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经皮电穴位电刺激足三里穴对胃癌患者术后血清 IgG、IgM 水平的影响 *

郭 键 王 凯 翟 茜 刘 瞰 王 强[△]

(第四军医大学西京医院麻醉科 陕西 西安 710032)

摘要 目的:观察经皮穴位电刺激对胃癌根治术患者术后血清免疫球蛋白 M(IgM)、免疫球蛋白 G(IgG)水平的影响。**方法:**选择全麻择期行胃癌根治术的患者 102 例(男 88 例,女 14 例),年龄 40~75 岁,将其随机分为经皮穴位电刺激组、假电刺激组和对照组。经皮电刺激双侧"足三里"(ST 36)、"三阴交"(SP 6)穴,于手术当日、术后第 1 日和术后第 2 日进行经皮电刺激治疗。于术前 30 分钟、术后 24 h、术后 72 h 采集静脉血标本,测定免疫球蛋白 G(Immunoglobulin G, IgG)、免疫球蛋白 M(Immunoglobulin M, IgM)的水平。术后监测和记录肛门的排气时间。**结果:**在术后第 1 天,对照组外周血 IgG 水平显著低于术前 30 分钟($P<0.05$),TEAS 组外周血 IgM 水平显著高于术前 30 分钟($P<0.05$),TEAS 组外周血 IgG 和 IgM 水平显著高于对照组($P<0.05$)。在术后第 3 天,对照组外周血 IgG、IgM 水平显著低于术前 30 分钟($P<0.05$),TEAS 组外周血 IgG、IgM 水平均显著低于术后 1 天($P<0.05$)。三组患者术后肛门排气时间比较无统计学差异($P>0.05$)。**结论:**经皮穴位电刺激可以升高胃癌根治术患者术后 1 天降低的外周血 IgG 和 IgM 水平,减轻其术后免疫抑制。

关键词:经皮穴位电刺激;胃癌;免疫球蛋白 M;免疫球蛋白 G;肛门排气时间

中图分类号:R454.1;R735.2 **文献标识码:**A **文章编号:**1673-6273(2015)18-3406-04

Effect of Transcutaneous Electrical Acupoint Stimulation on the Postoperative Immunologic Function in Patients with Gastric Cancer Undergoing Radical Surgery*

GUO Jian, WANG Kai, ZHAI Qian, LIU Tun, WANG Qiang[△]

(Department of Anesthesiology, Xi Jing Hospital, the Fourth Military Medical University, Xi'an, Shaanxi, 710032, China)

ABSTRACT Objective: To observe the effect of TEAS (Transcutaneous Electrical Acupoint Stimulation, TEAS) on the postoperative Immunoglobulin M (IgM) and Immunoglobulin G (IgG) levels in patients with gastric cancer undergoing radical surgery. **Methods:** Totally 102 patients with gastric cancer undergoing elective radical surgery under general anesthesia were randomly assigned to three groups, control group, TEAS group and sham group. TEAS group receiving TEAS before general anesthesia induction, 1st day and 2nd day after surgery. TEAS was given through electrodes attached to zusanli(ST 36) and sanyinjiao(SP 6) acupoints. The time for TEAS was 30 min. Venous blood samples from all groups(control group, TEAS group and sham group) were collected before general anesthesia induction, 1st day and 3rd day after surgery. The peripheral blood IgG and IgM levels were measured. Anal exhaust time after surgery was also compared among the groups. **Results:** IgG levels in peripheral blood decreased significantly compared with those at 30 min before surgery and 1st day after surgery in the control group. It increased significantly compared with those at 30 min before surgery and 1st day after surgery in TEAS group. The peripheral blood IgG and IgM levels in TEAS groups increased significantly compared with that of control group at 1st day after surgery; IgG and IgM levels in peripheral blood decreased significantly compared with those at 30min before surgery and 2nd day after surgery in the control group. They also decreased significantly compared with those at 1st and 2nd day after surgery in the TEAS group. **Conclusion:** TEAS could increase the low peripheral blood IgG and IgM levels in patients with gastric cancer undergoing radical surgery on the 1st day after surgery. It partially reduced the postoperative immune suppression.

