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微创穿刺引流联合开颅血肿清除术对高血压脑出血合并脑疝患者神经功能、炎症反应及脑部血流的影响*

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摘要 目的:探讨开颅血肿清除术联合微创穿刺引流对高血压脑出血(HICH)合并脑疝患者神经功能、炎症反应及脑部血流的影响。**方法:** 回顾性选择2014年4月~2019年11月期间我院收治的HICH合并脑疝患者80例，按照手术方式的不同分为A组(n=38,行开颅血肿清除术)和B组(n=42,行微创穿刺引流联合开颅血肿清除术),对比两组疗效、神经功能、炎症反应、脑部血流及预后情况。**结果:**B组的总有效率为92.86%(39/42),高于A组的76.32%(29/38),差异有统计学意义(P<0.05)。两组术后7 d血清神经元特异性烯醇化酶(NSE)、S100β蛋白水平以及术后3个月美国国立卫生研究院卒中量表(NIHSS)评分均较术前降低,且B组低于A组(P<0.05)。两组术后7 d血清白介素-6(IL-6)、肿瘤坏死因子-α(TNF-α)、超敏-C反应蛋白(hs-CRP)均较术前降低,且B组低于A组(P<0.05)。两组术后1个月、术后3个月大脑中动脉平均流速(Vm)均较术前增加,且B组高于A组(P<0.05);两组术后1个月、术后3个月大脑中动脉搏动指数(PI)较术前降低,且B组低于A组(P<0.05)。两组预后良好率无差异(P>0.05)。**结论:**与开颅血肿清除术相比,开颅血肿清除术联合微创穿刺引流治疗HICH合并脑疝患者可有效恢复患者脑部血流速度,降低炎症反应,有利于患者神经功能的恢复。

关键词:微创穿刺引流;开颅血肿清除术;高血压脑出血;脑疝;神经功能;炎症反应;脑部血流

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Effects of Minimally Invasive Puncture Drainage Combined with Craniotomy Hematoma Clearance on Neurological Function, Inflammatory Reaction and Cerebral Blood Flow in Patients with Hypertensive Intracerebral Hemorrhage and Cerebral Hernia*

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ABSTRACT Objective: To investigate the effects of minimally invasive puncture drainage combined with craniotomy hematoma clearance on neurological function, inflammatory reaction and cerebral blood flow in patients with hypertensive intracerebral hemorrhage (HICH)and cerebral hernia. **Methods:** 80 patients with HICH and cerebral hernia who were admitted in our hospital from April 2014 to November 2019 were retrospectively selected, they were divided into Group A (n=38, underwent craniotomy hematoma clearance) and group B (n=42, underwent minimally invasive puncture drainage combined with craniotomy hematoma clearance) according to the different surgical methods, the curative effect, neurological function, inflammatory reaction, cerebral blood flow and prognosis were compared between the two groups. **Results:** The total effective rate of group B was 92.86% (39/42), which was higher than 76.32% (29/38) of group A the difference was statistically significant (P<0.05). The serum neuron specific enolase(NSE), S100 β protein at 7d after operation and national institutes of health stroke scale (NIHSS)scores at 3 months after operation in the two groups were lower than those of before operation, and group B was lower than group A (P<0.05). The levels of serum interleukin-6 (IL-6), tumor necrosis factor-α (TNF-α)and high sensitivity C-reactive protein (hs-CRP)in the two groups at 7d after operation were lower than those of before operation, and group B was lower than group A (P<0.05). The mean velocity of middle cerebral artery (Vm) at 1 month after operationin, 3 months after operation in two groups were higher than those of before operation, and group B was higher than group A (P<0.05). Pulsatility index of middle cerebral artery(PI)at 1 month after operation, 3 months after operation in two groups were lower than those of before operation (P<0.05), and group B was lower than group A(P<0.05). There was no significant difference in the good prognosis rate between the two groups (P>0.05). **Conclusion:** Compared with craniotomy hematoma clearance, craniotomy hematoma removal combined with

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minimally invasive puncture and drainage in the treatment of HICH patients with cerebral hernia can effectively restore the cerebral blood flow velocity, reduce the inflammatory reaction, which is conducive to the recovery of neurological function.

