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脑血疏口服液与大骨瓣减压硬膜扩大减张缝合术治疗大面积脑梗死的疗效及对血清 NSE 和 hs-CRP 水平的影响 *

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摘要 目的：探讨脑血疏口服液配合大骨瓣减压硬膜扩大减张缝合术对大面积脑梗死患者的临床疗效及对血清超敏 C 反应蛋白(hs-CRP)及神经元特异性烯醇化酶(NSE)水平的影响。**方法：**选取 2013 年 1 月 ~2015 年 1 月我院收治的大面积脑梗死患者 87 例，采用随机单盲取法分为试验组 44 例，对照组 43 例。两组患者均给予标准大骨瓣减压硬膜扩张缝合术治疗，对照组术后给予常规及对症治疗，试验组在对照组基础上给予脑血舒口服液治疗。观察两组患者治疗前后 hs-CRP、NSE 水平变化，同时进行日常生活活动能力量表(ADL)评分、神经功能缺损量表(NIHSS)评分及生活质量指数(BI)测定，并评定和比较治疗效果。**结果：**治疗 1 疗程后，试验组总有效率为 97.73%，显著高于对照组 81.40%(P<0.05)。两组血清 hs-CRP、NSE 水平 ADL、NIHSS 评分均显著低于治疗前(P<0.05)，BI 指数明显高于治疗前，且试验组血清 hs-CRP、NSE 水平 ADL、NIHSS 评分明显低于对照组(P<0.05)，BI 指数明显高于对照组(P<0.05)。两组治疗期间均未见严重不良反应。**结论：**脑血舒口服液配合大骨瓣减压硬膜扩大减张缝合术治疗大面积脑梗死患者可有效提高临床疗效，且安全性高，可能与其降低血清 NSE、hs-CRP 水平有关。

关键词：脑血疏口服液；大骨瓣减压硬膜扩大减张缝合术；大面积脑梗死；超敏 C 反应蛋白；经元特异性烯醇化酶

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Effect of Naoxueshu Oral Liquid Combined with Large Bone Flap Decompression on Treatment of Large Area Cerebral Infarction and NSE and hs-CRP in Patients*

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ABSTRACT Objective: To investigate the effect of Naoxueshu oral liquid combined with large bone flap decompression dural suture surgery on the patients with large area of cerebral infarction and the serum high-sensitivity C reactive protein (hs-CRP) and neuron specific enolase (NSE) levels. **Methods:** 87 patients with large area of cerebral infarction admitted in our hospital from January 2013 to January 2015 were randomly divided into the trial group and the control group. Both groups of patients were given standard big bone flap decompression of dural suture expansion treatment, while the control group was given routine and symptomatic treatment, the experimental group was given naoxueshu oral liquid treatment. Then the serum levels of hs-CRP and NSE, and activities of daily living the ability to scale (ADL) score, neural function defect scale (NIHSS) score and quality of life index (BI) were measured and compared between two groups before and after treatment. **Results:** After treatment, the total effective rate of experimental group was significantly higher than that of the control group (P<0.05). The serum hs-CRP, NSE levels of ADL and NIHSS scores in both groups were significantly lower than those before treatment (P<0.05); BI index in the two groups were significantly higher than that before treatment, and the serum hs-CRP, NSE levels of ADL and NIHSS in experimental group were significantly lower than those of the control group (P<0.05); BI index in the experimental group was significantly higher than that of the control group (P<0.05). No serious adverse reactions was observed in both groups. **Conclusion:** Naoxueshu oral liquid combined with large bone flap decompression dural suture surgery was effective to improve the clinical efficacy and the safety of in the treatment of massive cerebral infarction, which might be related to reduce the serum levels of NSE and hs-CRP.

Key words: Cerebral blood thinning oral liquid; Large bone flap decompression and reduction of the suture; Large area cerebral infarction; High sensitive C reactive protein; Meta specific

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前言

大面积脑梗死属急性脑梗死中严重的神经系统疾病,发生率约 10%~15%,发生部位为颈内动脉、大脑中动脉主干或皮质层支,临床表现以颅内压增高、脑水肿及偏瘫为主,且迅速恶化,易形成脑疝等危及患者生命[1-3],治疗以手术治疗为主。我国 2010 年急性缺血性脑卒中诊治指南推荐意见中指出术后应辅以降颅压、溶栓、保护神经、改善微循环、清除自由基等提高治疗效果[4],但临床结果显示治疗效果及预后并不满意,多数患者存在严重神经功能缺损、生活功能障碍等。研究表明神经元的损伤程度及炎性因子的再损伤对治疗效果及预后的影响严重。我院大骨瓣减压硬膜扩大减张缝合术治疗大面积脑梗死术后给予脑血舒口服液治疗,取得了一定效果,现报道如下。

