肿体积呈持续缩小趋势($P<0.05$);研究组治疗第 28 d 血肿体积、脑水肿体积小于对照组($P<0.05$)。**结论:**针灸联合奥拉西坦治疗可有效改善脑出血患者的临床症状,减轻炎症反应及神经功能损害,安全性较好。

关键词: 针灸;奥拉西坦;脑出血;疗效;神经功能;炎性因子

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The Effect of Acupuncture Combined with Oxiracetam on Cerebral Hemorrhage and Its Influence on Nerve Function and Inflammatory Factors*

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ABSTRACT Objective: To investigate the effect of acupuncture combined with Oxiracetam on cerebral hemorrhage and its influence on nerve function and inflammatory factors. **Methods:** 90 patients with cerebral hemorrhage who were admitted to our hospital in February 2015 and July 2018 were selected, they were divided into control group ($n=45$) and study group ($n=45$) according to random number table method. Patients in the control group were treated with oxiracetam, while those in the study group were treated with acupuncture on the basis of the control group. The clinical effect, hematoma volume, brain edema volume, nerve function, cognitive function and inflammatory factors were compared between the two groups, Adverse reactions during treatment were recorded in the two groups. **Results:** The clinical effect of the study group at 2 courses after treatment was 91.11% (41/45), which was higher than that of the control group 71.11% (32/45) ($P<0.05$). 2 courses after treatment, mini-mental state examination (MMSE) score of the two groups increased, and that of the study group was higher than that of the control group ($P<0.05$). The national institutes of health stroke scale (NIHSS) score decreased, and that of the study group was lower than that of the control group ($P<0.05$). The interleukin-8 (IL-8), tumor necrosis factor- α (TNF- α), and hypersensitive C-reactive protein (hs-CRP) were all decreased in the two groups, and those of the study group were lower than those of the control group ($P<0.05$). There was no significant difference in the incidence of adverse reactions between the two groups ($P>0.05$). Compared with the first day of treatment, the hematoma volume of the two groups increased first and then decreased on the 7th and 28th day of treatment ($P<0.05$), the volume of brain edema of the two groups decreased continuously ($P<0.05$). The volume of hematoma and brain edema of the study group were smaller than those of the control group at 28th day after treatment ($P<0.05$). **Conclusion:** Acupuncture combined with oxiracetam can effectively improve the clinical symptoms of cerebral hemorrhage patients, reduce the damage of neurological function and inflammation, and it has a good safety.

Key words: Acupuncture; Oxiracetam; Cerebral hemorrhage; Efficacy; Neurological function; Inflammatory factors

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前言

脑出血是临床常见的急性脑血管疾病,具有病情发病急骤、进展迅速、病死率高、致残率高等特点,若未能及时予以治疗,还可引起患者神经系统功能障碍及认知障碍,严重者甚至导致死亡^[1-3]。据统计,脑出血的急性期病死率为30%~40%,预后较差^[4]。可见,早期合理有效的治疗对于改善脑出血患者预后具有积极的临床意义。奥拉西坦可有效减轻脑水肿、降低颅内压,是常见的临床脑出血处方药^[5,6],但仍有部分患者经奥拉西坦治疗后,效果欠佳,无法迅速改善患者临床症状,尚需优化治疗。近年来,中西医结合治疗脑出血取得了较大进展,中医学认为脑出血是患者机体阴亏或阳亢等原因引起的肝阳暴涨、阳升风动、血随气逆,进而蒙蔽清窍、血液阻滞,进而反溢于脉外,发为本病^[7]。针灸作为中医治疗方式的一种,治疗脑出血可达到损其有余、治其不足的作用^[8]。本研究通过对我院收治的脑出血患者给予针灸联合奥拉西坦治疗,疗效显著,整理报道如下。

