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小骨窗显微手术治疗基底节区高血压脑出血的效果分析及对血清CCCK-18、CTRP-3水平的影响*

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摘要 目的:探讨小骨窗显微手术治疗基底节区高血压脑出血的效果及对血清 gaspase 切割的细胞角蛋白 18(CCCK-18)、补体 C1q 肿瘤坏死因子相关蛋白 3(CTRP-3)水平的影响。方法:选取 2016 年 5 月至 2018 年 5 月我院收治的 160 例基底节区高血压脑出血患者,按照随机数表法将其分为观察组(n=82)和对照组(n=78)。对照组采用传统大骨瓣开颅术治疗,观察组采用小骨窗显微手术治疗。观察和比较两组的临床疗效,血肿清除率、术中出血量、术后意识恢复时间、住院时间,治疗前后 NIHSS、ADL 评分、血清 CCCK-18、CTRP-3 水平的变化及并发症的发生情况。结果:治疗后,观察组总有效率显著高于对照组[95.12% vs. 79.48%]($P<0.05$);血肿清除率、术中出血量、术后意识恢复时间、住院时间均显著优于对照组[(93.62±3.58)% vs. (85.40±2.19)%, (92.47±12.56) mL vs. (189.25±26.47) mL, (2.01±0.58) d vs. (8.69±2.03) d, (13.39±2.08) d vs. (19.45±3.76) d]($P<0.05$);NIHSS 评分显著低于对照组[(9.76±1.42)分 vs. (20.57±3.26)分]($P<0.05$);ADL 评分显著高于对照组[(86.42±8.64)分 vs. (75.39±7.02)分]($P<0.05$);血清 CCCK-18 水平显著低于对照组[(201.76±32.59) U/L vs. (237.57±39.20) U/L, (29.59±5.19) ng/mL vs. (42.97±7.94) ng/mL]($P<0.05$);CTRP-3 水平显著高于对照组[(289.59±35.19)ng/mL vs. (232.97±27.94)ng/mL]($P<0.05$);并发症总发生率显著低于对照组[3.65%(3/82) vs. 14.10%(11/78)]($P<0.05$)。结论:小骨窗显微手术治疗基底节区高血压脑出血的疗效显著,可更有效清除血肿,缓解血肿压迫,改善神经功能,减少继发性损伤,安全性高,可能与其降低血清 CCCK-18 水平及升高 CTRP-3 水平有关。

关键词:小骨窗显微手术;基底节区高血压脑出血;血肿清除率;并发症;预后

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Clinical Efficacy of Microsurgery with Small Bone Window in the Treatment of Hypertensive Cerebral Hemorrhage in Basal Ganglia and Its Effect on the Levels of CCCK-18 and CTRP-3 in Serum*

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ABSTRACT Objective: To investigate the clinical efficacy of microsurgery with small bone window in the treatment of hypertensive cerebral hemorrhage in basal ganglia and its effect on the levels of CCCK-18 and CTRP-3 in Serum. **Methods:** 160 patients with hypertensive cerebral hemorrhage in basal ganglia who were treated from May 2016 to May 2018 in our hospital were selected as research objects. According to random number table, those patients were divided into the observation group (n=82) and the control group (n=78). The control group was treated with traditional large bone flap craniotomy, while the observation group treated with microsurgery of small bone window. The clinical effect, hematoma clearance rate, intraoperative bleeding volume, postoperative consciousness recovery time, hospital stay time, NIHSS, ADL scores before and after treatment, changes in serum ccck-18, CTRP-3 levels and the incidence of complications were observed and compared between the two groups. **Results:** After treatment, the total effective rate of observation group was significantly higher than that of the control group [95.12% vs. 79.48%]($P<0.05$). The hematoma clearance rate, intraoperative bleeding volume, postoperative consciousness recovery time and hospitalization time were significantly better than those in the control group [(93.62±3.58)% vs. (85.40±2.19)%, (92.47±12.56) mL vs. (189.25±26.47) mL, (2.01±0.58) d vs. (8.69±2.03) d, (13.39±2.08) d vs. (19.45±3.76) d]($P<0.05$). NIHSS score was significantly lower than that of the control group[(9.76±1.42) scores vs. (20.57±3.26) scores]($P<0.05$). ADL score was significantly higher than that of the control group [(86.42±8.64) scores vs. (75.39±7.02) scores]($P<0.05$). The levels of ccck-18 in serum were significantly lower than those in the control group [(201.76±32.59) U/L vs. (237.57±39.20) U/L]($P<0.05$). The level of CTRP-3 was significantly higher than that of the control group[(289.59±35.19)ng/mL vs. (232.97±27.94)ng/mL]($P<0.05$). The total incidence of complications was significantly lower than that of the control group [3.65%(3/82) vs. 14.10%(11/78)]

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($P<0.05$)。 **Conclusion:** Microsurgery combined with small bone window is effective on hypertensive intracerebral hemorrhage in basal ganglia. It can clear hematoma more effectively relieve the hematoma compression, improve the nerve function, reduce the secondary injury, which may be related to the decrease of serum CCK-18 level and increase of CTRP-3 level.