Key words: Minimally invasive puncture drainage; Craniotomy hematoma clearance; Hypertensive intracerebral hemorrhage; Cerebral hernia; Neurological function; Inflammatory response; Cerebral blood flow

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前言

高血压脑出血(HICH)以呕吐、肢体偏瘫、头痛、意识障碍等症状为主要表现，是高血压患者常见的严重并发症之一[1,2]。该病多发于50～70岁年龄段,男性略多,具有起病急、病情发展快和病死率高的特点,已成为我国人口中主要的致死和致残原因之一[3]。HICH发病后,由于血肿的占位效应,部分脑组织被压迫,损害神经功能,导致脑疝,继而引发脑干损伤,对患者的生命安全造成极大的隐患[4-6]。手术治疗是挽救HICH合并脑疝患者生命的重要方法,传统的开颅血肿清除术虽可获得一定的治疗效果,但仍有部分患者效果一般,无法彻底清除血肿[7,8]。微创穿刺引流作为一项新技术,在临床上用于HICH合并脑疝的治疗,其操作简单、有效,有利于血肿的清除[9],然而单用此术式会引发血肿周边半暗带不能及时供血的风险,其中生成的氧化物、炎症因子、自由基团可毒害脑细胞造成二次损伤[10]。鉴于此,本研究对比了单纯行开颅血肿清除术与其联合微创穿刺引流术治疗HICH合并脑疝患者的疗效,现报道如下。

1 资料与方法

1.1 一般资料

本研究为回顾性研究,选择2014年4月~2019年11月期间我院收治的HICH合并脑疝患者80例。纳入标准:(1)所有患者均满足美国卒中协会卒中理事会等关于HICH合并脑疝的诊断标准[11];(2)经头颅CT等影像学确诊;(3)均符合手术指征,手术操作均由同一组医师完成操作;(4)首次发病且入院时间在24 h内。排除标准:(1)伴有凝血功能障碍、血管畸形、其他严重慢性疾病、蛛网膜下腔出血、出血破入脑室、血管炎等;(2)由于颅内血管畸形、脑干出血等引起的血肿者;(3)合并颅内或全身感染性疾病;(4)长期使用糖皮质激素、抗生素及免疫抑制剂等治疗;(5) 合并严重意识障碍或精神性疾病者;(6)发病前1个月有外科手术史和创伤史者。按照手术方式的不同分为A组(n=38,行开颅血肿清除术)和B组(n=42,行微创穿刺引流联合开颅血肿清除术),其中A组男女病例数分别为20例、18例,年龄47~74岁,平均(61.92± 5.67)岁;出血量22~35 mL,平均(28.67± 1.72)mL;出血部位:丘脑17例,基底节区12例,小脑9例。B组男女病例数分别为24例、18例,年龄46~70岁,平均(61.13± 4.83)岁;出血量23~34 mL,平均(28.57± 1.64)mL;出血部位:基底节区14例,丘脑15例,小脑13例。两组上述一般资料对比无差异(P>0.05),均衡可比。

1.2 方法

(1)术前基础治疗:入院之后均给予脱水、控制血糖和血压、降低颅内压、控制感染、维持水电解质平衡及防治消化道出血等治疗。(2)手术方法:B组患者给予微创穿刺引流联合开颅血肿清除术,CT定位血肿位置,剃头备皮后,消毒铺巾,使用2%的利多卡因5 mL实施局麻，以血肿中心点经皮钻透颅骨、硬脑膜,使用YL-1型血肿穿刺针缓慢送至血肿腔内,试抽吸确认后将未凝固的血液15~40 mL及部分的脑脊液予以吸出,安置并固定引流管。随后复查头部CT,全麻状态下实施开颅血肿清除手术,依照穿刺针及血肿部位,做出皮质切口,清除残余血肿。A组患者则常规给予开颅血肿清除手术治疗。(3)术后处理及随访:两组术后给予脱水降颅内压及神经营养性药物,术后对所有患者进行门诊、住院等方式的随访,时间为3个月,终点为患者死亡或者到达随访时间。

1.3 观察指标

(1)记录两组术后3个月的总有效率。总有效率=治愈率+显效率+有效率。无效：美国国立卫生研究院卒中量表(NIHSS)评分无变化或上升。好转:NIHSS评分下降幅度为10%~50%。显效:NIHSS评分下降幅为>50%~90%,病残度1~3级。治愈:病残评估为0级,NIHSS评分下降幅度>90%[12]。(2)收集患者术前、术后7 d的清晨空腹静脉血4 mL，经4200 r/min的转速离心12 min,离心半径14 cm,分离上清液待测。采用酶联免疫吸附法检测神经功能指标:神经元特异性烯醇化酶(NSE)和S100β蛋白,炎症因子指标:白介素-6(IL-6)、肿瘤坏死因子-α(TNF-α)、超敏-C反应蛋白(hs-CRP)。试剂盒购自北京四环生物制药有限公司,严格遵守操作步骤进行。(3)使用德国产EMS-9000型彩色经颅多普勒超声仪检查患者术前、术后1个月、术后3个月大脑中动脉血流情况[大脑中动脉平均流速(Vm)、大脑中动脉搏动指数(PI)]。(4)采用NIHSS[13]评价患者术前、术后3个月的神经功能,NIHSS量表包括感觉、语言、意识水平、面瘫、肢体运动等15项,总分42分,分数越高神经受损越严重。(5)术后3个月采用改良Rankin量表问卷(mRS)[14]评价患者预后。mRS分为0~5级:5级:需卧床,完全需要人看护照料。4级:中重度残疾,日常生活需要照料,无法独立行走。3级:中度残疾,日常生活需要帮助,可独立行走。2级:有轻度残疾,不需要人照料日常生活。1级:症状轻微,能完成日常生活和工作。0级:患者症状完全消失。将0~2级定义为预后良好。

