

及早经皮穴位电针刺激对高龄老年髋部骨折术后认知的影响

孙柯,梁丽萍,呼小雪,王刚

广东省人民医院/广东省医学科学院麻醉科,广东 广州 510080

【摘要】目的:研究经皮穴位电针刺激及早干预对老年髋部骨折术后认知功能及炎症因子的影响。**方法:**80岁以上髋部骨折患者40例,随机分为对照组(A组,20例)和电刺激组(B组,20例)。两组患者均采用腰-硬联合麻醉。B组患者术前2 d选取百会穴和风池穴行经皮电针刺激,3次/d,30 min/次;麻醉操作完成后行穴位持续刺激至手术结束。A组患者仅在相应穴位贴电极未行电针刺激。于入院时、术后24、72 h 3个时点对患者进行MMSE评定,若术后评分降低一个标准差或以上者即认定发生术后认知功能障碍(POCD)。所有患者在入院时、术毕即刻、术后24和72 h抽取静脉血,测定血清IL-6、IL-10和S100 β 蛋白水平。**结果:**A组术后24、72 h POCD发生率分别为65%(13/20)和60%(12/20),高于B组的35%(7/20)和25%(5/20),差异有统计学意义($P<0.05$);B组术后各时间点血清IL-6、IL-10和S100 β 蛋白水平均显著低于对照组同时点,差异有统计学意义($P<0.05$)。**结论:**及早经皮穴位电针干预有利于改善高龄老年髋部骨折术后的认知功能状态,有效降低患者POCD的发生率。这可能与抑制其血清IL-6、IL-10、S100 β 蛋白的过度表达、减轻患者脑损伤的程度有关。

【关键词】经皮穴位电针刺激;髋部骨折;术后认知功能;老年患者

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Effects of early transcutaneous acupoint electrical stimulation on postoperative cognition of elderly patients with hip fractures

SUN Ke, LIANG Liping, HU Xiaoxue, WANG Gang

Department of Anesthesiology, Guangdong Academy of Medical Sciences/Guangdong General Hospital, Guangzhou 510080, China

Abstract: Objective To assess the effects of early transcutaneous acupoint electrical stimulation (TAES) on postoperative cognitive function and inflammatory factors of the elderly with hip fractures. **Methods** Forty patients aged over 80 years with hip fractures were randomly divided into control group (group A, 20 cases) and electrical stimulation group (group B, 20 cases). All patients were treated with spinal-epidural combined anesthesia. Patients in group B received TAES at Baihui (DU20) and fengchi (GB20) (3 times a day, 30 minutes a time) since 2 days before operation until the operation finished. In group A, the electrodes were only applied at the corresponding acupoints without electrical stimulation. At admission, and 24, 72 h after finishing operation, all patients were assessed with MMSE. If the postoperative score was reduced by one standard deviation or more, postoperative cognitive dysfunction (POCD) was identified. The levels of serum IL-6, IL-10 and S100 β proteins were also measured at admission, the end of operation, and 24, 72 h after finishing operation. **Results** The incidence of POCD at 24 and 72 h after finishing operation was 65% (13/20) and 60% (12/20) in group A, higher than 35% (7/20) and 25% (5/20) in group B, with statistical significance ($P<0.05$). At all postoperative time points, the levels of serum IL-6, IL-10 and S100 β proteins in group B were significantly lower than those in group A, with statistical significance ($P<0.05$). **Conclusion** Early TAES can improve the postoperative cognitive function of elderly patients with hip fractures and reduce the incidence of POCD, which may be related to inhibiting the over-expression of serum IL-6, IL-10 and S100 β proteins, and reducing the degree of brain injury in patients.

Keywords: transcutaneous acupoint electrical stimulation; hip fracture; postoperative cognitive function; elderly patient

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【作者简介】孙柯,医学博士,医师,E-mail: 715493169@qq.com

【通信作者】王刚,主任医师,主要研究方向为老年患者围手术期重要器官的保护,E-mail: wggdry@sina.com

前言

术后认知功能障碍(Postoperative Cognitive Dysfunction, POCD)是麻醉手术后常见的中枢神经系统并发症,多见于老年患者,主要表现为精神错乱、焦虑、人格改变以及记忆受损,社交能力及认知

