

doi: 10.13241/j.cnki.pmb.2023.21.018

神经外科颅脑手术患者发生术后颅内感染的危险因素 及应用中医外科“托法”效果分析*

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摘要 目的:探讨神经外科颅脑手术患者术后发生颅内感染的危险因素,并研究中医外科“托法”辅助治疗颅内感染的临床疗效。

方法:回顾性分析 2017 年 1 月到 2022 年 12 月在我院神经外科进行颅脑手术的 260 例患者临床资料,分析影响患者发生术后颅内感染的影响因素。发生术后发生颅内感染的患者在常规抗感染治疗的基础上加用中医“托法”治疗,分析其临床治疗疗效、抗感染治疗后脑脊液白细胞计数、蛋白含量和中性粒细胞,以及血清白介素-8(IL-8),超敏 c 反应蛋白(hs-CRP)和降钙素(PCT)。

结果:260 例神经外科颅脑手术患者,术后出现颅内感染的患者有 21 例,术后颅内感染发生率为 8.08%。多因素 Logistic 回归分析显示:手术时间、脑脊液分流术、脑室外引流以及脑脊液漏是影响神经外科颅脑手术患者术后是否发生颅内感染的独立影响因素。经中医外科“托法”辅助抗感染治疗后,21 例术后颅内感染患者脑脊液白细胞计数、蛋白含量和中性粒细胞均较治疗前显著降低($P<0.05$),并且血清 IL-8、hs-CRP 和 PCT 均较治疗前降低($P<0.05$)。21 例术后颅内感染患者治疗总有效率、抗感染治疗时间和总费用分别为 90.48%、(11.43±1.57) 天和(7571.68±2541.29) 元。**结论:**手术时间、脑脊液分流术、脑室外引流以及脑脊液漏是影响神经外科颅脑手术患者术后是否发生颅内感染的独立影响因素,中医外科“托法”可用于术后颅内感染患者抗感染治疗。

关键词:颅脑手术;颅内感染;中医外科;危险因素

中图分类号:R651.1 文献标识码:A 文章编号:1673-6273(2023)21-4096-04

Risk Factors of Postoperative Intracranial Infection in Neurosurgery Patients Undergoing Craniocerebral Surgery and the Analysis of the Effect of Applying "Support Therapy" in Traditional Chinese Medicine Surgery*

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ABSTRACT Objective: To explore the risk factors of intracranial infection in neurosurgery patients after craniocerebral surgery, and to study the clinical efficacy of traditional Chinese medicine surgery "Tufa" as an auxiliary treatment for intracranial infection. **Methods:** Retrospectively analyze the clinical data of 260 patients who underwent craniocerebral surgery in neurosurgery of our hospital from January 2017 to December 2022, and analyze the influencing factors of postoperative intracranial infection. Patients with postoperative intracranial infection were treated with traditional Chinese medicine "Tuofe" on the basis of conventional anti infection treatment, and their clinical therapeutic efficacy, cerebrospinal fluid leukocyte count, protein content and neutrophils, as well as serum interleukin-8 (IL-8), hypersensitive C-reactive protein (hs CRP) and Calcitonin (PCT) after anti infection treatment were analyzed. **Results:** Among 260 patients undergoing neurosurgery craniocerebral surgery, 21 patients had intracranial infection after surgery, and the incidence of postoperative intracranial infection was 8.08%. Multivariate logistic regression analysis showed that operation time, cerebrospinal fluid shunt, external ventricular drainage and cerebrospinal fluid leakage were independent factors influencing whether intracranial infection occurred after neurosurgery craniocerebral surgery. After using the traditional Chinese medicine surgical "support method" to assist in anti infection treatment, the cerebrospinal fluid white blood cell count, protein content, and neutrophils of 21 patients with postoperative intracranial infection were significantly reduced compared to before treatment($P<0.05$), and serum IL-8, hs CRP, and PCT were all reduced compared to before treatment ($P<0.05$). The total effective rate, anti infection treatment time, and total cost of 21 postoperative intracranial infection patients were 90.48%(11.43±1.57) days, and (7571.68±2541.29) yuan, respectively. **Conclusion:** Operation time, cerebrospinal fluid shunt, external ventricular drainage and cerebrospinal fluid leakage are independent influencing factors that affect whether intracranial infection occurs after craniocerebral surgery in neurosurgery patients. Traditional Chinese medicine surgery "support therapy" helps to improve the anti infection treatment effect of patients with intracranial infection after surgery.

