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经皮穴位电刺激联合全身麻醉对腹腔镜结直肠癌根治术患者炎性因子、T细胞亚群和认知功能的影响*

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摘要目的:探讨经皮穴位电刺激(TEAS)联合全身麻醉对腹腔镜结直肠癌根治术患者炎性因子、T细胞亚群和认知功能的影响。
方法:选取2018年6月~2019年9月期间我院收治的行腹腔镜结直肠癌根治术患者90例,根据随机数字表法分为对照组(n=45)和研究组(n=45),对照组给予全身麻醉处理,研究组在对照组的基础上联合TEAS,比较两组患者炎性因子、T细胞亚群、认知功能及疼痛情况。
结果:研究组术后1d、术后5d白介素-6(IL-6)、白介素-1(IL-1)和肿瘤坏死因子-α(TNF-α)低于对照组($P<0.05$)。研究组术后1d、术后5d CD3⁺、CD4⁺/CD8⁺、CD4⁺高于对照组,CD8⁺则低于对照组($P<0.05$)。研究组术后1d、术后3d、术后5d、术后7d简易智力状态检查表(MMSE)评分高于对照组($P<0.05$)。研究组术后6h、术后12h、术后24h、术后48h视觉模拟评分法(VAS)评分低于对照组($P<0.05$)。两组术后5d、术后7d认知功能障碍(POCD)发生率比较差异无统计学意义($P>0.05$);研究组术后1d、术后3d POCD发生率低于对照组($P<0.05$)。
结论:TEAS联合全身麻醉治疗腹腔镜结直肠癌根治术患者,可降低炎性反应,减轻免疫抑制,同时还可降低对机体认知功能的损害。

关键词:经皮穴位电刺激;全身麻醉;腹腔镜结直肠癌根治术;炎性因子;T细胞亚群;认知功能

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Effects of Transcutaneous Acupoint Electrical Stimulation Combined with General Anesthesia on Inflammatory Factors, T Cell Subsets and Cognitive Function in Patients Undergoing Laparoscopic Radical Resection of Colorectal Cancer*

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ABSTRACT Objective: To investigate the effect of transcutaneous acupoint electrical stimulation (TEAS) combined with general anesthesia on inflammatory factors, T cell subsets and cognitive function in patients undergoing laparoscopic radical resection of colorectal cancer. **Methods:** 90 patients who underwent laparoscopic colorectal cancer radical surgery in our hospital were selected from June 2018 to September 2019, they were divided into control group (n=45) and study group (n=45) according to the random number table method. The control group was given general anesthesia. The study group combined with TEAS on the basis of the control group. Inflammatory factors, T cell subsets, cognitive function and pain were compared between the two groups. **Results:** The levels of interleukin-6 (IL-6), interleukin-1 (IL-1), tumor necrosis factor-α (TNF-α) in the study group at 1 d after operation, 5 d after operation were lower than those in the control group ($P<0.05$). CD3⁺, CD4⁺/CD8⁺ and CD4⁺ in the study group were higher than those in the control group at 1d after operation, 5d after operation, while CD8⁺ was lower than that in the control group ($P<0.05$). The scores of simple mental state Checklist (MMSE) in the study group were higher than those in the control group at 1d after operation, 3 d after operation, 4 d after operation, 7d after operation ($P<0.05$). The visual analogue scale (VAS) score of the study group was lower than that of the control group at 6 h after operation, 12 h after operation, 24 h after operation, 48 h after operation ($P<0.05$). There was no significant difference in the incidence of cognitive impairment (POCD) between the two groups on the 5th and 7th postoperative days ($P>0.05$); the incidence of POCD in the study group at 5d after operation, 7d after operation was lower than that in the control group ($P<0.05$). **Conclusion:** TEAS combined with general anesthesia can reduce inflammatory response, immune suppression and cognitive impairment in patients undergoing laparoscopic colorectal cancer radical resection.