1.4 统计学方法

采用SPSS19.0统计学软件,以($\bar{x}\pm s$)的形式表示计量资料,经t检验分析,以%的形式表示计数资料,经x^2检验分析,以P<0.05为差异有统计学意义。

2 结果

2.1 两组总有效率比较

B组的总有效率为92.86%(39/42)，高于A组的76.32%(29/38)(P<0.05),详见表1。

表 1 两组总有效率比较 [n(%)]

Table 1 Comparison of total effective rate between two groups [n(%)]

Groups	Clinical recovery	Obvious effect	Effective	Invalid	Total effective rate
Group A(n=38)	7(18.42)	12(31.58)	10(26.32)	9(23.68)	29(76.32)
Group B(n=42)	11(26.19)	16(38.10)	12(28.57)	3(7.14)	39(92.86)
x^2					4.281
P					0.039

2.2 两组神经功能指标比较

两组术前血清 NSE、S100β 蛋白水平及 NIHSS 评分对比组间无统计学差异(*P*>0.05),两组术后 7 d 血清 NSE、S100β 蛋白水平以及术后 3 个月 NIHSS 评分均较术前降低，且 B 组低于 A 组(*P*<0.05),详见表 2。

表 2 两组神经功能指标比较($\bar{x}\pm s$)

Table 2 Comparison of neurological function indexes between the two groups($\bar{x}\pm s$)

Groups	NSE(μg/L)		S100β protein(μg/L)		NIHSS(score)	
	Before operation	7 d after operation	Before operation	7 d after operation	Before operation	7 d after operation
Group A(n=38)	45.92± 4.53	38.54± 3.48[a]	1.97± 0.25	1.43± 0.24[a]	29.77± 4.36	18.67± 3.57[a]
Group B(n=42)	46.34± 5.48	32.35± 4.52[a]	1.91± 0.22	1.15± 0.18[a]	29.19± 3.24	9.25± 2.98[a]
t	0.371	6.810	1.142	5.938	0.679	12.855
P	0.711	0.000	0.257	0.000	0.499	0.000

Note: Compared with before operation, [a]*P*<0.05.

2.3 两组炎症因子指标比较

两组术前 IL-6、TNF-α、hs-CRP 对比组间无统计学差异(*P*>0.05),两组术后 7 d IL-6、TNF-α、hs-CRP 均较术前降低,且 B 组低于 A 组(*P*<0.05),详见表 3。

表 3 两组炎症因子指标比较($\bar{x}\pm s$)

Table 3 Comparison of inflammatory factors between the two groups($\bar{x}\pm s$)

Groups	IL-6(ng/L)		TNF-α(μg/L)		hs-CRP(mg/L)	
	Before operation	7 d after operation	Before operation	7 d after operation	Before operation	7 d after operation
Group A(n=38)	38.23± 3.07	28.97± 4.96[a]	75.64± 5.38	52.05± 4.32[a]	19.85± 2.39	12.94± 2.36[a]
Group B(n=42)	37.67± 4.14	19.23± 3.82[a]	75.08± 5.52	39.41± 5.29[a]	19.59± 2.45	7.41± 2.31[a]
t	0.681	9.892	0.459	11.631	0.480	10.583
P	0.798	0.000	0.648	0.000	0.633	0.000

Note: Compared with before operation, [a]*P*<0.05.

2.4 两组血流指标比较

两组术前 Vm、PI 对比组间无统计学差异(*P*>0.05),两组术后 1 个月、术后 3 个月 Vm 均较术前依次升高,且 B 组均高于 A 组(*P*<0.05),PI 较术前降低，且 B 组均低于 A 组(*P*<0.05),详见表 4。

表 4 两组血流指标比较($\bar{x}\pm s$)

Table 4 Comparison of blood flow indexes between the two groups($\bar{x}\pm s$)

Groups	Vm(cm/s)			PI		
	Before operation	1 month after operation	3 month after operation	Before operation	1 month after operation	3 month after operation
Group A(n=38)	37.62± 4.21	49.64± 6.32[a]	67.32± 9.34[ab]	1.51± 0.28	1.21± 0.29[a]	0.85± 0.22[ab]
Group B(n=42)	38.07± 4.37	64.25± 6.29[a]	82.54± 8.07[ab]	1.54± 0.25	0.93± 0.21[a]	0.61± 0.16[ab]
t	0.468	10.351	7.818	0.506	4.980	5.617
P	0.641	0.000	0.000	0.614	0.000	0.000

Note: Compared with before operation, [a]*P*<0.05, compared with 1 month after operation, [b]*P*<0.05.