* 基金项目:广东省 2021 年中医药局科研项目(20212249)

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(收稿日期:2023-04-06 接受日期:2023-04-28)

Key words: Craniocerebral surgery; Intracranial infection; Traditional Chinese Medicine Surgery; Risk factors

Chinese Library Classification(CLC): R651.1 **Document code:** A

Article ID: 1673-6273(2023)21-4096-04

前言

颅内感染是神经外科颅脑手术最常见的并发症之一,虽然不同医院、不同疾病、不同手术方式及不同诊断标准的神经外科颅脑手术术后颅内感染发生率不尽相同,但发生术后颅内感染的高死亡率和致残率的临床预后结果是一致的^[1,2]。据统计,术后出现颅内感染的患者死亡率比未发生颅内感染的患者高30%,并且其住院时间也因此延长,医疗费用显著增加^[3,4]。此外,颅内感染引起的发热也会对患者脑组织产生二次伤害,导致患者临床预后较差和致残率升高^[5,6]。因此,在临床实践中强调明确影响颅脑手术后颅内感染的危险因素,在围手术期进行预见性预防干预以降低患者术后颅内感染风险。对于已经出现术后颅内感染的患者,临幊上多采用抗感染治疗,对于出现脑脓肿的患者施以外科手术联合抗感染治疗,而中医药用于术后颅内感染的报道较少。中医理论认为^[7]:颅脑手术后患者,气血津液大亏,正气已虚;此时邪气乘虚而入而导致颅内感染。毒邪炽盛,正邪相争,故见发热或恶寒,气血津液亏虚,不能濡养清窍,故见神昏、疲倦、自汗、食少,其人多舌苔黄腻或灰腻,舌质淡红,脉象虚数或沉细。而中医外科中的“托法”治疗是用补益气血和透脓的药物,扶助正气、托毒外出,以免毒邪扩散和内陷的治疗法则,非常适合于抗感染的治疗^[8]。本研究首先回顾性分析2017-2022年间我院神经外科颅脑手术患者临床资料,对比分析各种可能影响患者术后颅内感染的因素,并同时运用中医“托法”辅助治疗术后颅内感染患者以研究其用于术后颅内感染患者的临床疗效。

1 资料与方法

1.1 临床资料

2017年1月到2022年12月在我院神经外科进行颅脑手术的260例患者被纳入本次研究,其中男性患者132例,女性患者128例,年龄介于35-56周岁之间,平均年龄(46.98±8.62)岁,手术原因是颅内肿瘤、外伤、脑血管疾病以及其他患者分别有18例、120例、92例和30例。所有参与本次研究的患者均对本次研究内容知情,签订知情同意书。此外,本研究经我院伦理委员会批准实施。

1.2 研究方法

1.2.1 术后颅内感染影响因素分析 根据患者术后是否出现颅内感染分为颅内感染组和非颅内感染组,收集并比较两组患者年龄、性别、美国麻醉师协会(American Society of Anesthesiologists, ASA)评分、格拉斯哥昏迷评分法(Glasgow Coma Scale, GCS)、颅骨修补术、颅内血肿清除、二次手术以、气管切开、手术时间、脑脊液分流、脑室外引流、脑脊液漏、使用激素以及颅脑内植入异物的差异。然后将存在显著差异的临床资料纳入Logistic回归分析,以是否发生术后颅内感染为因变量,以存在差异的临床资料为自变量。