Key words: Transcutaneous acupoint electrical stimulation; General anesthesia; Laparoscopic radical resection of colorectal cancer;

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前言

结直肠癌是我国常见的恶性肿瘤之一,近年来随着人们生活方式的改变及饮食结构的变化,其发病率呈逐年递增趋势^[1,2]。腹腔镜结直肠癌根治术是治疗结直肠癌的有效方案,其术后五年生存率在50%至70%之间^[3,4]。然而此类手术麻醉方法、术中CO₂气腹以及手术创伤等,易发生机体内环境紊乱,细菌和内毒素能穿越损伤的肠黏膜进入患者的组织和血液中,产生强烈的应激反应,影响患者术后恢复,甚至造成其术后免疫功能抑制、认知功能障碍(POCD)等,影响手术疗效^[5-7]。近年来加速康复外科(ERAS)主张使用多重方式进行术中麻醉的管理和术后镇痛以减轻应激和疼痛等围术期不良反应,以加速术后康复^[8]。经皮穴位电刺激(TEAS)是一种传统针灸穴位疗法与经皮神经电刺激结合的新型针灸治疗方法,具有镇静、镇痛、维持内环境稳定等作用,应用于全身麻醉不同阶段,发挥着减少麻醉药的用量、降低炎性反应、调节免疫功能、改善患者预后等作用^[9]。鉴于此本研究通过对部分我院收治的行腹腔镜结直肠癌根治术患者给予TEAS联合全身麻醉,观察其对于炎性因子、免疫功能及认知功能的影响,报道如下。

1 资料与方法

1.1 一般资料

选取2018年6月~2019年9月期间我院收治的行腹腔镜结直肠癌根治术患者90例为研究对象,本研究已获得医院伦理学委员会批准并经患者或授权人签署知情同意书。纳入标准:(1)均经实验室检查、组织病理结果确诊为结直肠癌,符合手术指征,择期行腹腔镜结直肠癌根治术者;(2)美国麻醉医师协会(ASA)分级I或II级者;(3)对本次研究用药无禁忌者;(4)既往无经穴循行部位神经损伤、手术史者。排除标准:(1)伴有自身免疫缺陷疾病者;(2)近3个月参加其他临床试验者;(3)合并其他恶性肿瘤者;(4)术中、术后出现重大并发症者;(5)经穴局部有皮肤感染者;(6)合并精神疾患,无法正常沟通交流者。上述患者根据随机数字表法分为研究组(n=45)、对照组(n=45),其中对照组女20例,男25例,ASA分级I级24例,II级21例;年龄38~67岁,平均(49.82±4.19)岁;体质指数21.5~26.4kg/m²,平均(23.84±0.76)kg/m²。研究组男23例,女22例,ASA分级I级26例,II级19例;年龄37~68岁,平均(50.17±4.82)岁;体质指数21.2~26.1kg/m²,平均(23.96±0.83)kg/m²。两组一般资料比较无差异($P>0.05$)。

1.2 方法

两组均给予全身麻醉,术前常规禁饮禁食,入室后开放静脉通道,常规监测患者心电图、动脉血压、脉搏氧饱和度、麻醉深度等,麻醉诱导:依次静脉注射咪达唑仑(国药准字H20031037,江苏恩华药业股份有限公司,规格:5mL:5mg)0.05mg/kg,舒芬太尼(国药准字H20054172,宜昌人福药业有限责任公司,规格:按舒芬太尼计1mL:50μg)0.5μg/kg,丙泊

酚(国药准字H20133360,广东嘉博制药有限公司,规格:20mL:200mg)1.5~2.0mg/kg,维库溴铵(国药准字H20065437,山西振东泰盛制药有限公司,规格:4mg)0.1mg/kg,麻醉诱导成功后气管插管,行机械通气。麻醉维持:术中吸入1.0%的七氟烷(国药准字H20173156,河北一品制药股份有限公司,规格:250mL),静脉输注丙泊酚3~6mg/kg·h、瑞芬太尼(国药准字H20143315,江苏恩华药业股份有限公司,规格:以瑞芬太尼计2mg)3~10μg/kg·h,维持麻醉深度(Narcotrend监测)45~60之间,间断注射维库溴铵2mg维持肌松满意。手术结束前5min,给予舒芬太尼0.1μg/kg,停用所有麻醉药。研究组患者于术前半小时由专人负责TEAS操作,经皮肤消毒后,采用北京产LH-202型韩式穴位神经刺激仪,取电极片贴于双侧合谷、足三里、内关穴,刺激强度为2~3mA,疏密波设置为2/15Hz,以患者舒适为度,诱导30min,持续至手术结束。