Key words: Transcutaneous electrical acupoint stimulation; Immunologic function; Anal exhaust time

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前言

免疫抑制是手术后常见的并发症,容易导致术后感染,同

时增加肿瘤免疫逃逸的风险。有大量文献报道了针刺具有免疫调节作用和促进肠蠕动的作用。本研究拟在围术期应用经皮穴位电刺激(Transcutaneous Electrical Acupoint Stimulation,

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作者简介:郭键(1981-),男,硕士研究生,主治医师,主要研究方向:脑保护,电话:15877673530, E-mail:249826424@qq.com

△ 通讯作者:王强,男,副教授,博士研究生导师, E-mail:wangqiang@fmmu.edu.cn

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TEAS) 以观察 TEAS 对胃癌患者术后免疫功能及肠蠕动功能恢复的影响。

1 资料与方法

1.1 病例选择及分组

选择 2014 年 7 月至 11 月在西京消化病医院消化外科住院, 拟行择期胃癌根治术患者 102 例, 年龄 40~75 岁, ASA I 级或 II 级, 术前无严重心脏病、中重度贫血、免疫系统疾病史, 近期末接受过免疫抑制剂治疗, 围术期未输血。所有受试者均签署知情同意书。将所有患者随机分为经皮穴位电刺激组 (TEAS group)、假经皮穴位电刺激组 (Sham group) 和对照组 (Control group), 每组 34 例。对照组不进行 TEAS 治疗, TEAS 组采用 SDZ-V 型电子针疗仪(江苏医疗器械公司), 从麻醉诱导前至切皮前行 TEAS 治疗, 术后连续 2 日行 TEAS 治疗, 每次治疗时间均为 30 min。穴位选择为双侧足三里穴和三阴交穴。电针刺激参数: 疏密波, 频率 2/15Hz, 刺激强度为受试者能耐受的最大程度。Sham TEAS 组刺激双侧足三里穴内侧和三阴交穴前侧旁开 2 cm 处的非穴位, 其余均同 TEAS 组。

1.2 麻醉过程

患者入室后开放外周静脉, 静脉注射咪达唑仑 0.05 mg/kg、芬太尼 3-5 μ g/kg、顺式阿曲库铵 0.2 mg/kg、异丙酚 1-2 mg/kg 诱导气管插管后行机械通气, 吸入 1.5%~2.5%七氟烷、持续泵注瑞芬太尼 0.1-0.2 μ g/kg·min, 间断静脉注射顺式阿曲库铵维持麻醉。术中静脉输注乳酸钠林格液 10~15 mL/kg·h, 术中根据需要输入羟乙基淀粉(万汶)。

1.3 术后镇痛

关腹时嘱外科医生用 0.375%左布比卡因 20 mL 行局部浸润麻醉。手术结束前静脉给予非甾体类抗炎镇痛药塞来昔布 1 mg, 镇痛泵配方: 舒芬太尼 200 μ g+ 地佐辛 5mg+ 托烷司琼 5 mg+0.9%氯化钠注射 93 mL, 共 100mL。设定参数: 0.8-1.2 mL/h, 锁定时间 15 min, 单次剂量为 0.2 mL。

1.4 测定指标

分别于术前 30 分钟、术后 24、72 小时抽取外周静脉血 2 mL。于 4℃ 冰箱冷藏, 于 2 h 内离心分离血清, 离心(3000 r/min) 10 min, 移液器提取上清液, 注入 2 mL 冰冻管内, 标号后保存于 -80℃ 冰箱, 有明显红细胞溶血的血清样本被剔除。待标本收集齐全后每组随机抽取 10 例患者血样标本由北京 BD 生物科技公司采用 BD LSR II 型高通量流式细胞仪测定血清 IgM、IgG 的水平。