2.5 两组预后比较

B 组 mRS 预后情况:0 级 11 例,1 级 17 例,2 级 9 例,3 级 4 例,4 级 1 例, 预后良好率为 88.10%(37/42);A 组 mRS 预后情况:0 级 8 例,1 级 14 例,2 级 10 例,3 级 4 例,4 级 2 例,预后良好率为 84.21%(32/38); 两组预后良好率对比组间无统计学差异(x^2=0.254,P=0.614)。

3 讨论

HICH 发病的主要病理机制为机体长期处于高血压状态下,颅内动脉血管壁强度减弱,进而出现小动脉瘤,颅内动脉粥样硬化,当患者剧烈活动、情绪过度激动时,血压可瞬间飙升,造成脑出血原发性损伤;出血未能控制的情况下,出血区域可形成血肿,血肿的占位效应、凝血酶等细胞毒性物质以及出血灶周围微循环的损害均会对脑细胞造成损害,形成继发性脑损伤[15-17]。而 HICH 突发脑疝使神经、脑干和重要脑血管等受到压迫,严重危害患者生命健康[18]。HICH 合并脑疝患者预后极差 ,病死率极高,且患者颅内压呈现病理性升高,此时降低颅内压、及时清除血肿、减轻脑神经损伤成为治疗该病的主要目标[19,20]。

开颅血肿清除术是现阶段治疗 HICH 合并脑疝的常用手术方式,但术后存在不同程度的认知障碍、运动障碍和语言障碍[21]。微创穿刺引流术是近年来发展的治疗 HICH 合并脑疝的一种新术式,可充分降低颅内压,在短时间内清除大部分血肿[22-24]。临床尝试将微创穿刺引流联合开颅血肿清除术治疗,以期更好地控制颅内压,清除血肿。S100β 蛋白主要存在于脑组织的神经胶质细胞, 与细胞增殖关系密切,NSE 是一类神经细胞质中广泛分布的烯醇化酶,NSE 及 S100β 蛋白在脑组织中均具有较高活性, 脑损伤后其水平会出现快速升高 [25]。而 NIHSS 评分则是评价人体神经功能缺损的客观性指标,信效度较好。本次研究结果显示, 术后两组的 NSE、S100β 蛋白、NIHSS 评分及脑部血流指标均有所改善,且联合微创穿刺引流术治疗后其改善效果更为明显,这说明微创穿刺引流联合开颅血肿清除术治疗 HICH 合并脑疝患者, 可有效恢复脑部血流,促进患者早期神经功能的改善,具有较好的疗效。究其原因,可能是微创穿刺引流术虽然不能清除所有血肿,但可在短时间进行降压处理,为开颅血肿清除术争取了时间,可尽早恢复患者脑血流速度,减少脑组织继发性损伤,利于术后患者神经功能的恢复。越来越多的研究显示[26,27],IL-6、TNF-α、hs-CRP 作为炎症反应、免疫应答的重要调节因子参与着脑损伤病情进展,HICH 合并脑疝存在明显脑损伤, 亦会引起机体免疫应答及炎症反应,故上述炎性因子会出现异常升高。TNF-α 在病理状态下可作为机体炎症的重要调节因子。IL-6 具有修复神经系统及免疫介导等作用,可活化巨噬细胞,使脑水肿程度加重。hs-CRP 作为一种急性期高敏反应蛋白,可损害脑血管内膜,加重脑损伤。本研究中术后两组炎症因子均降低,且 B 组的效果更佳,原因可能是微创穿刺引流对机体损伤小,同时可及时解除血肿压迫、清除坏死组织,减少炎性因子的大量分泌,因此降低了血清内各炎症因子的含量[28-30]。另两组预后良好率对比组间无统计学差异,但联合治疗者的预后良好率仍然较单用开颅血肿清除术治疗者更高,究其原因,可能是本研究中样本量更少导致,此结论尚需进一步的大样本量结合长期随访予以证实。此外,结合笔者的临床经验,笔者认为微创穿刺引流术虽不失为一种快速降低颅内压效的有效方法,但仍需注意以下几点:穿刺有可能损伤血管,引发感染扩散,因此施术者需仔细辨认血管,以免误伤;术后应严密观察病情变化,加强护理和全身支持;引流血肿不宜过快,以免颅内压降低过快出现意外。

综上所述, 开颅血肿清除术联合微创穿刺引流治疗 HICH 合并脑疝患者,可有效恢复脑部血流,降低炎症反应,有利于患者早期神经功能的恢复。

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