Key words: Microsurgery of small bone window; Hypertensive cerebral hemorrhage in basal ganglia; Hematoma clearance rate; Complication; Prognosis

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前言

脑出血是临床上常见的脑血管疾病,大量血肿组织会产生占位效应,可诱发脑部继发性损害,致残率和死亡率较高^[1]。高血压是诱导脑出血死亡独立危险因素之一,临床研究^[2,3]表明高血压导致脑出血是极其危重的疾病,病情较轻的患者通过治疗可恢复神智,但病情较重的患者会出现昏迷,残留后遗症,对患者的日常生活及生命健康均造成了严重的影响。基底节区是高血压脑出血的好发部位,因出血部位接近功能区,手术时容易造成较大的创伤,通常预后较差。及时有效清除血肿、减少神经功能损害、改善预后是治疗的目的^[4,5]。

目前,临床上治疗基底节区高血压脑出血的方法较多,以往传统的术式创伤较大。本研究以小骨窗显微手术和传统大骨瓣开颅术对患者展开治疗,其中小骨窗显微手术能够有效清除血肿,促进术后神经功能恢复;传统大骨瓣开颅术降压充分且迅速,可使患者术后颅内压迅速得到缓解,解除占位效应。观察治疗疗效及其作用机制。有研究^[6]显示血清 gaspase 切割的细胞角蛋白 18 (CCK-18)、补体 C1q 肿瘤坏死因子相关蛋白 3 (CTRP-3)与高血压脑出血患者的预后情况有关,现报道如下。

1 资料与方法

1.1 一般资料

收集 160 例基底节区高血压脑出血患者,均符合第四届全国脑血管学术会议制定的诊断标准。纳入标准^[7]:经 CT 确诊为基底节区脑出血;有明确的高血压病史;配合研究者;符合手术指征;脑血肿体积超过 30 mL;发病至手术时间不超过 24 h;排除标准:入院时出血迅速增多;生命体征不稳定者;创伤性脑出血;既往脑创伤、脑卒中;患有其他严重器官疾病者;妊娠期或哺乳期者;患有恶性肿瘤疾病;患有感染疾病;患有精神疾病;同时参与其他研究者。

按照随机数表法将所有患者分为观察组($n=82$)和对照组($n=78$)。观察组男 47 例,女 35 例,年龄 40~80 岁,平均 (68.02 ± 7.30) 岁,发病至手术时间 5 h~2 d,平均 (12.58 ± 1.17) h,血肿量平均 (39.24 ± 3.08) mL,GCS 评分:13~15 分 10 例,9~12 分 34 例,6~8 分 38 例;对照组男 42 例,女 36 例,年龄 41~80 岁,平均 (67.93 ± 7.16) 岁,发病至手术时间 6 h~2 d,平均 (11.96 ± 1.09) h,血肿量平均 (40.37 ± 3.21) mL,GCS 评分:13~15 分 12 例,9~12 分 30 例,6~8 分 36 例。两组患者一般资料均无明显差异($P>0.05$),具有可比性。

1.2 治疗方法

两组均于发病后 24 h 内实施手术,行气管插管麻醉,术常规降低颅内压,营养神经补给及抗感染,对照组采用传统大骨瓣开颅术治疗,清除血肿后行硬膜减张修补术缝合切口,保

留骨瓣。

观察组采用小骨窗显微手术治疗,确定血肿具体位置和侧裂皮层最近的层面后,将其作为切口点作长约 6 cm 的切口,采用铣刀作一 3 cm 长的骨窗,充分切开硬膜,在显微镜的观察下进行操作,分开蛛网膜,于额叶皮质无血管的部位作一 2 cm 长的入口,沿额颞间隙解剖,经大脑动脉分支,剥离至岛叶表面,将岛叶在无血管区切开长度 1 cm,向下稍分离至血肿部位,低负压清除血肿,注意不易摘除的血肿切勿强行清除,采用电凝处理活动性血管出血。

1.3 观察指标

观察两组治疗疗效,各项治疗指标(血肿清除率、术中出血量、术后意识恢复时间、住院时间),NIHSS、ADL 评分,血清 CCK-18、CTRP-3 水平,并发症发生率。