1 资料与方法

1.1 基线资料

于2015年2月~2018年7月期间选取我院收治的90例脑出血患者。纳入标准:(1)诊断参考第六届全国脑血管病会议制订的相关标准^[9];(2)经颅脑CT检查证实;(3)患者及其家属知情本研究且签署了同意书;(4)对本次研究治疗用药无禁忌症者;(5)均为初次发病。排除标准:(1)外伤创伤性引起的脑出血;(2)合并精神疾病,无法配合本次研究治疗者;(3)合并心、肝、肾等脏器功能障碍者;(4)妊娠或哺乳期妇女;(5)脑出血严重需进行手术者;(6)合并免疫缺陷、急慢性感染者。根据数字量表将患者分为对照组(n=45)和研究组(n=45),其中对照组男24例,女21例,年龄32~64岁,平均(49.67±3.82)岁;格拉斯哥昏迷量表(Glasgow coma scale, GCS)评分^[10]为1~5分,平均(2.81±0.72)分;合并高血压18例,合并糖尿病11例。研究组男26例,女19例,年龄31~65岁,平均(49.93±4.02)岁;GCS评分为1~4分,平均(2.73±0.66)分;合并高血压20例,合并糖尿病12例。两组一般资料对比未见无差异($P>0.05$)。

1.2 方法

两组入院后给予绝对卧床静养、积极控制原发疾病、保护脑细胞、维持水电解质平衡、止血、降低颅内压等常规干预治疗。在此基础上,对照组给予奥拉西坦注射液(国药准字H20100040,石药集团欧意药业有限公司,规格:1.0 g)治疗,将4~6 g奥拉西坦注射液加入5%的葡萄糖溶液200 mL中,静脉

滴注,1次/d。研究组则在对照组的基础上给予针灸治疗,具体操作如下:穴位选取内关、三阴交、人中、委中、尺泽、极泉,对于口张目合、大小便失禁者加神阙、百会穴针刺,对于昏迷但两手紧握、牙关紧闭者,加太冲穴针刺,对于肢体偏瘫者加环跳、合谷、曲池、足三里针刺。针灸20 min/次,2次/d。两组均以2周为1个疗程,治疗2个疗程,每个疗程之间间隔2d。

1.3 观察指标

(1)于治疗第1 d、治疗第7 d、治疗第28 d行颅脑CT检查,以多田公式计算出总占位效应体积和血肿体积,脑水肿体积=总占位效应体积-血肿体积。(2)记录两组治疗2个疗程后的临床疗效,判定标准如下:判定标准参考《神经外科学》^[11],显效:患者头痛、恶心等临床症状消失,颅内CT检查显示无继续出血或残留血肿;有效:患者头痛、恶心等临床症状有所改善,血肿较治疗前缩小30%以上;无效:临床症状未见改善甚至加重,血肿较治疗前缩小<30%,总有效率=显效率+有效率。(3)于治疗前、治疗2个疗程后采用美国国立卫生院卒中量表(National institutes of health stroke scale, NIHSS)^[12]、简易精神状态量表(Mini-mental state examination, MMSE)^[13]评价患者神经功能变化,其中NIHSS包括意识水平、视野、面瘫、意识水平指令、四肢运动、感觉、肢体障碍、意识水平提问、凝视、语言障碍、消退及不注意,总分42分,分数越高,神经损伤越严重。MMSE包括定向力、语言能力、注意力和计算力、记忆力、回忆能力,总分30分,分数越高,认知功能越好。(4)于治疗前、治疗2个疗程后清晨抽取患者4 mL空腹静脉血。经离心半径13 cm,3800 r/min离心12 min,分离上清液待测。经酶联免疫吸附试验检测血清白介素-8 (Interleukin-8, IL-8)、肿瘤坏死因子- α (Tumor necrosis factor- α , TNF- α)、超敏C反应蛋白(Hypersensitive C-reactive protein, hs-CRP)水平,严格按照说明书进行操作(武汉博士德生物科技有限公司)。(5)记录治疗期间不良反应发生情况。

1.4 统计学方法

数据分析采用SPSS25.0进行,以率表示计数资料,行 χ^2 检验,计量资料以($\bar{x} \pm s$)的形式表示,行t检验。检验标准设置为 $\alpha=0.05$ 。

2 结果

2.1 临床疗效比较

治疗2个疗程后,研究组的临床总有效率为91.11%(41/45),高于对照组的71.11%(32/45)($P<0.05$);详见表1。

表1 临床疗效比较[例(%)]

Table 1 Comparison of clinical effects [n(%)]

Groups	Markedly effective	Effective	Invalid	Total effective rate
Control group(n=45)	10(22.22)	22(48.89)	13(28.89)	32(71.11)
Study group(n=45)	15(33.33)	26(57.58)	4(8.89)	41(91.11)
χ^2				5.872
P				0.015