1.5 统计学处理

采用 SPSS 19.0 统计学软件进行分析, 计量资料以均数 $\pm$ 标准差($\bar{x} \pm s$)表示, 组间比较采用成组 t 检验, 组内比较采用单因素方差分析, 以 $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 三组患者的一般临床特征比较

三组患者的年龄、性别、身高体重、手术时间、手术方式、术中输血量及失血量、麻醉药物用量比较差异均无统计学意义 ($P > 0.05$), 见表 1、2。

表 1 三组患者的一般临床特征及术中输血量、失血量的比较($\bar{x} \pm s$)

Table 1 Comparison of the baseline clinical characteristics and intraoperative transfusion volume, bleeding volume between three groups($\bar{x} \pm s$)

	Control group	TEAS group	Sham group
n	30	31	26
male/female	26/4	27/4	23/3
Age (year)	58 $\pm$ 7.8	54.6 $\pm$ 9	54 $\pm$ 7
Height(cm)	169 $\pm$ 6	169 $\pm$ 9	167 $\pm$ 8
Weight(kg)	62 $\pm$ 10	64 $\pm$ 11	61 $\pm$ 11
Part/Whole gastrectomy	8 $\pm$ 22	7 $\pm$ 24	6 $\pm$ 20
Operation time(h)	3.1 $\pm$ 1.1	3.1 $\pm$ 0.8	3.1 $\pm$ 0.9
Anesthesia time (h)	3.5 $\pm$ 1.1	3.6 $\pm$ 0.9	3.4 $\pm$ 0.9
Blood lost volume (mL)	200 $\pm$ 105	182 $\pm$ 130	146 $\pm$ 70
Urine amount (mL)	130 $\pm$ 91	150 $\pm$ 176	134 $\pm$ 99
Transfusion volume (mL)	2524 $\pm$ 526	2393 $\pm$ 639	2113 $\pm$ 515

2.2 三组患者各时间点 IgG 和 IgM 水平的比较

组内比较: Control 组外周血 IgG 水平在术后 1 天和术后 3 天显著低于术前 30 分钟, TEAS 组外周血 IgG 水平在术后 3 天显著低于术后 1 天, sham 组外周血 IgG 水平在各时间点无统计学差异 (见图 1); Control 组外周血 IgM 水平在术后第 3 天显著低于术前 30 分钟, TEAS 组外周血 IgM 水平在术后 1 天显著高于术前 30 分钟, 在术后 3 天显著低于术后 1 天, sham

组外周血 IgM 水平在各时间点无统计学差异 (见图 2)。

组间比较: TEAS 组外周血 IgG 和 IgM 水平在术后 1 天显著高于 Control 组, sham 组外周血 IgG 和 IgM 水平在各时间点与 Control 组和 TEAS 组比较无统计学差异 (见图 1、2)。

2.3 三组患者术后肛门排气时间的比较

如图 3 所示, 三组患者术后肛门排气时间比较无统计学差异 ($P > 0.05$)。

表 2 三组患者麻醉药物用量的比较($\bar{x} \pm s$)

Table 2 Comparison of the Dosages of Anesthesia Drug between three groups

	Control group	TEAS group	Sham group
n	30	31	26
Midazolam(mg)	1.07± 0.2	1.08± 0.3	1.04± 0.1
Fentanyl (mg)	0.21± 0.04	0.22± 0.05	0.22± 0.04
Propofol (mg)	102± 21	102± 29	108± 21
Cis-atracurium(mg)	26.9± 5.7	28± 3.9	24± 4.2

表 3 三组患者各时间点 IgG 和 IgM 水平的比较($\bar{x} \pm s$)

Table 3 Comparison of the serum IgG and IgM levels at different time points between three groups