能力减退,严重影响患者术后康复^[1]。髌部骨折多见于高龄老年患者,常合并多种基础疾病,机体代偿能力差,在手术、麻醉等多种因素作用下,更易发生POCD。国外最新一项Meta分析发现,髌部骨折的老年患者有14.8%在术前就发生了认知功能减退,而术后发生率则高达55.5%^[2]。有报道证实电针刺激治疗能够有效预防和治疗老年患者全麻腹部手术后POCD^[3]。经皮穴位电针刺激是一种改良的无创电刺激穴位治疗方法,它将经皮电神经刺激疗法与针灸穴位相结合,通过皮肤将特定的低频脉冲电流输入人体内,具有与电针相似的效应。本次研究旨在研究经皮穴位电针刺激对高龄患者髌部骨折术后认知功能的影响及其可能机制。

1 资料与方法

1.1 研究对象

2017年6月至2017年12月在广东省人民医院拟接受矫形手术的80岁以上髌部骨折患者40例,排除标准:(1)中枢神经系统合并症,如脑血管疾病、老年性痴呆;(2)凝血功能障碍;(3)精神疾病,如抑郁症等;(4)医患交流困难,无法配合完成认知功能测定;(5)拟刺激穴位局部皮肤感染。研究已获本院伦理委员会批准,并与患者签署知情同意书。按入组先后顺序编号,采用随机数字表法将40例患者随机分为对照组(A组)电刺激组(B组)。

1.2 麻醉方法

两组患者均采用腰-硬联合麻醉:术前6 h禁食,2 h禁饮;监测心电图、血氧饱和度、心率、血压;开放外周静脉通路,以6 mL/(kg·h)输入醋酸林格式液;消毒铺巾后行腰L₃₋₄椎间隙硬膜外穿刺,穿刺成功后置入25G腰穿针,见清亮脑脊液流出后鞘内缓慢匀速注入0.5%布比卡因1.0~1.5 mL,退出腰穿针,向头端置入硬膜外导管3 cm;控制麻醉平面在T10。术中给予右美托咪定0.2 μg/(kg·h)辅助镇静并行持续脑电Nacrotrend监测;术中积极纠正贫血,出室时HB>100 g/L;维持血流动力学稳定,通过适当输液和血管活性药物控制血压波动范围在术前基础值

的20%以内。术后两组患者均使用单次硬膜外腔吗啡1 mg+0.1%布比卡因5 mL镇痛。

B组患者术前2 d开始,选取百会穴和风池穴,行经皮穴位电针刺激,3次/d,30 min/次,直至术前晚;麻醉操作完成后行穴位持续刺激至手术结束。经皮穴位刺激仪器采用LH402韩式2/100 Hz的疏密波,刺激强度从1 mA开始,逐步加大电流强度以患者能耐受的最大电流为适度(8~10 mA之间调节)。A组患者仅在相应穴位贴电极未行电刺激。

1.3 疗效观察

由参加过培训但不了解试验分组情况的医师运用简易智能量表(MMSE)于入院时、术后24 h、术后72 h 3个时点对患者进行认知功能评定,并根据患者术后24 h、术后72 h的MMSE评分与首次评分比较,若降低一个标准差或以上者即为认知功能下降,认定发生了POCD;所有患者在入院时、术毕即刻、术后24 h和术后72 h抽取静脉血,用酶联免疫吸附法(ELISA)测定血清IL-6、IL-10和S100β蛋白水平。采用美国Uscn Life公司提供的试剂盒,严格按照说明书进行操作。

1.4 统计学处理

应用SPSS 17.0统计软件进行分析,计量资料以均数±标准差表示,组间比较采用独立样本 t 检验,自身治疗前后比较采用配对 t 检验,组间不同时间点的比较采用重复测量方差分析,计数资料以率表示,比较采用 χ^2 检验。 $P<0.05$ 为差异有统计学意义。

2 结果

2.1 基本情况比较

两组患者一般资料和手术时间、麻醉时间、术中出血量、输血量比较差异无统计学意义($P>0.05$),见表1和表2。

2.2 MMSE评分和POCD发生率比较

两组患者术后24 h和术后72 h MMSE评分较入院时均有所降低,差异有统计学意义($P<0.05$,表3);B组术后24 h和术后72 h POCD发生率明显低于A组,差异有统计学意义($P<0.05$,表3)。

表1 两组一般资料比较($n=20$, $\bar{x}\pm s$)

Tab.1 Comparison of general characteristics in two groups ($n=20$, $Mean\pm SD$)