1 资料与方法

1.1 临床资料

收集我院 2013 年 1 月 ~2015 年 1 月收治大面积脑梗死患者 87 例,所有患者均经 MRI 及颅脑 CT 检查确诊。经本院医学伦理委员会批准,进行本次研究。采用随机单盲取法将患者分为试验组 44 例,对照组 43 例,两组患者年龄、性别等临床资料对比差异无统计学意义(P<0.05),具有可比性,见表 1。

表 1 两组的一般临床资料对比

Table 1 Comparison of the general clinical data between two groups

Groups	n	Age(Year)	Gender(Example)		Time of onset(d)
			Male	Female	
Experimental group	44	58.46± 8.56	24	20	2.01± 0.24
Control group	43	58.41± 8.58	22	21	2.11± 0.18
P	-	0.489	0.752		0.015

1.2 纳入与排除标准

纳入标准:(1) 符合第四届脑血管病学术会议修订诊断标准,脑梗死直径 >3 cm,脑解剖部位累积 2 支主血管供应区;(2)发病时间 <3 d;(3)发病至入院时间 <72 h;(4)首次发病;(5)年龄 40~80 岁;(6)入院前未进行溶栓、抗凝等治疗;(7)患者或直系亲属愿意参加本次研究,并签订知情同意书。排除标准:(1)合并脑部肿瘤、颅内感染等其它脑部疾病;(2)严重心、肝、肾等脏器功能障碍;(3)合并恶性疾病;(4)伴有全身系统性疾病及免疫功能障碍患者;(5)对本次研究药物过敏患者。

1.3 方法

两组患者均给予大骨瓣减压硬膜扩大减张缝合术治疗。均在气管插管全麻下进行,患者取仰卧位,头偏向健侧。于耳屏前 1.5 cm 处,做 " 大 " 字形切口,期间注意保护颞浅表动脉。以铣刀切开颅骨,骨窗下缘与中颅窝底保持平行,咬除蝶骨嵴,制造 10 cm~15 cm 立方大小骨瓣。悬吊硬脑膜并剪开,充分暴露顶叶、额叶及颞叶等,术中均采用内减压,不切除脑组织,并以人工硬脑膜或颞肌筋膜实施硬膜扩大减压缝合,对颅腔进行重建修补。对照组术后参照相关标准常规给予脑细胞保护剂、自由基清除剂及脱水、对症治疗及对症支持疗法等。试验组在对照组基础上给予脑血舒口服液(批准文号:Z20070059;厂家山东沃华医药科技股份有限公司;规格:10 mL/ 支)治疗,3 次 /d,10 mL/ 次,口服 1 个月为 1 疗程。

1.4 观察指标与检测方法

两组患者于术前及服用 1 疗程抽取空腹肘静脉血 4 mL 送检,采集及送检过程严格按照相关标准进行。进行超敏 C 反应蛋白(hs-CRP)及神经元特异性烯醇化酶(NSE)测定,hs-CRP 以奥林巴斯全自动生化分析仪进行测定,试剂盒为原厂配套试剂;NSE 采用罗氏电化学发光免疫分析仪测定,试剂盒为原厂配套试剂。同时进行日常生活活动能力量表(ADL)评分、神经功能缺损量表(NIHSS)评分及生活质量指数(BI)测定,均采用相应量表进行;于用药 1 疗程后进行疗效评定;治疗期间详细记录两组患者治疗期间并发症发生情况。

1.5 评定标准

采用神经功能缺损量表(NIHSS)[5]评定两组患者治疗前后神经功能缺损情况,采用日常生活活动能力量表(ADL)[6]及生活质量指数量表(BI)[7]进行生活质量评定,综合评定治疗效果。治疗后 NIHSS 评分较治疗前减少 100.00%,BI>85 分,无伤残为临床痊愈;治疗后较治疗前 NIHSS 评分减少 46%~90%以上,BI>85 分,伤残程度 1~3 级为显著进步;治疗后较治疗前 NIHSS 评分减少 18%~45%,BI>85 分,伤残程度为 1~3 级为进步;治疗后较治疗前 NIHSS 评分减少 <18%,BI<20 分,伤残程度重度为无效;治疗后较治疗前各项评分均加重为恶化。总有效率为(基本痊愈 + 显著进步 + 进步)/n× 100.00%。