	Time point	Control group	TEAS group	Sham group
n		10	10	10
IgG(mg/ml)	30 min before surgery	1.43± 0.21	1.43± 0.16	1.42± 0.12
	24h after surgery	1.31± 0.19 ^a	1.49± 0.23 ^{ac}	1.44± 0.14
	72h after surgery	1.31± 0.20 ^a	1.38± 0.18	1.37± 0.13
IgM(mg/ml)	30min before surgery	0.78± 0.44	0.96± 0.53	0.96± 0.36
	24h after surgery	0.72± 0.43	1.27± 0.53 ^{ac}	0.97± 0.46
	72h after surgery	0.63± 0.43 ^a	0.91± 0.48 ^a	0.80± 0.53

注:组内比较:a 与术前 30 min 比较差异有统计学意义,b 与术后 24 h 比较差异有统计学意义;组间比较:c 与对照组比较差异有统计学意义(P<0.05)。

Note: ^a compared with 30min before surgery, there was a significant difference within the group, ^b compared with 24 h after surgery, there was a significant difference within the group (P<0.05); ^c compared with control group, there was significant difference (P<0.05).

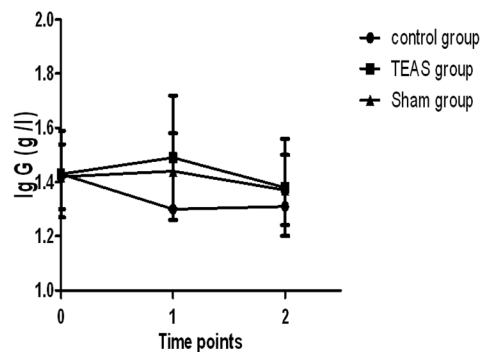


Fig.1 IgG Levels in three groups at three time points. T0: 30 min before surgery, T1: 24 h after surgery, T2: 72 h after surgery

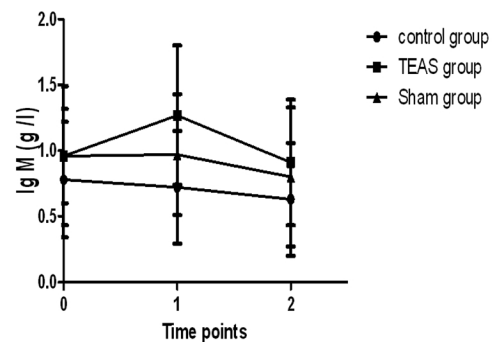


Fig.2 IgM Levels in three groups at three time points. T0: 30 min before surgery, T1: 24 h after surgery, T2: 72 h after surgery

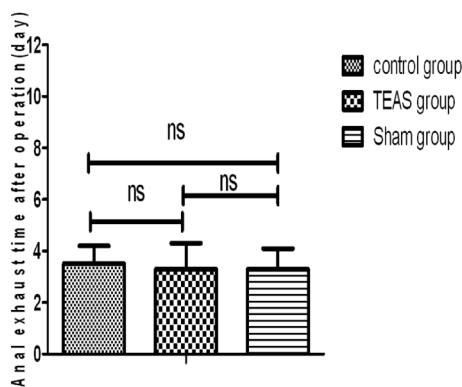


Fig. 3 Anal exhaust time after operation in three groups

有研究指出手术的应激和术后疼痛^[1]、麻醉药物^[2,3]、失血、输血^[4,5]和轻度低温^[6]等容易导致术后免疫抑制,不同的麻醉方法对免疫功能的影响也不相同^[7]。另外,肿瘤患者本身即有一定的免疫紊乱^[8,9]。免疫球蛋白是指具有抗体活性或化学结构上与抗体相似的球蛋白,IgG、IgM 是活化 B 淋巴细胞产生的主要免疫球蛋白,反映体液免疫状况^[10]。在本试验中,我们也发现手术后对照人群外周血 IgG 和 IgM 水平降低,说明手术对机体有一定的免疫抑制作用。

有大量文献报道针刺可以减轻手术后的免疫抑制。如隔日针刺合谷、曲池、足三里、三阴交、血海穴等,每次治疗 30 分钟,共治疗 1 个月,可以降低慢性荨麻疹病人增高的血清 IgE 水平^[11]。有学者观察了艾灸百会穴对顽固性面瘫的治疗作用以及其对免疫球蛋白的调节作用,结果发现顽固性面瘫与免疫球蛋白