Group	Age/years	ASA (I/II)	Weight/kg	Gender (Male/Female)	Education (Primary/Junior/Senior)
A	85.8±4.2	5/15	58.2±6.2	8/12	10/6/4
B	86.3±4.4	7/13	57.7±7.1	7/13	12/5/3

Group A: Control group; Group B: Electrical stimulation group

表2 两组手术过程相关指标比较($n=20$, $\bar{x} \pm s$)Tab.2 Comparison of intraoperative data in two groups ($n=20$, $Mean \pm SD$)

Group	Duration of operation/min	Blood loss/mL	Fluid/mL	HB/g · L ⁻¹
A	114.7±23.2	237.2±35.8	874.7±227.5	112.7±18.3
B	108.3±22.4	230.5±42.1	866.2±250.8	119.4±13.3

表3 两组术后认知功能比较($n=20$, $\bar{x} \pm s$)Tab.3 Comparison of cognitive function after operation in two groups ($n=20$, $Mean \pm SD$)

Group	MMSE score			POCD [cases(%)]	
	Before operation	24 h after finishing operation	72 h after finishing operation	24 h after finishing operation	72 h after finishing operation
A	28.6±1.9	20.8±5.7*	22.6±3.2*	13(65)	12(60)
B	28.2±1.8	24.3±3.5* [#]	25.3±2.3* [#]	7(35) [#]	5(25) [#]
t/χ^2 value	0.585	2.431	2.273	4.563	4.821
P value	0.352	0.021	0.028	0.032	0.029

MMSE: Mini-mental state examination; POCD: Postoperative cognitive dysfunction; Compared with before operation, * $P<0.05$; Compared with Group A, [#] $P<0.05$

2.3 围术期血清炎症因子比较

术毕两组患者血清IL-6、IL-10和S100β蛋白水平较组内其余各时段均显著升高,差异有统计学意义($P<0.05$,表4);B组术后各时间点血清IL-6、IL-10和S100β蛋白水平均显著低于A组同时时间点($P<0.05$,表4)。

表4 两组围术期血清炎症因子比较($n=20$, $\bar{x} \pm s$)Tab.4 Comparison of perioperative serum inflammatory factors in two groups ($n=20$, $Mean \pm SD$)

Group	S100β	IL-6	IL-10
A			
Admission	62.2±15.3 ^a	11.8±6.7 ^a	4.9±1.8 ^a
End of operation	135.6±39.1	231.3±66.8	22.3±6.3
24 h after finishing operation	117.5±27.9 ^a	38.5±9.7 ^a	9.9±3.7 ^a
72 h after finishing operation	85.2±18.2 ^a	17.8±5.9 ^a	7.1±3.5 ^a
B			
Admission	61.8±16.1 ^a	12.3±7.2 ^a	4.7±1.9 ^a
End of operation	103.4±30.5 ^b	127.5±38.1 ^b	11.8±4.7 ^b
24 h after finishing operation	88.2±22.8 ^{ab}	25.7±6.2 ^{ab}	5.7±3.3 ^{ab}
72 h after finishing operation	68.6±16.9 ^{ab}	13.2±4.1 ^{ab}	4.5±2.1 ^{ab}

Intra-group comparison between admission and other time points, ^a $P<0.05$; Compared with group A at the same time point, ^b $P<0.05$

3 讨论

我国传统医学尤其是针灸技术在改善认知功能方面具有一定的作用。POCD属于中医的“健忘”、“痴呆”等范畴,此病病位在脑,故治法应立足于通络启闭、醒神开窍。因此历代医家素有“病变在脑,首取督脉”之说。百会为督脉之要穴,是诸阳之会,具有开窍启闭、推动督脉气血运行、改善脑部缺血之功。风池穴为足少阳阳维之会,具有壮阳益气、安神醒脑之功。针刺百会、风池穴可改善脑的低灌注与脑代谢功能,减轻炎症反应,使脑神经细胞机能再恢复而增强学习记忆功能^[4]。

