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亚低温联合穿刺碎吸术治疗高血压脑出血的疗效 及对患者血清 TNF- α , IL-6, CRP 水平的影响 *

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摘要 目的:探讨亚低温联合穿刺碎吸术治疗高血压脑出血的疗效及对患者血清 TNF- α 、IL-6、CRP 水平的影响。**方法:**选取我院 2015 年 2 月~2016 年 8 月收治的 112 例高血压脑出血患者作为研究对象,采取随机数字表将其分成两组,每组 56 例。两组患者均给予微创穿刺碎吸术治疗,观察组联合给予亚低温治疗,对比两组手术疗效、并发症、短期预后及手术前后不同时点血清 TNF- α 、IL-6、CRP 水平变化情况。**结果:**观察组治疗总有效率为 92.86%,与对照组(76.79%)相比明显上升($P<0.05$)。观察组 MODS、总并发症的发生率分别为 0%、26.79%,均明显低于对照组($P<0.05$)。观察组术后 3d、7d 血清 TNF- α 、IL-6、CRP 水平逐渐下降,且均明显低于术前($P<0.01$);对照组术后 3d 血清 TNF- α 、IL-6、CRP 水平与术前相比无明显变化($P>0.05$),术后 7d 则明显下降,并显著低于术前($P<0.01$);观察组术后 3、7d 血清 TNF- α 、IL-6、CRP 水平均明显低于同时点对照组($P<0.01$)。观察组术后 3 个月预后良好率为 80.36%,与对照组(62.50%)比较明显上升($P<0.05$)。**结论:**亚低温联合穿刺碎吸术治疗高血压脑出血可有效减轻神经功能缺损,抑制体内炎症反应,降低病死率,疗效确切。

关键词:亚低温;穿刺碎吸术;高血压脑出血;疗效;炎症反应

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Clinical Effect of Mild Hypothermia Combined with Puncture Aspiration Operation on the Hypertensive Intracerebral Hemorrhage and Its Effect on the Serum TNF- α , IL-6 and CRP Levels*

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ABSTRACT Objective: To explore the clinical effect of mild hypothermia combined with puncture aspiration operation on the hypertensive intracerebral hemorrhage and its effect on the serum TNF- α , IL-6 and CRP levels. **Methods:** 112 cases of patients with hypertensive intracerebral hemorrhage admitted in our hospital from February 2015 to August 2016 were selected as the research objectives and randomly divides into 2 groups with 56 cases in each group. Both groups were treated with minimally puncture aspiration, and mild hypothermia was performed in the observation group additionally, the clinical effect, complication, short-term prognosis, serum TNF- α , IL-6, CRP levels at different time points before and after operation were compared between two groups. **Results:** The overall effective rate of observation group was 92.86%, which was significantly higher than of the control group(76.79%. $P<0.05$). The incidence of MODS and complications were 0% and 26.79% respectively, which were significantly lower than those of the control group($P<0.05$). The serum TNF- α , IL-6, CRP levels of observation group were significantly decreased on the 3rd and 7th day postoperation, which were significantly lower than those before operation ($P<0.01$). The serum TNF- α , IL-6, CRP levels of control group on the 3rd day postoperation were similar to those before operation ($P>0.05$), but the serum TNF- α , IL-6, CRP levels on the 7th day postoperation were significantly decreased ($P<0.01$). The serum TNF- α , IL-6, CRP levels on the 3rd, 7th day postoperation were significantly lower than those of the control group at same time points ($P<0.01$). The favorable prognosis of observation group was 80.36%, which was significantly higher than that of the control group (62.50%, $P<0.05$). **Conclusion:** Mild hypothermia combined with puncture aspiration operation could effectively reduce the neurological deficits, inhibit the inflammatory response and decrease the mortality.

Key words: Mild hypothermia; Puncture aspiration operation; Hypertensive intracerebral hemorrhage; Clinical effect; Inflammatory response

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前言

高血压脑出血是高血压最严重并发症之一,临床十分多见,高发人群为 50~75 岁男性。由于高血压脑出血病情严重且进展迅速,致残率及致死率高,故及时给予有效的治疗是改善患者预后的关键^[1]。手术治疗可起到迅速清除血肿,解除血肿及脑水肿的占位效应,进而减轻神经损害的作用,其中穿刺碎吸术由于具有创伤小、疗效好等优点而被临床广泛使用^[2]。亚低温疗法则是临床辅助用于颅内手术治疗的一种常用物理疗法,在预防及减轻脑水肿方面效果突出^[3]。为进一步探讨穿刺碎吸术与亚低温联合治疗在高血压脑出血中的应用价值,本研究在我院伦理委员会的批准下,对我院近年来收治的高血压脑出血患者分别给予了亚低温联合穿刺碎吸术及单用穿刺碎吸术治疗,现作如下报道。