3 讨论

的异常增加有关,每日艾灸百会穴 1 次,连续治疗 15 日,可以显著降低血清 IgA、IgG 和 IgM 抗体水平,从而起到治疗顽固性面瘫的作用^[12]。还有研究者报道,每隔 2 日(每周 3 次)针刺过敏性哮喘病人大椎、肺腧、风门穴 30 分钟,治疗五周后,可以降低其唾液 sIgA、总 IgA 以及血清 IgE 水平。此外,该研究者指出针刺可以辅助治疗过敏性哮喘,总有效率达 85%^[13]。赖敏等研究发现,电针"足三里"、"合谷"、"三阴交"对大鼠胃癌根治术后低下的 IgG、IgM、IgA、C3、C4 水平有明显的改善作用^[14]。还有研究者发现在幕上开颅术的患者,电针可以减轻手术所致的免疫球蛋白降低^[15]。而本研究结果显示围术期经皮穴位电刺激可以升高胃癌患者术后 1 日的外周血 IgG 和 IgM 水平,减轻手术所致的免疫抑制。

针刺调节免疫的确切机制尚不清楚。有文献报道神经-内分泌-免疫网络是针刺作用途径的一个重要组成部分。其中,神经系统起着主导作用,内分泌、免疫系统对其具有一定的调节作用^[16]。据文献报道电针刺激脊髓损伤大鼠能改善其免疫功能使 CD3、CD4、CD4/CD8(%) 升高,CD8 降低。脊髓损伤后大鼠血浆促肾上腺皮质激素和血清皮质醇较正常对照组明显升高,说明脊髓损伤后大鼠下丘脑-垂体-肾上腺 (Hypothalamic Pituitary Adrenal, HPA) 轴功能紊乱,电针刺激使脊髓损伤大鼠血浆促肾上腺皮质激素和血清皮质醇较阴性对照组明显降低,恢复 HPA 轴功能状态^[17]。还有文献报道长期剧烈运动应激导致 HPA 轴功能过度亢进、皮质醇持续高水平,从而引起神经内分泌紊乱、免疫功能抑制。而电针对长期高强度运动应激所致的机体免疫功能下降及 HPA 轴具有一定的良性调节作用^[18]。

目前,临床上普遍将腹部手术后第 1 次肛门排气作为术后肠道蠕动功能恢复的标志。肠道蠕动功能恢复延迟往往容易引起患者腹胀,严重的腹胀还会影响患者腹部切口和吻合口的愈合,不利于患者早期恢复。有研究者将 180 例接受腹部手术的患者随机分为电针组和对照组,电针组电针刺激患者双侧足三里穴,每次刺激时间 30 分钟,2 次/日,直至胃肠功能恢复为止,结果发现电针组患者术后肛门排气时间(45.2-3.1)h 短于对照组(59.7-4.20)h^[19]。本研究中,我们未发现围术期经皮穴位电刺激能够促进胃癌根治术患者术后肠道功能恢复,这和文献中报道的不一致。这可能与本试验在观察术后肛门排气时间以"日"作为测量单位有关。而文献中大多都是以小时作为术后肛门排气时间的测量单位^[19,20],这可能导致试验敏感度下降,因而没有阳性发现;也可能与我们电刺激治疗的疗程较短有关。此外,Teas 组和 Sham 组年龄的均值(54.6±9 岁和 54±7 岁)略低于 control 组年龄的均值(58±7.8 岁),尽管对照组、TEAS 组和 Sham 组间年龄的差异没有统计学意义,但这种差异也可能也会对本试验的结果产生一定的影响。

总之,本研究结果表明经皮穴位电刺激可以升高胃癌患者术后 1 天降低的外周血 IgG 和 IgM 水平,减轻其术后免疫抑制,其具体机制尚待进一步研究阐明。

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