1.2.2 治疗方法 发生术后颅内感染的患者在常规抗感染治

疗的基础上辅助使用中医外科“托法”进行治疗。选用托里消毒散加减,组方如下:党参20 g、川芎10 g、当归10 g、白芍10 g、白术10 g、银花15 g、茯苓15 g、白芷10 g、皂角刺10 g、甘草10 g、桔梗10 g、黄芪60 g,随证加减,日一剂,水煎服,每日两次。

1.2.3 临床疗效评价 通过比较患者治疗前后实验室检查指标、病原学检查、临床症状以及体征等判定患者临床疗效,即:治疗后以上全部指标恢复正常为治愈,治疗后以上全部指标有好转或仅有1项指标未恢复正常为有效,治疗后4项指标均未见好转或出现病情恶化为无效/恶化。总有效率=(治愈+好转)/总病例数×100%。

1.2.4 生化指标 患者治疗前后取脑脊液进行白细胞计数、蛋白和中性粒细胞百分含量检测。分别在治疗前和治疗后取患者外周血5 mL,离心(1000×g,10分钟,室温)以分离血清,使用酶联免疫吸附法检测血清清白介素-8(interleukin-8, IL-8),超敏c反应蛋白(hypersensitive C-reactive protein, hs-CRP)和降钙素(procalcitonin, PCT)含量。

1.3 统计学分析方法

对本研究数据使用SPSS20.0软件进行统计学分析,计数资料以百分比展示,卡方检验比较两组间计数资料差异;以(均值±标准差)表示计量数据,非配对t检验比较两组计量数据间差异。 $P<0.05$ 表示差异显著具有统计学意义。

2 结果

2.1 影响颅脑感染的单因素分析

260例神经外科颅脑手术患者,术后出现颅内感染的患者有21例,术后颅内感染发生率为8.08%。比较术后颅内感染和非感染患者临床资料,结果显示:两组患者在年龄、性别、ASA评分、颅骨修补术、颅内血肿清除、二次手术以及气管切开上比较无显著差异($P>0.05$),但术后颅内感染组患者手术时间、脑脊液分流、脑室外引流、脑脊液漏、使用激素以及颅脑内植入异物患者比例均高于术后无颅内感染组患者($P<0.05$);但术后颅内感染组患者GCS评分低于术后无颅内感染组患者($P<0.05$)。见表1。

2.2 影响颅脑感染的因素的 Logistic 回归分析

以神经外科颅脑手术患者术后是否发生颅内感染为因变量,以手术时间、GCS评分、CSF分流术、脑室外引流、脑脊液漏、使用激素以及颅脑内植入异物等作为变量进行多因素 Logistic 回归分析,结果显示:手术时间、脑脊液分流、脑室外引流以及脑脊液漏是影响神经外科颅脑手术患者术后是否发生颅内感染的独立影响因素($P<0.05$)。见表2。

2.3 治疗前后脑脊液检测指标比较

经抗感染治疗后,术后颅内感染患者脑脊液白细胞计数、蛋白含量和降钙素原均较治疗前显著降低($P<0.05$)。见表3。

2.4 治疗前后血清炎症因子含量比较

经抗感染治疗后,术后颅内感染患者血清IL-8, hs-CRP和降钙素原均较治疗前显著降低($P<0.05$)。见表4。

表 1 神经外科颅脑手术患者术后颅内感染影响因素单因素分析

Table 1 Single factor analysis of influencing factors of postoperative intracranial infection in neurosurgery patients undergoing craniocerebral surgery

