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• 临床研究 •

微创下置管抽吸液化引流术联合依达拉奉对脑出血患者的疗效分析*

郭清保¹ 李立宏¹ 杨彦龙¹ 马 涛¹ 谢曼丽^{2Δ}

(1 第四军医大学唐都医院 神经外科 陕西 西安 710000; 2 西安市中心医院 职业病科 陕西 西安 710004)

摘要 目的:探讨微创下置管抽吸液化引流术联合依达拉奉对脑出血患者的疗效及血清超敏 C 反应蛋白(hs-CRP)、白细胞介素-6(IL-6)、肿瘤坏死因子- α (TNF- α)水平的影响。**方法:**研究对象选自我院 2015 年 2 月~2016 年 12 月收治的 146 例脑出血患者,采取随机数字表将其分成两组,每组 73 例。两组患者均采取微创下置管抽吸液化引流术治疗,观察组联合给予依达拉奉治疗,对比两组疗效及治疗前后血清 hs-CRP、IL-6、TNF- α 水平变化情况。**结果:**观察组治疗总有效率高于对照组,差异有统计学意义($P<0.05$)。与治疗前相比,治疗后 14d 两组患者的 NIHSS 评分、血清 hs-CRP、IL-6、TNF- α 水平均明显下降,BI 指数评分明显上升($P<0.01$);且观察组 NIHSS 评分、血清 hs-CRP、IL-6、TNF- α 水平均较对照组明显下降($P<0.01$)。**结论:**在微创下置管抽吸液化引流术治疗基础上联合给予依达拉奉治疗脑出血能有效促进炎症反应的缓解,改善神经功能缺损状况,疗效确切。

关键词:依达拉奉;微创置管抽吸液化引流术;脑出血;炎症因子

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Clinical Effects of Minimally Invasive Catheterized Suction Drainage Combined with Edaravone on Cerebral Hemorrhage*

GUO Qing-bao¹, LI Li-hong¹, YANG Yan-long¹, MA Tao¹, XIE Man-li^{2Δ}

(1 Department of Neurosurgery, Tangdu Hospital, The Fourth Military Medical University, Xi'an, Shaanxi, 710000, China;

2 Occupation department, Central Hospital of Xi'an, Xi'an, Shaanxi, 710004, China)

ABSTRACT Objective: To explore clinical effects of minimally invasive catheterized suction drainage combined with edaravone on the patients with cerebral hemorrhage and the serum levels of high sensitivity C reactive protein (hs-CRP), interleukin-6 (IL-6) and tumor necrosis factor- α (TNF- α). **Methods:** 146 patients with cerebral hemorrhage in our hospital from February 2015 to December 2016 were selected as the research objects and randomly divided into two groups with 73 cases in each group. Minimally invasive catheterized suction drainage was given to two groups while edaravone was given to the observation group additionally. The clinical effect and changes of serum hs-CRP, IL-6 and TNF- α levels before and after treatment were compared between two groups. **Results:** The total effective rate of observation group was significantly higher than that of the control group ($P<0.05$). Compared with before treatment, the NIHSS scores and serum hs-CRP, IL-6 and TNF- α levels of two groups significantly decreased at 14 d after treatment, while the scores of BI index significantly increased ($P<0.01$). The NIHSS score and serum hs-CRP, IL-6 and TNF- α levels of observation group were significantly lower than those of the control group ($P<0.01$). **Conclusion:** Minimally invasive catheterized suction drainage combined with edaravone effectively enhance the alleviate the inflammatory response and improve the neurological function of patients with cerebral hemorrhage.

Key words: Edaravone; Minimally invasive catheterized suction drainage; Cerebral hemorrhage; Inflammatory factor

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前言

脑出血是由非创伤因素引起的脑实质内出血,具有病情进展快、致残率及致死率高等特点^[1]。对于出血量较小者,保守治疗多可收到满意效果,但对于出血量较多者,手术是其最有效的治疗方法^[2]。在手术方式的选择上,微创手术因具有的创伤

小、疗效好、恢复快等优点而被广泛应用于脑出血的治疗中,其中微创下置管抽吸液化引流术临床应用较多^[3]。脑出血的病理生理改变主要是血肿引起的占位效应以及脑水肿的形成,其涉及到炎症反应、氧自由基损伤等。研究表明^[4]脑出血后血肿释放的大量炎症因子及自由基是诱发脑水肿及神经细胞损伤的主要原因。依达拉奉是重要的氧自由基清除剂,能对炎症反应起