1.3.1 指标检测 分别于两组治疗前后分别采集 5 mL 静脉血,离心分离血清,采用酶联免疫吸附法检测血清 CCK-18、CTRP-3 水平;CCK-18 试剂盒来自广州易科生物科技有限公司,CTRP-3 试剂盒来自试剂盒来自美国 R&D 公司。采用神经功能缺损程度(NIHSS)评估患者的神经功能,分数越低表明情况越好;采用日常生活能力量表(ADL)评估患者的生活自理能力,分值为 0~100 分,分数越高表明自我能力越好。

1.3.2 疗效评定标准 意识恢复,生活自理,NIHSS 减少 91%及以上为治愈^[8]。意识恢复或轻微模糊,NIHSS 减少 45%~90%为有效;意识有所恢复,NIHSS 减少 18%~45%为有效;以上指标均未改善为无效。

1.4 统计学分析

使用 SPSS18.0 统计软件进行数据分析,数据均符合正态分布,计数资料以[(例)%]表示,组间比较采用 χ^2 检验,计量资料以($\bar{x}\pm s$)表示,组间比较采用 t 检验,组内比较使用配对样本 t 检验,以 $P<0.05$ 为差异有统计学意义。

2 结果

2.1 两组治疗疗效

治疗后,观察组总有效率为 95.12%(78/82),与对照组的 79.48%(62/78)比较具有统计学意义($P<0.05$),见表 1。

2.2 两组各项治疗指标比较

观察组血肿清除率、术中出血量、术后意识恢复时间、住院时间均显著优于对照组($P<0.05$),见表 2。

2.3 两组治疗前后 NIHSS、ADL 评分的变化

治疗前,两组 NIHSS、ADL 评分比较无明显统计学差异($P>0.05$);治疗后,两组 NIHSS 评分较治疗前显著降低($P<0.05$),而 ADL 评分较治疗前显著升高 ($P<0.05$),且观察组 NIHSS 评分显著低于对照组 ($P<0.05$),ADL 评分明显高于对照组($P<0.05$),见表 3。

表 1 两组治疗疗效的比较[例(%)]

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

Groups	n	Cure	Markedly effective	Effective	Invalid	Total effective rate
Observation group	82	39(47.56)	16(19.51)	21(25.60)	4(4.87)	78(95.12)*
Control group	78	31(39.74)	14(17.94)	17(21.79)	16(20.51)	62(79.48)
t		0.993	0.064	0.321	8.934	8.934
P		0.319	0.800	0.571	0.003	0.003

表 2 两组各项治疗指标比较($\bar{x} \pm s$)

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

Groups	n	Hematoma clearance rate	Intraoperative hemorrhage	Postoperative consciousness	Length of stay(d)
		(%)	(mL)	recovery time(d)	
Observation group	82	93.62 $\pm$ 3.58*	92.47 $\pm$ 12.56*	2.01 $\pm$ 0.58*	13.39 $\pm$ 2.08*
Control group	78	85.40 $\pm$ 2.19	189.25 $\pm$ 26.47	8.69 $\pm$ 2.03	19.45 $\pm$ 3.76
t		17.413	29.775	28.600	12.696
P		0.000	0.000	0.000	0.000

表 3 两组治疗前后 NIHSS、ADL 评分的变化($\bar{x} \pm s$, 分)

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

Groups	n	NIHSS		ADL	
		Before treatment	After treatment	Before treatment	After treatment
Observation group	82	36.02 $\pm$ 5.81	9.76 $\pm$ 1.42**	55.39 $\pm$ 6.82	86.42 $\pm$ 8.64**
Control group	78	36.91 $\pm$ 5.76	20.57 $\pm$ 3.26 [#]	56.02 $\pm$ 6.75	75.39 $\pm$ 7.02 [#]
t		0.973	27.420	0.587	8.836
P		0.332	0.000	0.558	0.000

2.4 两组治疗前后血清 CCCK-18、CTRP-3 水平变化

治疗前, 两组血清 CCCK-18、CTRP-3 水平比较无明显统计学差异($P>0.05$); 治疗后, 两组血清 CCCK-18 水平较治疗前

显著降低 ($P<0.05$), 而血清 CTRP-3 水平较治疗前显著升高 ($P<0.05$), 且观察组血清 CCCK-18 水平显著低于对照组 ($P<0.05$), 血清 CTRP-3 水平明显高于对照组 ($P<0.05$), 见表 4。

表 4 两组治疗前后血清 CCCK-18、CTRP-3 水平的变化($\bar{x} \pm s$)

Table 4 Comparison of the changes of serum ccck-18 and CTRP-3 levels between two groups before and after treatment($\bar{x} \pm s$)

Groups	n	CCCK-18(U/L)		CTRP-3(ng/mL)	
		Before treatment	After treatment	Before treatment	After treatment
Observation group	82	246.81 $\pm$ 51.07	201.76 $\pm$ 32.59**	65.03 $\pm$ 10.85	289.59 $\pm$ 35.19**
Control group	78	247.09 $\pm$ 50.86	237.57 $\pm$ 39.20 [#]	64.89 $\pm$ 10.02	232.97 $\pm$ 27.94 [#]
t		0.035	6.296	0.085	11.235
P		0.972	0.000	0.933	0.000