1 资料与方法

1.1 一般资料

研究选取 2015 年 2 月~2016 年 8 月我院收治的高血压脑出血患者 112 例。纳入标准:(1)经临床表现及头颅 CT 检查确诊为脑出血,具有明确的高血压病史,符合高血压脑出血诊断标准;(2)年龄 30~80 岁,性别不限;(3)血肿量 30~90 mL;(4)心肺肝肾功能正常;(5)未出现急性脑疝;(6)患者家属对本研究知情,自愿签署知情同意书。排除标准:(1)合并严重心肺肝肾功能疾病或并发症;(2)合并急性脑疝;(3)血管畸形、凝血障碍等引起的脑出血;(4)合并急性慢性感染;(5)痴呆或精神疾病史。采取随机数字表将这 112 例患者随机分成两组,每组 56 例。观察组男 34 例,女 22 例,年龄 38~78 岁,平均(58.0±6.3)岁,出血量(74.6±12.5)mL,出血部位为丘脑 9 例,基底节区 36 例,脑叶 11 例。对照组男 37 例,女 19 例,年龄 39~76 岁,平均(56.9±7.9)岁,出血量(71.8±14.2)mL,出血部位为丘脑 7 例,基底节区 39 例,脑叶 10 例。两组一般临床资料对比差异无明显统计学意义($P>0.05$),具有可比性。

1.2 治疗方法

两组患者均给予包括降颅压、抗感染、营养神经、纠正电解质紊乱等在内的基础规范化治疗。在此基础上采取微创穿刺碎吸术,剃头、备皮,CT 定位设计穿刺点与穿刺方向,并选取适宜的穿刺针,长度以针头能进入血肿中心为准,注意避开脑功能区。局麻后,于 CT 引导下穿刺,YL-1 粉碎穿刺针依次穿透颅骨与硬脑膜后,将碎吸针缓缓送至血肿中心,随后将针芯拔除,接

上侧管,并连接引流管,将血肿液化部分缓慢抽出,注意首次抽出量控制在总量的 1/2 左右。随后注入生理盐水反复冲洗,至生理盐水清亮为止。待持续引流 12 h 后,将 2 万 U 尿激酶注入,夹管 4 h 左右开放。CT 下观察血肿,若血肿残留量不足 20%即可拔除引流管。

观察组术后给予亚低温治疗,患者头戴冰帽,以降温毯进行全身降温,肌松冬眠剂按照 2~4 mL/h 速度持续泵入,肛温与腋温 3~8 h 内降至 33~35℃,并维持 3~5d 左右,待脑水肿高峰期过后即可停止治疗,复温时,逐渐减少肌松冬眠剂用量,先停降温毯,再停冰帽,体温自然恢复。严密观察生命体征。

1.3 疗效评定

神经功能缺损评分采取美国国立卫生院神经功能缺损量表(NIHSS)^[4]评价。于术后 2 周根据 NIHSS 减分率进行疗效评价。基本治愈:病残程度为 0 级,NIHSS 评分减少 91%~100%;显著进步:病残程度为 1~3 级,NIHSS 评分减少 46%~90%;进步:NIHSS 评分减少 18%~45%;无变化:NIHSS 评分减少不及 17%;恶化:NIHSS 评分增加超过 18%,或患者死亡。以基本治愈、显著进步、进步为总有效。

1.4 观察指标

(1)并发症:统计两组患者并发症发生情况,包括肺部感染、上消化道出血、肾功能不全、多器官功能障碍综合征(MODS)。(2)血清炎症因子:晨起空腹抽取 3 mL 静脉血,3000 r/min 速度离心后取上清液,放置于 -80℃冰箱内保存待测。采取酶联免疫吸附法检测两组患者血清肿瘤坏死因子(TNF)- α 、白细胞介素(IL)-6、C 反应蛋白(CRP)水平。(3)短期预后:于术后 3 个月采取格拉斯哥预后评分(GOS)评价两组短期预后情况。GOS 评分共分为 5 个等级,其中 I 级为死亡,计 1 分;II 级为植物生存,计 2 分;III 级为重度残疾,日常生活需他人照料,计 3 分;IV 级为轻度残疾,生活可以自理,计 4 分;V 级为恢复良好,可正常学习及工作,计 5 分。以 IV 级及 V 级为预后良好。

1.5 统计学分析

采取统计软件 SPSS19.0 处理数据,计量资料采用 t 检验,计数资料采用 χ^2 检验,以 $P<0.05$ 表示差异有统计学意义。

2 结果

2.1 两组临床疗效对比

观察组与对照组总有效率分别为 92.86%、76.79%,观察组总有效率显著高于对照组($P<0.05$)。见表 1。

表 1 两组疗效对比[例(%)]