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作者简介:郭清保(1980-),男,硕士,主治医师,研究方向:多模态监测对颅脑损伤的精准化治疗、高血压脑出血的基础和临床研究

Δ 通讯作者:谢曼丽(1980-),女,本科,主治医师,研究方向:化学药物中毒的基础和临床研究

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到有效的抑制作用,清除因缺血再灌注损伤产生的氧自由基,从而使血管内皮细胞与神经细胞的氧化损伤受到抑制,在脑出血患者的治疗中可发挥有效的保护脑组织细胞的作用^[9]。本研究在微创下置管抽吸液化引流术治疗的基础上联合依达拉奉治疗后疗效明显提高,现报道如下。

1 资料与方法

1.1 一般资料

选取2015年2月~2016年12月我科确诊的脑出血患者146例,纳入对象:(1)符合1995年第四届全国脑血管病学术会议通过的《各类脑血管疾病诊断要点》中脑出血的诊断标准^[10];(2)发病时间不超过48 h,出血量在30 mL以上;(3)年龄低于80岁,性别不限;(4)患者或家属知情同意,签署知情同意书。排除标准:(1)凝血功能异常或严重出血倾向;(2)心肺肝肾功能不全、严重糖尿病、免疫系统疾病、恶性肿瘤;(3)颅内血管畸形、动脉瘤、外伤性出血;(4)严重感染或合并其他部位损伤;(5)妊娠及哺乳期妇女。

采取随机数字表将这146例患者随机分成两组,每组73例。观察组男46例,女27例,年龄43~79岁,平均 (62.7 ± 5.6) 岁;出血量34~88 mL,平均 (66.7 ± 7.3) mL;出血部位:基底节区37例,丘脑19例,脑叶17例;入院时意识状况:清醒18例,浅昏迷24例,重度昏迷31例。对照组男49例,女24例,年龄46~78岁,平均 (61.5 ± 7.3) 岁;出血量36~86 mL,平均 (64.6 ± 9.4) mL;出血部位:基底节区41例,丘脑16例,脑叶16例;入院时意识状况:清醒21例,浅昏迷25例,重度昏迷27例。两组资料差异无统计学意义($P>0.05$),具有可比性。

1.2 治疗方法

两组患者均给予常规治疗,包括脱水降低颅内压、抗生素抗感染、控制血压及血糖、早期营养支持等。对照组在此基础上采取微创下置管抽吸液化引流术治疗,CT定位血肿部位及大小,选择适宜的穿刺路径与穿刺点,注意避开主要大血管以及重要功能区。采用小颅锥进行颅骨钻孔,穿透至硬膜下,再将脑穿刺针经穿刺点进入血肿腔内,将针芯拔出后,接5 mL无菌注

射器,抽出50%~70%积血时,于血肿腔置入软塑带侧孔引流管,并接脑室外引流瓶。每隔8 h于血肿腔中注入5万U尿激酶,引流夹夹闭2 h后开放引流,引流3~5 d积血基本可以清除,随后将引流管拔除。

观察组在对照组基础上联合依达拉奉治疗,将30 mg依达拉奉注射液(国药集团国瑞制药,批号150112)加入100 mL生理盐水中静脉滴注,时间控制在30 min内。2次/d,连续用药14 d。

1.3 观察指标

(1)血清炎性因子:分别于治疗前、治疗后14 d抽取肘静脉血5 mL,做离心处理后取其上清液,放置在 -70°C 冰箱内待检。超敏C反应蛋白(hs-CRP)检测采取免疫比浊法,采取酶联免疫法检测白细胞介素-6(IL-6)、肿瘤坏死因子- α (TNF- α)。(2)神经功能:采取美国国立卫生院神经功能缺损评分(NIHSS)评价两组患者治疗前、治疗后14 d神经功能缺损情况,该量表总分45分,评分越高提示神经功能缺损越严重。(3)日常生活能力:采取Barthel指数(BI)评价两组患者治疗前、治疗后14 d日常生活能力,总分100分,得分越高提示日常生活能力越好。