Factors	Infection group (n=21)	No-Infection group (n=239)	t/ χ^2	P
Male	12	120	0.371	0.549
Age (year)	47.03± 8.35	46.98± 7.41	0.029	0.977
Surgical time (hour)	3.79± 1.38	2.82± 1.04	3.144	0.005
GCS score	8.92± 1.34	12.16± 2.46	5.951	<0.001
ASA score	2.15± 0.42	2.08± 0.42	0.732	0.465
Cerebrospinal fluid shunt (n)	3	5	9.624	0.002
Cranial repair (n)	8	129	1.953	0.162
Removal of hematoma (n)	4	43	0.015	0.904
Reoperation (n)	5	19	1.471	0.225
Extracentricular drainage (n)	3	5	4.388	0.036
Cerebrospinal fluid leakage (n)	6	10	9.263	0.002
Tracheotomy (n)	2	10	0.143	0.709
Using hormones (n)	12	48	14.935	<0.001
Foreign body implantation (n)	10	46	9.195	0.002

表 2 影响颅脑手术患者术后颅内感染独立危险因素分析

Table 2 Analysis of independent risk factors for postoperative intracranial infection in patients undergoing craniocerebral surgery

Factors	β	SE	OR	95%CI	Wald χ^2	P
Surgical time	2.703	0.945	15.621	2.131-90.234	2.305	0.021
GCS score	1.325	0.926	0.31	0.051-1.708	2.135	0.167
Cerebrospinal fluid shunt	0.712	1.328	11.325	4.235-15.318	7.965	0.013
Extracentricular drainage	2.187	1.816	9.421	3.652-17.329	8.943	0.002
Cerebrospinal fluid leakage	4.325	1.923	19.324	4.625-29.654	6.662	0.014
Using hormones	1.352	0.923	4.152	0.710-24.325	2.413	0.328
Foreign body implantation	-0.325	0.884	0.513	0.983-2.154	0.882	0.614

表 3 治疗前后脑脊液白细胞计数、蛋白质和中性粒细胞含量比较

Table 3 Comparison of white blood cell count, protein content and neutrophils in cerebrospinal fluid before and after treatment

Time	n	Leukocyte ($10^6/L$)	Protein (g/L)	Neutrophils (%)
Pre-treatment	21	3016.57± 192.35	3.02± 1.21	77.82± 20.34
Post-treatment	21	148.32± 35.21	0.94± 0.15	25.25± 9.08
t		67.217	7.818	10.815
P		<0.001	<0.001	<0.001

表 4 治疗前后血清 IL-8, hs-CRP 和 PCT 含量比较

Table 4 Comparison of white blood cell count, protein content and neutrophils in cerebrospinal fluid before and after treatment

Time	n	IL-8 (pg/mL)	hs-CRP (mg/L)	PCT ($\mu g/L$)
Pre-treatment	21	5.52± 1.24	15.11± 3.48	1.89± 0.54
Post-treatment	21	4.35± 0.62	6.92± 1.08	0.42± 0.05
t		3.867	10.300	12.422
P		<0.001	<0.001	<0.001

2.5 临床疗效、住院时间和抗感染治疗费用

21例出现术后颅内感染患者经抗感染治疗后治愈10例、好转9例和无效/恶化2例,临床治疗总有效率为90.48%。21例出现术后颅内感染患者抗感染治疗时间和费用分别为(11.43±1.57)天和(7571.68±2541.29)元。

3 讨论

颅脑手术后颅内感染是神经外科手术后致病和致死率最高的并发症之一,颅内感染患者常常伴有癫痫、颅内高压以及颅内脓肿等多种临床症状。术后颅内感染及其引发的并发症不仅会对患者带来直接身体伤害,而且会大大延长患者住院时间和增加治疗费用,在增加患者及其家属精神和经济负担的同时还会严重影响患者预后,严重者会引起患者死亡^[3,4]。因此,在围手术期做好预防性措施以避免颅内感染意义重大。本文回顾性分析在我院神经外科接受颅脑手术的260例患者临床资料,结果显示:21例患者在颅脑手术后出现颅内感染,颅脑术后颅内感染发生率为8.08%,这与Zhou J等人^[9]报道的2.1%-8.9%的颅脑手术后颅内感染的发生率一致。颅脑手术后颅内感染的发生率在不同医院、同一医院不同疾病、不同人群以及不同手术方式都是不完全相同的,但总体而言我国颅内感染发生率处于较低水平,大概发生率在2%到8%之间^[10-12]。然而,开颅手术之后的颅内感染发生率较高,大约0.2%-28%^[13]。