2.2 血肿体积、脑水肿体积比较

两组治疗第 1 d、第 7 d 血肿体积、脑水肿体积比较无差异 ($P>0.05$); 两组治第 7 d、治疗第 28 d 血肿体积呈先升高后降低

趋势 ($P<0.05$), 脑水肿体积呈持续下降趋势 ($P<0.05$); 研究组治疗第 28 d 血肿体积、脑水肿体积小于对照组 ($P<0.05$); 详见表 2。

表 2 血肿体积、脑水肿体积比较($\bar{x} \pm s$, mL)

Table 2 Comparison of hematoma volume and brain edema volume($\bar{x} \pm s$, mL)

Groups	Hematoma volume			Brain edema volume		
	1th day after treatment	7th day after treatment	28th day after treatment	1th day after treatment	7th day after treatment	28th day after treatment
Control group(n=45)	28.54 $\pm$ 3.64	32.07 $\pm$ 3.35 ^a	13.12 $\pm$ 2.89 ^{ab}	23.44 $\pm$ 2.28	17.15 $\pm$ 2.24 ^a	13.38 $\pm$ 3.76 ^{ab}
Study group(n=45)	28.49 $\pm$ 4.93	31.10 $\pm$ 3.27 ^a	8.93 $\pm$ 2.43 ^{ab}	23.56 $\pm$ 3.72	16.47 $\pm$ 3.93 ^a	7.46 $\pm$ 1.34 ^{ab}
t	0.055	1.390	7.444	0.184	1.831	9.949
P	0.956	0.168	0.000	0.854	0.153	0.000

Note: Compared with the 1th day after treatment, ^a $P<0.05$; compared with the 7th day after treatment, ^b $P<0.05$.

2.3 神经功能和认知功能比较

两组治疗前 MMSE、NIHSS 评分比较无差异 ($P>0.05$); 两

组治疗 2 个疗程后 MMSE 升高, 且研究组高于对照组 ($P<0.05$); NIHSS 降低, 且研究组低于对照组 ($P<0.05$); 详见表 3。

表 3 神经功能和认知功能比较($\bar{x} \pm s$, 分)

Table 3 Comparison of neural function and cognitive function($\bar{x} \pm s$, scores)

Groups	MMSE score		NIHSS score	
	Before treatment	2 courses after treatment	Before treatment	2 courses after treatment
Control group(n=45)	12.09 $\pm$ 2.94	18.31 $\pm$ 2.69 ^a	24.26 $\pm$ 3.35	15.95 $\pm$ 3.04 ^a
Study group(n=45)	12.15 $\pm$ 2.87	24.67 $\pm$ 2.71 ^a	24.73 $\pm$ 4.85	9.31 $\pm$ 2.51 ^a
t	0.098	11.173	0.535	11.299
P	0.922	0.000	0.594	0.000

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

2.4 炎症因子水平比较

两组治疗前 IL-8、TNF- α 、hs-CRP 比较无差异 ($P>0.05$); 两

组治疗 2 个疗程后 IL-8、TNF- α 、hs-CRP 均下降, 且研究组低于对照组 ($P<0.05$); 详见表 4。

表 4 炎症因子水平比较($\bar{x} \pm s$)

Table 4 Comparison of inflammatory factors($\bar{x} \pm s$)

Groups	IL-8(ng/L)		TNF- α (ng/L)		hs-CRP(mg/L)	
	Before treatment	2 courses after treatment	Before treatment	2 courses after treatment	Before treatment	2 courses after treatment
Control group(n=45)	22.23 $\pm$ 2.25	16.53 $\pm$ 2.87 ^a	22.16 $\pm$ 2.21	17.49 $\pm$ 2.24 ^a	41.75 $\pm$ 5.13	29.05 $\pm$ 5.91 ^a
Study group(n=45)	22.71 $\pm$ 3.36	11.98 $\pm$ 2.95 ^a	22.33 $\pm$ 2.45	12.38 $\pm$ 3.04 ^a	42.16 $\pm$ 7.94	17.62 $\pm$ 3.95 ^a
t	0.796	7.416	0.346	9.078	0.291	10.786
P	0.428	0.000	0.730	0.000	0.772	0.000