1.3 观察指标

于术前、术后1d、术后5d采集患者肘静脉血4mL,离心半径13cm,3100r/min离心9min分离血清,取上清液置于-30℃冰箱中待测。选用深圳晶美生物科技有限公司试剂盒,采用酶联免疫吸附实验检测白介素-6(IL-6)、白介素-1(IL-1)和肿瘤坏死因子-α(TNF-α)水平。采用美国贝克曼公司生产的CX9大型全自动生化分析仪检测T淋巴细胞亚群:CD3⁺、CD4⁺、CD8⁺,计算CD4^{+/}CD8⁺。记录两组患者术后6h、术后12h、术后24h、术后48h、术后72h的视觉模拟评分法(VAS)^[10]评分,VAS总分0~10分,分数越高,疼痛感越强。于术前、术后1d、术后3d、术后5d、术后7d采用简易智力状态检查表(MMSE)^[10]评分,评估患者认知功能状况。MMSE评分主要包括语言即刻回忆、计算能力、注意力、定向力、短期回顾和复制图形的能力,最高分值为30分,分数越高,认知功能越好。统计两组患者术后POCD发生率,其中MMSE评分<27分即表示发生POCD。

1.4 统计学方法

采用SPSS 24.0统计学软件进行统计学分析。计数资料以[n(%)]表示,实施卡方检验,计量资料以均值±标准差表示,实施t检验,检验标准设置为 $\alpha=0.05$ 。

2 结果

2.1 两组炎性因子指标比较

两组术前IL-6、IL-1、TNF-α比较差异无统计学意义($P>0.05$);两组术前~术后5dIL-6、IL-1、TNF-α呈先升高后下降趋势($P<0.05$);研究组术后1d、术后5dIL-6、IL-1、TNF-α低于对照组($P<0.05$);详见表1。

2.2 两组T淋巴细胞亚群比较

两组患者术前CD3⁺、CD4^{+/}CD8⁺、CD4⁺、CD8⁺比较差异无统计学意义($P>0.05$);两组患者术前~术后5dCD3⁺、CD4^{+/}CD8⁺、CD4⁺呈先降低后升高趋势,CD8⁺呈先升高后降低趋势($P<0.05$);研究组术后1d、术后5dCD3⁺、CD4^{+/}CD8⁺、

表 1 两组炎性因子指标比较($\bar{x} \pm s$)Table 1 Comparison of inflammatory factors between the two groups($\bar{x} \pm s$)

Groups	Time	IL-6(pg/mL)	IL-1(ng/mL)	TNF- α (pg/mL)
Control group(n=45)	Before operation	53.25±6.19	1.20±0.27	19.73±1.65
	1d after operation	93.92±6.41 ^a	2.69±0.23 ^a	37.54±2.53 ^a
	5d after operation	72.37±7.83 ^{ab}	2.08±0.24 ^{ab}	29.27±2.27 ^{ab}
Study group(n=45)	Before operation	54.27±6.14	1.27±0.20	19.87±1.25
	1d after operation	82.01±8.63 ^{ac}	1.94±0.18 ^{ac}	30.42±1.63 ^{ac}
	5d after operation	61.97±7.31 ^{abc}	1.55±0.13 ^{abc}	24.37±1.26 ^{abc}

Note: compared with before operation, ^a $P<0.05$; compared with 1d after operation, ^b $P<0.05$; compared with control group, ^c $P<0.05$.