1.6 统计学分析

采用 SPSS17.0 软件进行统计分析,血清 NSE、CRPADL、NIHSS 水平及 BI 资料均以($\bar{x}$± s)表示,采用 t 检验,计数资料以百分率表示,采用 x^2 检验,以 P<0.05 为差异具有统计学意义。

2 结果

2.1 两组治疗效果比较

经一疗程治疗后,试验组总有效率为 97.73%,对照组为 81.40%,两组总有效率对比差异具有统计学意义(P<0.05),见表1。

2.2 两组治疗前后 ADL 评分、NIHSS 及 Bi 的变化

两组治疗前 ADL、NIHSS 及 BI 对比差异均无统计学意义(P>0.05)。治疗后,与同组同指标治疗前对比,两组 ADL、NIHSS 评分均显著下降,BI 均明显升高 (P<0.05),且实验组 ADL、

NIHSS 评分明显高于对照组，BI 显著低于对照组 (P<0.05)，见 表 2。

表 2 两组的治疗效果比较(例)

Table 2 Comparison of the treatment effect between two groups(n)

Groups	n	Cure	Excellent	Progress	Unchanged	Deteriorate	Total effective rate(%)
Experimental group	44	12	29	2	1	0	97.73
Control group	43	5	20	10	5	3	81.40

表 3 两组治疗前后 ADL、NIHSS 评分及 BI 的比较($\bar{x}\pm s$)

Table 3 Comparison of the ADL, NIHSS scores and BI before and after treatment between two groups($\bar{x}\pm s$)

Groups	ADL(branch)		NIHSS(branch)		BI	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Experimental group	63.85± 11.24	30.12± 7.66[a]	14.41± 4.20	6.27± 3.78[a]	2.48± 2.02	10.68± 3.20[a]
Control group	62.54± 12.16	48.68± 8.37[a]	14.37± 4.32	10.63± 3.86[a]	2.41± 1.94	5.26± 2.37[a]
t	0.522	10.794	0.044	5.323	0.165	8.961
P	0.302	0.000	0.483	0.000	0.434	3.237

Note: compared with the same group before treatment, [a]P<0.05; Compared with the control group after treatment, [b]P<0.05.

2.3 两组治疗前后血清 NSE 及 hs-CRP 水平的变化

两组治疗前血清 hs-CRP 及 NSE 水平比较差异均无统计学意义。治疗后，与同组治疗前对比，两组血清 hs-CRP 及 NSE 水平均显著下降，差异均具有统计学意义(P<0.05)，且实验组血清 hs-CRP 及 NSE 水平显著低于对照组(P<0.05)，见表 3。

表 4 两种治疗前后血清 NSE 及 hs-CRP 水平比较($\bar{x}\pm s$)

Table 4 Comparison of the serum levels of NSE and CRP before and after treatment between two groups($\bar{x}\pm s$)

Groups	hs-CRP(mg/L)		NSE(μg/L)	
	Before treatment	After treatment	Before treatment	After treatment
Experimental group	12.71± 5.44	2.67± 1.33[ab]	40.56± 7.18	17.35± 4.69[ab]
Control group	12.53± 6.70	6.54± 1.62[a]	38.37± 8.39	28.65± 5.76[a]
P	0.445	0.000	0.097	0.000

Note: Compared with the same group before treatment, [a]P<0.05; Compared with the control group after treatment, [b]P<0.05.

2.4 两组不良反应发生情况的比较

两组治疗期间均未见严重不良反应，试验组仅 1 例出现心慌、出汗等不适症状，经查为滴速过快导致，减慢速度后好转，余未见其它不良反应。

3 讨论

急性脑梗死临床常见，致病原因为脑血管动脉粥样硬化形成，病理基础为栓塞，具有病死率、致残率高的特点。大面积脑梗死属急性脑梗死严重类型，较急性脑梗死具有病情重、进展快、预后差、治疗困难等特点。大面积脑梗死发生使局部脑组织缺血、缺氧，产生水肿，水肿对周围脑组织造成压迫，致使脑血管受压、颅内压增高、脑组织及中线偏移，易形成脑疝[8-11]。其次，脑组织缺血、缺氧，可使大量脑细胞坏死，增加局部代谢产物及炎性产物堆积，增加脑组织损害，加重临床症状，促使病情迅速恶化，最终导致患者死亡[12]。单纯的内科保守治疗不能迅速减轻脑水肿、减低颅压、改善脑组织血液供应等，故单纯的内科保守治疗病死率高达 80%左右。故临床多给于外科大骨瓣减压术，以迅速缓解颅高压，减少颅高压对脑血管压迫，改善缺血半暗带脑组织供血，降低脑组织及神经功能进一步损害[13-15]。相关文献显示，给予大骨瓣减压术可致残率降低至 20.65%~52.4%。但仍偏高，且术后多需结合内科治疗，以进一步降低致残率。