Table 1 Comparison of the curative effect between two groups[n(%)]

Groups	n	Basic cure	Significant progress	Progress	Unchanged	Deteriorate	Total effective rate
Observation group	56	12	24	16	3	1	52(92.86)
Control group	56	8	21	14	9	4	43(76.79)
P							0.018

2.2 两组并发症发生情况对比

观察组 MODS、总并发症发生率分别为 0%、26.79%,均明

显低于对照组($P<0.05$)。见表 2。

表 2 两组并发症发生情况对比[例(%)]

Table 2 Comparison of the complication occurrence between two groups[n(%)]

Groups	n	Lung infection	Upper gastrointestinal bleeding	Renal insufficiency	MODS	Complication rate
Observation group	56	8(14.29)	3(5.36)	4(7.14)	0(0)	15(26.79)
Control group	56	10(17.86)	5(8.93)	4(7.14)	6(10.71)	25(44.64)
P		0.607	0.463	1.000	0.012	0.049

2.3 两组治疗前后不同时点血清 TNF- α 、IL-6、CRP 水平变化情况对比

观察组术后 3 d、7 d 血清 TNF- α 、IL-6、CRP 水平逐渐下降,且均明显低于术前($P<0.01$);对照组术后 3d 血清 TNF- α 、

IL-6、CRP 水平与术前相比无明显变化($P>0.05$),术后 7d 则明显下降,并显著低于术前 ($P<0.01$);观察组术后 3、7d 血清 TNF- α 、IL-6、CRP 水平均明显低于同时点对照组($P<0.01$)。见表 3。

表 3 两组治疗前后不同时点血清 TNF- α 、IL-6、CRP 水平变化情况对比($\bar{x}\pm s$)Table 3 Comparison of the serum TNF- α , IL-6, CRP levels at different time points before and after the treatment between two groups ($\bar{x}\pm s$)

Groups	Time	TNF- α (μ g/L)	IL-6(μ g/L)	CRP(mg/L)
Observation group(n=56)	Preoperation	9.76 $\pm$ 2.24	72.78 $\pm$ 14.35	26.25 $\pm$ 4.87
	3 rd day Postoperation	6.74 $\pm$ 1.82 ^{*#}	52.35 $\pm$ 16.48 ^{*#}	17.46 $\pm$ 4.33 ^{*#}
	7 th day Postoperation	3.15 $\pm$ 1.36 ^{*#}	16.73 $\pm$ 18.22 ^{*#}	4.94 $\pm$ 2.35 ^{*#}
Control group(n=56)	Preoperation	9.61 $\pm$ 2.18	70.12 $\pm$ 12.72	26.06 $\pm$ 5.13
	3 rd day Postoperation	9.24 $\pm$ 2.76	69.24 $\pm$ 14.56	25.55 $\pm$ 5.02
	7 th day Postoperation	7.23 $\pm$ 3.12 [*]	30.45 $\pm$ 15.78 [*]	15.43 $\pm$ 3.42 [*]

Note: compared with preoperative, $P^*<0.01$, compared with the control group at the same time, $^{\#}P<0.01$.

2.4 两组术后 3 个月预后对比

62.50%比较明显上升($P<0.05$)。见表 4。

观察组术后 3 个月预后良好率为 80.36%,与对照组的

表 4 两组术后 3 个月预后对比[例(%)]

Table 4 Comparison of the prognosis on the 3rd month after operation between two groups[n(%)]

Groups	n	Good recovery	Mild disability	Severe disability	Plants live	Death	Good prognosis rate
Observation group	56	22	23	7	3	1	45(80.36)
Control group	56	13	22	9	7	5	35(62.50)
P							0.037

3 讨论

高血压脑出血是因长期高血压引起的脑细小动脉玻璃样变性与纤维样坏死导致微动脉瘤形成,当患者出现情绪激动或劳累等因素时可引起血压突然升高,进而导致病变血管发生破裂出血^[5]。一般对于出血量 <30 mL 的患者采取内科保守治疗可取得满意效果,但对于出血量较大者,血肿占位效应可使血肿周围组织神经受压坏死,引起严重的继发性脑损害^[6]。此外,血肿分解出的血红素、铁离子等产物可对神经细胞产生毒性作用,加之脑组织受损后所释放的大量血管活性物质可引起超出血肿体积数倍的脑水肿,加重脑损伤,乃至引起脑疝。研究表明脑出血 6 h 以后血肿引起的脑损害多是不可逆的,故当发生脑出血后需及时清除血肿,解除颅内血肿及脑水肿产生的占位效应,同时采取有效的措施保护血肿周围正常的脑组织,减轻继发性脑损害,改善患者预后^[7,8]。