表 2 两组 T 淋巴细胞亚群比较($\bar{x} \pm s$)Table 2 Comparison of T lymphocyte subsets between the two groups($\bar{x} \pm s$)

Groups	Time	CD3 ⁺ (%)	CD4 ⁺ (%)	CD8 ⁺ (%)	CD4 ⁺ /CD8 ⁺
Control group(n=45)	Before operation	51.23±5.47	35.34±3.92	27.65±2.48	1.28±0.19
	1d after operation	40.59±4.59 ^a	25.24±3.17 ^a	36.87±3.62 ^a	0.68±0.12 ^a
	5d after operation	45.53±4.38 ^{ab}	29.38±3.69 ^{ab}	32.50±2.35 ^{ab}	0.90±0.17 ^{ab}
Study group(n=45)	Before operation	51.48±5.42	35.49±3.31	27.39±3.28	1.30±0.21
	1d after operation	45.81±5.32 ^{ac}	30.94±3.50 ^{ac}	32.88±2.46 ^{ac}	0.94±0.23 ^{ac}
	5d after operation	50.85±4.63 ^c	34.86±4.91 ^c	28.24±3.53 ^c	1.23±0.24 ^c

Note: compared with before operation, ^a $P<0.05$; compared with 1d after operation, ^b $P<0.05$; compared with control group, ^c $P<0.05$.

CD4⁺ 高于对照组, CD8⁺ 则低于对照组($P<0.05$);详见表 2。

2.3 两组 MMSE 评分比较

两组患者术前 MMSE 评分比较差异无统计学意义($P>0.05$)。

05); 两组患者术前~术后 7 d MMSE 评分呈先降低后升高趋

势($P<0.05$);但研究组术后 1 d、术后 3 d、术后 5 d、术后 7 d MMSE 评分高于对照组($P<0.05$);详见表 3。

表 3 两组 MMSE 评分比较($\bar{x} \pm s$, 分)Table 3 MMSE score comparison between the two groups($\bar{x} \pm s$, score)

Groups	Before operation	1d after operation	3d after operation	5d after operation	7d after operation
Control group(n=45)	29.21±0.25	26.56±0.28 ^a	27.93±0.29 ^{ab}	28.29±0.27 ^{abc}	28.83±0.24 ^{abcd}
Study group(n=45)	29.27±0.22	27.61±0.25 ^a	28.25±0.25 ^{ab}	28.63±0.29 ^{abc}	29.19±0.21 ^{bcd}
t	1.209	18.765	5.606	5.756	7.573
P	0.230	0.000	0.000	0.000	0.000

Note: compared with before operation, ^a $P<0.05$; compared with 1d after operation, ^b $P<0.05$; compared with 3d after operation, ^c $P<0.05$; compared with 5d after operation, ^d $P<0.05$.

2.4 两组 VAS 评分比较

两组术后 6 h~术后 72 h VAS 评分呈持续下降趋势($P<0.05$);研究组术后 6 h、术后 12 h、术后 24 h、术后 48 h VAS 评分

低于对照组 ($P<0.05$); 两组术后 72 h VAS 评分比较无差异

($P>0.05$);详见表 4。

表 4 两组 VAS 评分比较($\bar{x} \pm s$, 分)Table 4 Comparison of VAS scores between two groups($\bar{x} \pm s$, score)

Groups	6h after operation	12h after operation	24h after operation	48h after operation	72h after operation
Control group(n=45)	5.59±0.21	5.02±0.23 ^a	4.19±0.22 ^{ab}	2.44±0.29 ^{abc}	1.28±0.23 ^{abcd}
Study group(n=45)	4.73±0.25	4.27±0.26 ^a	3.38±0.21 ^{ab}	1.89±0.23 ^{abc}	1.21±0.19 ^{abcd}
t	17.670	14.494	17.866	9.968	1.574
P	0.000	0.000	0.000	0.000	0.119

Note: compared with 6h after operation, ^a $P<0.05$; compared with 12h after operation, ^b $P<0.05$; compared with 24h after operation, ^c $P<0.05$; compared with 48h after operation, ^d $P<0.05$.