脑梗死属中医 " 中风 " 范畴，与气血衰少、肝肾阴虚等有关，治当益气通络、活血化瘀为主[16]。脑血舒口服液为纯中药制剂，为黄芪、水蛭、石菖蒲、牡丹皮、川芎、牛膝等中药西制而成[17]。其中水蛭含有大量水解蛋白酶水蛭素，可发挥溶栓、阻滞纤维蛋白凝固、延长或抑制血栓形成等作用，且比西药作用温和，可降低出血风险；川芎素有 " 血中气药 "，具有祛风、活血、行气作用，可通过血脑屏障，发挥扩张脑血管、降低血黏度、改善局部供血功效，从而促进局部自由基及炎性因子代谢。黄芪为扶正祛邪药物，同时具有益气和血功效，对患者免疫功能具有改善作用，调节内循环稳定性，降低脑水肿严重度；当归活血养血，可降低缺血区脑细胞丢失；牛膝逐瘀、通经络；大黄及牡丹皮具有凉血、止血、祛瘀功效，可避免出血发生。诸药共同发挥改善脑梗死局部血液循环、促进代谢产物排泄、驱祛除瘀血、溶解血栓等，最终达到改善预后目的[18]。此外，脑血舒口服液对格子细胞具有激活或促进其吞噬作用，达到减轻脑水肿、减少脑组织丙二醛等产生[19]，用于脑梗死术后还可促进溶解残余红细胞，达到清除积血目的，同时还具有抗凝血酶、抗血小板聚集、促进纤维蛋白溶解等作用，可促进血栓溶解，预防过度溶栓出血等，达到迅速缓解半暗带供血，减少脑细胞进一步死亡。本研究结果显示服用脑血舒口服液 1 疗程后，患者 ADL、NIHSS 评分高于治疗前及对照组同期，BI 指数低于同组治疗前及对照组同

期,且试验组以总有效率 97.73%高于对照组 81.40%。可见,对大骨瓣减压硬膜扩大术具有提高治疗效果作用。大骨瓣减压硬膜扩大术虽可迅速缓解颅压增高, 减少脑疝发生率等目的,但栓塞及脑水肿仍为解除,给予内科溶栓、清除自由基及对症等治疗,如用量掌握不当,极易导致出血,增加病死率及治疗难度等[20]。联合脑血舒口服液可避免此弊端发生,且通过扩张局部血管,改善局部微循环作用,可促进西药达到局部,更好发挥溶栓、清除自由基等目的,且脑血舒口服液自身具有解除平滑肌痉挛、降低脑血管阻力等作用,有助于降低脑梗死患者神经功能缺损,促进神经功能重建,故术后给予脑血舒口服液可提高手术治疗效果。

研究表明脑梗死患者预后与 hs-CRP 及 NSE 水平具有相关性,可作为脑梗死预后判断指标。脑梗死发生后可缺血区神经元缺血性坏死,可产生大量 hs-CRP 及 NSE,通过细胞间隙进入脑脊液,在通过受损的血脑屏障进入血浆,均可作为神经组织受损的敏感指标,且与病情严重程度呈正相关。本研究结果显示试验组治疗后实验室指标 hs-CRP、NSE 均低于同组治疗前及对照组同期。术后给予脑血舒口服液可改善局部微循环,促使局部炎性因子代谢,降低 hs-CRP 及 NSE 水平,从而降低炎性因子对脑组织的再损伤。但本研究中的例数较少,未对患者治疗前后炎性因子水平、局部血流进行监测,有待于进一步扩大研究范围进行研究。

综上所述,脑血舒口服液配合大骨瓣减压硬膜扩大减张缝合术治疗大面积脑梗死患者可有效提高临床疗效, 且安全性高,可能与其降低血清 NSE、hs-CRP 水平有关。

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