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

2.5 不良反应

治疗期间, 对照组出现恶心呕吐 2 例, 胃肠道不适 1 例, 不良反应发生率为 6.67%(3/45); 研究组出现恶心呕吐 3 例, 皮疹 1 例, 不良反应发生率为 8.89%(4/45); 两组不良反应发生率对比无差异($\chi^2=0.158$, $P=0.694$)。

3 讨论

脑出血是脑卒中的一种, 约占全部脑卒中的 20%~30%^[14]。

据以往资料表明, 诱发脑出血的病因较多, 包括情绪激动、吸烟、高血压、酗酒、腹压增高等^[15,16]。若未能及时进行干预, 因脑出血引发的脑血肿及脑水肿可对人体脑组织造成压迫, 加重患者病情。此外, 脑出血患者在发病过程中引发的脑组织缺血、缺氧, 导致细胞内酸中毒, 神经细胞变性坏死以及胆碱能受体缺失, 致使患者痊愈后神经功能、认知功能均出现不同程度的障碍^[17]。另患者在脑出血发病后, 脑血肿和脑水肿的形成可能造成占位效应, 激活机体免疫系统, 释放大量炎症因子, 影响脑组

织修复^[18]。因此,临床治疗脑出血应以阻止患者病情进展、保护患者神经功能及认知功能、降低炎性因子水平为主要治疗目标。奥拉西坦属于人工合成药物,是临床常见的保护受损神经细胞的药物,在慢性脑功能不全、颅脑损伤、脑出血等病症中应用广泛^[19]。由于脑出血发病机制极其复杂,单一的药物治疗尚不能达到最理想的治疗效果。针灸治疗脑出血由来已久,历代医书中均有记载,《灵枢·刺节真邪篇》有云:"泄其有余,补其不足,阴阳平复,用针若此",可见针灸可治疗脑出血。

本次研究结果显示,两组患者临床疗效、血肿体积、脑水肿体积及神经功能、认知功能、血清炎性因子改善情况均优于对照组,可见针灸联合奥拉西坦治疗脑出血可保护患者神经功能及认知功能,改善患者临床症状。究其原因,奥拉西坦改善脑出血患者症状的作用机制主要有以下几点:奥拉西坦可直接作用于中枢网状结构,通过影响腺苷激酶,增加葡萄糖的合成,增加脑细胞内能量,进而恢复患者脑部代谢;脑循环代谢得到改善后,促使脑血液循环加快,并重新为受损区域的脑组织供血,使得患者脑部抗缺氧功能得以提升,促进患者认知功能提升;奥拉西坦可抑制神经兴奋性,缩小患者血肿体积、脑水肿体积,保护患者神经元,促进患者神经功能提升^[20-22]。针灸可使患者全身气机通畅,有利于调节神经和体液平衡,通过相关穴位的刺激,可促进神经系统进行自我修复,加快吸收病理产物,并提高脑组织的缺氧耐受性,进而缩小脑血肿体积和脑水肿体积,发挥较好的神经组织保护作用^[23-25]。近年来不少研究证实,炎症损伤在脑出血后引起的继发性脑损伤中发挥关键作用^[26-28],其中IL-8、TNF- α 、hs-CRP是参与脑内炎症的重要炎性因子,均可通过直接或间接的炎症反应向血肿周围聚集、活化,引起脑内组织局部炎症反应。本次研究结果中两组患者血清IL-8、TNF- α 、hs-CRP水平均下降,且研究组低于对照组,可见针灸联合奥拉西坦治疗脑出血,可有效降低体内炎性因子水平,这可能是因为针灸可通过改善血液循环进而加速自由基的转运清除,同时还可阻止钙离子超载与自由基生成,最终改善机体免疫的紊乱状态,使受损伤的脑血管、脑组织的炎症反应得到缓解,从而降低炎性因子水平^[29,30]。两组不良反应发生率对比未见差异,可见安全性较好,可能是因为针灸治疗只是对穴位进行刺激,没有药物的毒副作用,因而不增加不良反应。

综上所述,脑出血患者经针灸联合奥拉西坦治疗后,临床症状得到有效改善,神经功能、认知功能损害及炎症反应得到减轻,安全性较好,具有一定的临床应用价值。

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