2.5 两组POCD发生率比较

两组术后5 d、术后7 d POCD发生率比较差异无统计学意

义($P>0.05$);研究组术后1 d、术后3 d POCD发生率低于对照组($P<0.05$);详见表5。

表5 两组POCD发生率比较【例(%)】

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

Groups	1d after operation	3d after operation	5d after operation	7d after operation
Control group(n=45)	30(66.67)	23(51.11)	12(26.67)	4(8.89)
Study group(n=45)	18(40.00)	12(26.67)	6(13.33)	2(4.44)
χ^2	6.429	5.657	2.500	0.714
P	0.011	0.017	0.114	0.398

3 讨论

腹腔镜手术作为一种新型的微创手术，因其手术创伤小、术后恢复快等诸多特点而被广大外科医师所使用^[11,12]。随着结直肠癌检出率的不断升高，腹腔镜结直肠癌根治术的应用率也逐年递增。但多数结直肠癌患者本身生理条件较差，存在免疫功能低下的情况，手术又在二氧化碳气腹下完成操作，致使其产生不同程度的应激反应，增加全麻苏醒期风险，影响患者预后^[13,14]。此外，手术中若未能给予良好的麻醉环境，可引起患者中枢神经系统暂时性障碍，引发POCD^[15]。据统计^[16]，POCD在老年结直肠癌术后1周内的发病率为11.1%~68.9%。此类术后并发症不仅延长患者的住院时间及医疗费用，还可对患者出院后生活质量造成影响。全身麻醉是腹腔镜结直肠癌根治术患者常用的麻醉方式，但近年来不少临床实践表明，全身麻醉无法彻底阻止手术区域带来的应激传导，镇痛效果有待加强^[17,18]。既往研究结果及实验发现，针刺麻醉有一定的镇痛效果，且对患者内分泌、神经及免疫功能均有一定的调节作用^[19,20]。TEAS是针刺镇痛的方法之一，治疗范围涉及临床各科，疗效均得到了肯定。

本次研究结果显示，研究组术后6 h、术后12 h、术后24 h、术后48 h的VAS评分低于对照组，可见相比于单纯的全身麻醉，TEAS联合全身麻醉可获得更好的术后镇痛效果。TEAS本身即具有较好的止痛效果，加上联合全身麻醉还可减少麻醉药物的使用量，进而减轻其相应的副作用^[21]。此外，两组患者术后均有不同程度的炎性应激，免疫功能下降现象，但TEAS联合全身麻醉产生的炎性应激更轻，对机体免疫功能影响更小。究其原因，TEAS治疗中选取穴位为合谷、足三里、内关穴，其中合谷穴是手阳明大肠经之原穴，有通经活络、镇静止痛、解表泄热的作用；内关穴为手厥阴经之络穴，八脉交会穴，可以宽胸利膈、宁心安神、疏肝理脾、止痛之功效；足三里穴是“足阳明胃经”的主要穴位之一，有行气活血、和胃健脾、理气止痛、平衡阴阳的功效^[21-23]。TEAS通过穴位对机体的双向调节作用而发挥器官组织保护作用，减少应激反应，进一步减轻机体免疫抑制^[24,25]。由于在腹腔镜直肠癌切除手术过程中，体位和二氧化碳气腹对患者脑氧含量及脑血流有明显影响，可导致短暂性的脑组织氧供需失衡，进而对机体神经功能产生一定程度的不利影响^[26,27]。本研究中TEAS联合全身麻醉治疗者术后认知功能的损害程度更轻。现代医学临床实践证实^[28,29]：针刺足三里穴可激活大脑颞叶为主的大部分区域，进而改善认知功能障碍、运动

感觉障碍等；针刺内关穴可增强脑血流量，改善脑代谢功能，增强学习记忆功能。同时，TEAS还可通过降低围术期应激反应来降低脑组织氧、糖代谢，发挥脑保护作用^[30]。本次研究尚存在以下不足：纳入样本量偏少，观察时间仅维持在术后1周内，未能对患者远期预后进行考察。今后将通过采取多中心扩大样本量研究、增加随访时间的措施进行研究，以期获取更为精确的结果。

综上所述，TEAS联合全身麻醉治疗腹腔镜结直肠癌根治术患者，可降低炎性反应，减轻免疫抑制，同时还可降低对机体认知功能的损害。

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