2.5 两组并发症发生情况的比较

治疗过程中, 观察组并发症总发生率为 3.65%, 显著低于对照组 ($P<0.05$), 见表 5。

3 讨论

高血压脑出血是在高血压状态下发生的脑实质出血, 病情发展迅速, 病理生理特点是脑血管发生变化, 颅内小动脉改变, 出现严重的动脉粥样硬化^[9-11]。临床上针对出血量在 30 mL 内

患者多采用保守治疗, 而超过 30 mL 且在 60 mL 内被认定为中等量出血, 需要采用手术治疗^[12,13]。临床研究表明^[14-16]脑出血后, 血肿周围会行程一个组织损伤和水肿形成的加重区域, 如果及时采取有效的治疗, 可改善该区域的病理改变, 恢复受损组织功能。血肿周围病变会随着病情的及病程的发展而加重, 从局部水肿、缺血发展到坏死^[17]。研究表明^[18]血肿会造成压迫损伤, 导致神经功能恶化, 还会在凝结及液化分解过程中产生大量的毒性物质, 不利于患者预后, 且随着时间的变化, 该病的发

生率也越来越高。目前,临床上治疗该病的术式较多,其中传统大骨瓣开颅手术视野充足,术中可充分暴露,能够彻底止血,但

由于开颅创伤较大,手术时间较长,术后容易诱发并发症,不利于预后^[19,20]。

表 5 两组并发症发生率比较[例(%)]

Table 5 Comparison of the incidence of complications between the two groups[n(%)]

Groups	n	pulmonary infection	Gastrointestinal hemorrhage	Urinary tract infection	Renal insufficiency	Total incidence rate
Observation group	82	1(1.21)	2(2.42)	0(0.00)	0(0.00)	3(3.65) #
Control group	78	3(3.84)	3(3.84)	3(3.84)	2(2.56)	11(14.10)
χ^2		1.132	0.262	3.214	2.129	5.461
<i>P</i>		0.287	0.609	0.073	0.145	0.019

随着临床的不断研究,与传统开颅手术相比,微创术式具有明显的优势^[21]。小骨窗显微手术具有术中视野清晰、创伤小等优点,可清除血肿彻底,及时有效缓解颅内压升高^[22,23]。在显微镜的观察下操作可最大程度的减少脑组织损伤;以侧裂岛叶入路,直达血肿腔,可避免损伤重要脑血管,可彻底止血,恢复神经功能^[24];可清楚显示出出血豆纹动脉,精确电凝,避免术后再次出血^[25];可有效降低并发症、可减少患者住院时间。临床研究表明^[26]微骨窗入路不会对细胞免疫造成较大的影响,可降低肺部感染发生率。本研究显示采用小骨窗显微手术治疗的患者的血肿清除率、术中出血量、术后意识恢复时间、住院时间及治疗疗效均显著优于对照组,说明小骨窗显微手术有利于促进患者预后恢复,疗效更佳^[27]。本研究通过对两组治疗期间并发症的发生情况观察,发现采用小骨窗显微手术治疗的患者的并发症总发生率更低,创伤小,可减少脑部继发性损害,安全有效^[28]。

近年来研究显示多种疾病中 CCK-18 含量显著高于正常水平,在脑出血的各个出血部位均存在,CCK-18 是神经系统疾病预后的潜在生物标志物,被确定为不良预后的独立预测因子,预测价值较高,其浓度与病情的严重程度相关^[29,31]。相关研究表明^[32]CCK-18 参与了脑出血的急性发病过程,与患者的预后存在一定的关系。CTRP-3 是一种新的脂肪因子,参与炎症反应、细胞凋亡、血管新生等多种生理过程,可促血管生成,抵抗脑出血继发性损伤,可保护血脑屏障^[33]。通过监测 CTRP-3 水平变化反映病情程度及预后^[34]。本研究显示两组患者血清 CCK-18、CTRP-3 水平均较治疗前显著改善,采用小骨窗显微手术治疗的患者的血清 CCK-18 水平显著低于采用传统大骨瓣开颅术治疗的患者,CTRP-3 水平显著高于采用传统大骨瓣开颅术治疗的患者,提示小骨窗显微手术可减少脑水肿,减少神经功能缺损,提高预后^[35]。

综上所述,小骨窗显微手术治疗基底节区高血压脑出血的疗效显著,可更有效清除血肿,缓解血肿压迫,改善神经功能,减少继发性损伤,安全性高,可能与其降低血清 CCK-18 水平及升高 CTRP-3 水平有关。

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