1.4 疗效评定

疗效评估时间为治疗后14 d,根据NIHSS评分及病残程度进行。基本治愈:NIHSS评分较治疗前减少超过90%,且病残程度0级;显著进步:NIHSS评分较治疗前减少46%~90%,且病残程度在1~3级之间;进步:相对于治疗前NIHSS评分减少18%~45%;无效:相对于治疗前NIHSS评分减少不及18%,或评分增加,或死亡。以基本治愈、显著进步与进步为治疗有效。

1.5 统计学分析

数据处理采取SPSS19.0,计数资料统计采取 χ^2 检验,计量资料采取t检验,以 $P<0.05$ 为差异有统计学意义。

2 结果

2.1 两组治疗后14d疗效对比

治疗2周后,观察组总有效率为90.41%,与对照组【78.08%】相比明显升高($P<0.05$)。见表1。

表1 两组治疗后14d的临床疗效对比[n(%)]

Table1 Comparison of the curative effect 14d after treatment between two groups [n(%)]

Groups	n	Basic cure	Significant progress	Progress	Invalid	Total effective rate
Observation group	73	29	31	6	7	66(90.41)
Control group	73	21	28	8	16	57(78.08)
P						0.041

2.2 两组治疗前、治疗后14d NIHSS评分、BI指数评分对比

与治疗前相比,治疗后14d两组患者的NIHSS评分均有明显下降,BI指数评分均有明显上升($P<0.01$);这两项指标观察组改善更显著($P<0.01$)。见表2。

2.3 两组治疗前、治疗后14d血清hs-CRP、IL-6、TNF- α 水平对比

两组治疗后14d血清hs-CRP、IL-6、TNF- α 水平均较治疗前明显下降($P<0.01$),观察组各项血清炎性指标改善更为明显

($P<0.01$)。见表3。

3 讨论

脑出血后产生的血肿可使脑组织出现占位效应,导致颅内压升高,从而使脑组织正常的血液循环受到影响,诱发脑组织凝固性坏死^[11]。脑出血血管内释放出的激肽和组胺可导致局部脑组织缺血缺氧,引起一系列应激性改变。此外,血肿在形成与自然液化裂解时可产生凝血酶、坏死组织降解产物等具有神经

表 2 两组治疗前、治疗后 14d NIHSS 评分、BI 指数评分对比($\bar{x} \pm s$, 分)Table 2 Comparison of the NIHSS score and BI index score between two groups before and 14d after treatment ($\bar{x} \pm s$, scores)

Groups	n	NIHSS score		BI index score	
		Before treatment	14d after treatment	Before treatment	14d after treatment
Observation group	73	34.67± 5.23	20.12± 3.76*	31.34± 4.87	58.24± 5.35*
Control group	73	33.89± 4.67	26.56± 4.02*	32.57± 5.12	53.19± 7.02*
P		0.344	0.000	0.139	0.000

Note: Compared with this group before treatment, $P^* < 0.01$.

表 3 两组治疗前、治疗后 14d 血清 hs-CRP、IL-6、TNF- α 水平对比($\bar{x} \pm s$)Table 3 Comparison of the serum hs-CRP, IL-6 and TNF- α levels between two groups before and 14d after treatment ($\bar{x} \pm s$)

Groups	n	hs-CRP(mg/L)		IL-6(ng/L)		TNF- α (ng/L)	
		Before treatment	14d after treatment	Before treatment	14d after treatment	Before treatment	14d after treatment
Observation group	73	26.22± 7.37	11.67± 4.75*	86.24± 18.24	47.87± 10.35*	72.45± 17.13	32.65± 8.56*
Control group	73	25.78± 6.64	16.24± 4.28*	84.93± 17.81	62.45± 11.28*	70.82± 15.67	46.75± 10.24*
P		0.705	0.000	0.661	0.000	0.550	0.000

Note: Compared with this group before treatment, $P^* < 0.01$.

毒性作用的物质^[89]。研究证实^[10]一般脑出血后 20~30 min 即可形成血肿,3 h 内血肿周围尚不会形成水肿,通常 6~7 h 后会形成血肿,临近组织可出现相应坏死,并发生不可逆性损害,12 h 后血肿程度上升至中度血肿,24 h 后形成重度水肿。脑水肿程度越严重,颅内压升高越明显,周围受压组织缺血缺氧越严重。故脑出血发生后,采取有效的方法及时清除血肿,解除血肿的占位效应,减轻神经功能损伤程度,是改善患者预后的关键^[11]。在治疗方法的选择上,对于出血量较多者一般采取手术治疗,以往采取的手术主要是开颅血肿清除术,该术式尽管能有效清除颅内血肿,但手术创伤大,患者不易耐受,术中易对血肿周围正常的组织造成损害,术后感染风险大,致残率及致死率相对较高^[12]。而随着微创技术的不断进步,微创手术逐渐取代开颅术成为脑出血的主要治疗手段,其中微创置管抽吸液化引流术是最常使用的术式之一。该手术方式通过引流脑出血患者的脑脊液可使颅内压降低,改善颅内血氧状况,加快颅内血肿的吸收,使急性发作期缩短^[13]。