临床研究发现,手术的时间、手术方式、脑脊液渗漏以及患者年龄等都会影响颅脑手术后颅内感染的发生率。本文研究发现,手术时间、脑脊液分流术、脑室外引流以及脑脊液渗漏是影响我院神经外科颅脑手术患者术后发生颅内感染的独立危险因素,这与Han H, et al.^[10-12]等人的研究结果一致。之前的研究表明^[10-13],尽管影响不同颅脑手术患者术后颅内感染的影响因素不尽相同,但手术时间越长的患者术后出现感染的风险就越高。此外,脑脊液渗漏及后续所采用的引流措施是导致各种颅脑手术后颅内感染风险增加的主要因素^[14,15]。脑脊液渗漏是临幊上较为复杂的问题,其愈合比较困难,单纯修补再复发的风险比较高,所有治疗脑脊液渗漏的因素均会增加颅内感染的风险,比如脑脊液分流术和脑室外引流^[16-18]。

"消法"、"托法"、"补法"是中医外科内治法三大总则,由明代著名外科学家陈实功总结提出,记载于《外科正宗》书中。陈实功主张内外并治、刀针与药物结合,其中内治十分注意顾护脾胃、调理气血,临床主张消、托、补;外治强调"开户逐贼、使毒外出"为第一。中医外科"托法"是指用补益气血和透脓的药物,扶助正气、托毒外出,以免毒邪内陷,适用于外疡中期。托法分为透托法和补托法,其中补托法适用于毒势方盛、正气已虚,不能御毒外出者。补托法以托里消毒散为代表方,原方出自《医宗金鉴》,药物组成:人参、川芎、当归、白芍、白术、银花、茯苓、白芷、皂角刺、甘草、桔梗、黄芪,效用补益气血、托毒消肿。本研究以补托法中代表方托里消毒散对颅内感染患者进行辅助治疗,结果显示:加用托里消毒散辅助抗感染治疗患者临床治疗总有效率高达90.48%,表明中医外科"托法"辅助治疗颅内感染患者是有效的。目前,还未见有研究报道中医外科"托法"应用于颅内感染辅助治疗的文献,但梁祥翰等人^[20]研究指出,中医外科"托法"可以显著提高骨科手术患者术后感染

抗感染治疗的临床疗效。

此外,本研究还发现,辅以"托法"治疗的颅内感染患者治疗后脑脊液白细胞计数中性粒细胞、蛋白含量以及血清炎症因子均较治疗前显著降低,表明辅以"托法"治疗可以增加常规抗感染治疗疗效。进一步分析可知:白细胞是存在于机体血液中的重要血细胞,通常在机体发生感染后数量会增多,发挥杀死病原体保护机体的作用,是机体重要的防御成分,所以白细胞计数是目前评价感染最常见的指标之一,也是颅内感染临床治疗后疗效评价的重要指标之一^[21,22]。蛋白含量增高是颅内感染常见的生化变化之一,这主要是由于颅内感染造成蛋白的合成或者脑脊液循环的障碍而引起的^[23,24]。中性粒细胞是外周血最丰富的粒细胞类型,占人类所有白细胞的40%至70%,其是宿主抵抗入侵病原体的第一道防线^[25,26]。血清IL-8、hs-CRP和PCT是最常见的感染性疾病诊断实验室指标,广泛应用于临床感染性疾病的诊断及预后评估^[27]。

综上所述,神经外科颅脑手术后发生颅内感染的影响因素较多,其中以手术时间、脑脊液分流术、脑室外引流以及脑脊液漏对其影响较大。中医外科"托法"辅助治疗有助于提高颅内抗感染治疗疗效。

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