微创穿刺碎吸术目前是高血压脑出血最常使用的手术方式之一,具有手术创伤小、技术成熟、操作简单、耗时短等优点,在高血压脑出血的治疗中能快速清除血肿,减轻脑组织神经二次损伤^[9]。且由于该术式操作时能保证脑组织密闭性,故可减少外界因素对脑组织形成的刺激与干扰,因此感染的发生风险低。但也有研究显示该术式仅能引流清除血肿,无法有效止血,故具有较高的二次出血的风险^[10]。针对此,我们认为在实施微创穿刺碎吸术时做到以下几点有助于提高手术的安全性:应严格控制好患者的血压,采用镇静、镇痛药物保持患者情绪稳定;静注立止血;首次血肿抽吸量控制在 1/2 左右;引流 12 h 后可通过注入尿激酶促使血肿溶解。

亚低温疗法是常用的物理疗法之一,目前被广泛应用于脑出血术后的治疗中。研究表明对于继发性脑损害例如颅内血肿周围脑组织出现缺血缺氧性损害、脑神经细胞凋亡或炎性损伤时,通过亚低温可起到有效的预防与治疗效果^[11]。高血压脑出

血术后应用亚低温对脑组织进行保护的作用机制在于亚低温可减少脑耗氧量,使脑代谢减慢,脑组织乳酸堆积也可因此减少,进而起到保护血脑屏障的作用^[12];减少内源性毒性产物损害脑细胞,减少钙离子内流,从而使钙对神经的毒性作用被阻断;通过遗传信息传递的改变,促进蛋白质的合成,促使脑细胞结构蛋白破坏减少,进而恢复脑细胞结构与功能;减少脑代谢、降低颅内压、抑制酶促反应,使脑内氧自由基生成减少;避免脑出血后水钠潴留导致脑水肿加重,从而有效降颅内,促进脑细胞氧供改善;对脑出血后中枢性发热与继发感染引起的体温升高可起到抑制作用^[13]。本研究中,通过对比亚低温联合穿刺碎吸术与单用穿刺碎吸术,结果显示联合治疗组患者的总有效率可达 92.86%,与单用穿刺碎吸术相比明显上升,且联合治疗组术后 3 个月短期预后也明显优于单用穿刺碎吸术组。由此可见,在手术治疗基础上联合亚低温治疗能有效提高手术疗效,与相关研究一致^[14,15]。

肿瘤坏死因子与白细胞介素类细胞因子活性的增强可增加脑微血管以及血脑屏障的通透性,引起炎症细胞侵袭,诱发或加重脑水肿^[16]。Brouwers 等^[17]通过检测高血压脑出血患者手术前后血清 TNF- α 、IL-6、CRP 水平,发现术前患者的血清 TNF- α 、IL-6、CRP 水平呈明显的高表达状态,血肿周围也发生程度不同的脑水肿,而术后随着脑水肿范围的逐渐缩小,血清 TNF- α 、IL-6、CRP 水平逐渐下降。Wang 等^[18]的研究则显示高血压脑出血术后 TNF- α 、IL-6 等炎症细胞因子的表达及动态变化和患者的疗效及预后关系密切。由此可见,血清 TNF- α 、IL-6、CRP 水平可在一定程度上反映高血压脑出血患者机体内炎症反应状况以及脑水肿程度,同时还可作为疗效评估及预后判断的参考指标。本研究中,观察组术后 3 d、7 d 血清 TNF- α 、IL-6、CRP 水平逐渐下降,且均明显低于术前;对照组术后 3 d 血清 TNF- α 、IL-6、CRP 水平与术前相比无明显变化,术后 7 d 则明显下降,并显著低于术前;观察组术后 3、7 d 血清 TNF- α 、IL-6、CRP 水平均明显低于同时点对照组。由此可见,在穿刺碎吸术基础上联合亚低温治疗能有效减轻机体内炎症反应,这与亚低温疗法具有的减少脑耗氧量与脑代谢、减少脑组织乳酸堆积、减少脑内氧自由基生成等作用密切相关^[19]。另外,本研究中,两组肺部感染、上消化道出血、肾功能不全发生率比较无明显差异,但观察组 MODS 发生率显著低于对照组。高血压脑出血术后 12~24 h 属于脑水肿产生高峰期,该时间段内给予亚低温治疗有助于减少脑水肿的发生,从而减少 MODS 等并发症的发生^[20]。

综上所述,与单纯给予穿刺碎吸术相比,亚低温联合穿刺碎吸术治疗高血压脑出血可有效减轻神经功能缺损及病残程度,抑制体内炎症反应,改善患者预后。

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(上接第 4742 页)

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