脑出血后血肿可刺激周围组织产生炎症反应,多种炎症因子可出现过度表达,过度的炎症反应是脑出血继发性脑损伤的重要因素^[14]。研究显示^[15],脑出血后血肿的增多和血清炎症因子水平密切相关,IL-6、TNF- α 等炎症因子可使脑血管通透性增加,也可增加血脑屏障通透性,导致血脑屏障崩溃,炎症细胞因子大量入侵脑组织,诱发或加重脑水肿。因此,早期若能及时控制炎症反应,降低血清炎症因子水平,有助于减轻脑出血后导致的神经功能损害,改善患者预后。宛丰等^[16]通过对比治疗前后高血压脑出血患者的血清 hs-CRP、IL-6、TNF- α 指标发现,在脑出血治疗早期,血清 hs-CRP、IL-6、TNF- α 水平显著上升,血肿周围组织发生水肿,而随着水肿的逐渐缩小,血清 hs-CRP、IL-6、TNF- α 水平逐渐下降。故血清 hs-CRP、IL-6、TNF- α 水平的高低可反映出机体内炎症反应的严重程度以及血肿周围水肿的严重程度。本研究中,两组患者治疗后 14 d 血清

hs-CRP、IL-6、TNF- α 水平均较治疗前明显下降,但观察组各项血清炎症指标改善更为明显,提示在微创置管抽吸液化引流术治疗基础上联合依达拉奉治疗脑出血能进一步促进炎症反应的缓解,有利于增强术后神经功能的恢复效果。

依达拉奉是常用的氧自由基清除剂,可对体内活性氧分子与脑内羟自由基起到强效清除作用,并可抑制脂质过氧化,对血管内皮细胞损伤起到抑制作用,使迟发性神经细胞死亡受到抑制,对中枢神经系统可发挥有效的保护作用^[17]。研究证实^[18],依达拉奉对于由氧化应激引起的血管内皮细胞、星形胶质细胞、神经元损伤均可起到有效的保护作用。依达拉奉由于无纤溶作用,不会对血液凝固、纤维蛋白溶解、血小板聚集等产生影响,故不会导致再出血危险增加,在脑出血的治疗中安全可靠。有研究显示^[19],对行微创引流术治疗的脑出血患者联合使用依达拉奉能有效降低患者术后血清 IL-6、TNF- α 水平,减轻神经功能损害程度,并认为依达拉奉能有效抑制脑出血后机体内炎症反应的作用机制主要是其能使转录核因子的活性受到抑制,下调细胞间黏附分子-1 (ICAM-1) 的表达,使其对磷脂酶 A (PLA) 的激活作用被减弱,抑制花生四烯酸(AA)的释放,减少前列腺素(PG)与白三烯的生成。石滴坚等^[20]对高血压脑出血患者在微创碎吸术治疗基础上联合依达拉奉治疗后,与单用微创碎吸术治疗相比,患者的 TNF- α 与 IL-1 β 水平达峰时间更早,且水平显著降低,临床总有效率则明显高于单用微创碎吸术治疗组,指出在微创碎吸术治疗基础上联合依达拉奉治疗高血压脑出血能有效促进患者机体内炎症反应的缓解,促进预后的改善。本研究通过对比两组患者的疗效得出,观察组疗效显著好于对照组。另外,观察组 NIHSS、BI 指数评分这两项指标改善效果显著优于对照组。提示,在微创下置管抽吸液化引流术治疗基础上联合依达拉奉治疗脑出血能有效提高临床疗效,促进神经功能的恢复,增强患者的日常生活能力。

综上所述,与单用微创下置管抽吸液化引流术治疗相比,

微创下置管抽吸液化引流术联合依达拉奉治疗脑出血能有效促进患者机体内炎症反应的缓解,促进神经功能的恢复。

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