动物实验发现,电针对老年痴呆大鼠的认知功能有明显改善作用^[5-6];电针预处理可以有效改善脑损伤后的缺血再灌注损伤,提高神经预后功能^[7]。临床研究也证实电针对认知的治疗作用^[8]。进一步的研究发现电针穴位刺激改善认知的可能途径:(1)阿尔茨海默病的认知功能减退一定程度上与海马、杏仁核、后扣带回皮质等脑区对葡萄糖摄取能力下降有关;电针刺激百会穴可增加相关区域葡萄糖转运蛋白的表达而改善能量代谢^[9]。(2)海马胆碱能神经功能减退是阿尔茨海默病的重要病理改善改变,而电针刺激可以增加海马7-nAChR的表达而改善胆碱能神经功能^[10]。(3)创伤疼痛是老年认知功能减退的重要诱因,电针刺激可调节内源性的阿片通路,减轻痛觉过敏^[11]。

多数临床研究均采用3次/周、连续4周的百会穴电刺激,提示在治疗有明显中枢神经病理改变的认知疾病时,足够的疗程是非常关键的^[12-13]。多数POCD初期大脑并无新发的器质性病变,因此我们推测两者的疗程设计应有所不同。我们在前期预实验中发现,在麻醉前30 min直至手术结束这段时间给予经皮穴位电针刺激,多例患者术后当天的认知功能仍出现了明显下降;鉴于髋部骨折创伤巨大,部分老年患者骨折伊始就出现了认知减退,因此我们将穴位电针刺激提前至术前2 d,3次/d,30 min/次;手术当日自麻醉操作完成后持续刺激至手术结束。本研究中两组患者MMSE评分术后72 h较入院时有所降低,但B组评分高于A组,证明经皮穴位电针刺激可以降低高龄髋部骨折患者术后POCD的发生。

POCD在发病机制、危险因素及流行病学等方面尚存在很多争议,全麻药物是可能原因之一,如安定类药物、吸入麻醉药等。因此本研究中两组患者均采用椎管内麻醉,从而可以减少干扰因素,更准确地评价电针刺激的效果。现阶段可以肯定的是,POCD与患者机体老化、手术创伤等有较明确的关系,而神经内分泌和免疫系统紊乱可能发挥了重要作用^[14];手术创伤应激因素引起大量促炎细胞因子释放、促使部分神经细胞凋亡、对已存在和新形成空间记忆功能的长期损坏作用^[15-16];临床研究表明炎性细胞因子的大量表达可通过多种途径影响突触可塑性,损坏学习和记忆等认知功能^[17]。POCD患者外周IL-6水平明显升高,推测IL-6参与损坏突触可塑性,进而导致患者认知功能下降^[18]。本研究中两组患者血清IL-6水平在术毕、术后24、72 h均高于组内入院时,证实手术创伤、麻醉等应激可产生强烈的外周炎性反应,促使IL-6等炎性细胞因子大量产生,继而激活小胶质细胞引起中枢神经系统过度扩大的炎性反应^[17]。薛红等^[19]研究发现电针对血浆IL-10和IL-6具有双向调节作用。IL-6主要由单核巨噬细胞产生,是创伤急性期的关键促炎因子;IL-10主要由激活的T细胞、B细胞及单核细胞生产,是体内重要的抗炎性细胞因子。IL-6的变化可反映手术刺激及损伤的程度,而IL-10可以抑制炎性细胞因子IL-6的释放,起到抗炎作用。本研究中B组术毕、术后24 h和术后72 h的血清IL-6和IL-10水平显著低于A组,提示电针干预可有效地抑制促炎因子IL-6和IL-10的上调,从而调节患者机体的免疫抑制状态,使机体失衡的免疫功能趋向正常。S100 β 蛋白主要存在于星状细胞和雪旺细胞,作为神经胶质的标记蛋白,是脑特异性蛋白。高浓度的S100 β 蛋白对神经元具有毒性作

用,且与POCD密切相关。血清S100 β 蛋白含量可作为评价POCD的发病率、病程及结果的重要指标^[20]。本研究中两组患者血清S100 β 蛋白水平在术毕和术后24 h显著升高,B组各时点的S100 β 蛋白水平均显著低于A组同时点,差异有统计学意义,提示电针干预可降低S100 β 蛋白水平。

综上所述,经皮穴位电针刺激可以降低高龄老年患者髋关节置换术后POCD的发生,推测其原因可能是穴位电针刺激能抑制手术中炎性因子的反应水平,如减少IL-6释放、抑制S100 β 蛋白的过度表达,进而减轻中枢神经元的炎症损伤,使机体失衡的免疫功能趋向正常,有效降低患者POCD的发生率。由于脑脊液炎性细胞因子水平更能反映中枢炎症反应的程度,因此下一步研究收集脑脊液标本进行分析可能更具有意义。

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