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七氟烷与丙泊酚对腹腔镜直肠癌根治术患者认知功能、T 淋巴细胞及肝功能的影响 *

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摘要 目的:探讨七氟烷与丙泊酚对腹腔镜直肠癌根治术患者认知功能、T 淋巴细胞水平及肝功能指标的影响。**方法:**选择 2015 年 6 月 -2017 年 8 月期间于我院进行腹腔镜直肠癌根治术的 110 例患者为研究对象,按随机数字表法分为观察组和对照组,每组患者 55 例。观察组采用丙泊酚静脉全麻方式进行术前麻醉,对照组采用七氟烷吸入全麻方式进行术前麻醉。观察两组患者不同时间点平均动脉压(MAP)、心率(HR)情况,比较两组患者手术前后认知功能、T 淋巴细胞水平、肝功能各项指标及不良反应发生情况。**结果:**两组患者不同时间点 MAP、HR 组间比较差异无统计学意义($P>0.05$)。术后 6 h、12 h 观察组简易精神状态量表(MMSE)评分低于术前,术后 6 h、12 h、24 h 对照组 MMSE 评分低于术前和观察组($P<0.05$)。术后 3 d 两组患者 $CD3^+$ 、 $CD4^+$ 、 $CD4^+/CD8^+$ 水平均降低, $CD8^+$ 水平均升高,且观察组 $CD3^+$ 、 $CD4^+$ 、 $CD4^+/CD8^+$ 水平高于对照组, $CD8^+$ 水平低于对照组($P<0.05$)。术后 3 d 两组患者谷丙转氨酶(ALT)、谷草转氨酶(AST)、总胆红素(TBIL)、直接胆红素(DBIL)水平均升高,但观察组患者各项指标水平低于对照组($P<0.05$)。观察组不良反应发生率为 12.73%,与对照组的 7.27%比较差异无统计学意义($P>0.05$)。**结论:**七氟烷与丙泊酚在腹腔镜直肠癌根治术中的麻醉效果相当,无严重不良反应发生,但应用丙泊酚进行麻醉对患者术后的认知功能、T 淋巴细胞、肝功能指标的影响较小,值得临床推广应用。

关键词:七氟烷;丙泊酚;腹腔镜;直肠癌根治术;认知功能;T 淋巴细胞;肝功能

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Effects of Sevoflurane and Propofol on Cognitive Function, T Lymphocyte and Liver Function in Patients with Laparoscopic Radical Resection of Rectal Cancer*

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ABSTRACT Objective: To investigate the effects of sevoflurane and propofol on cognitive function, T lymphocyte level and liver function indexes in patients with laparoscopic radical resection of rectal cancer. **Methods:** 110 patients who were underwent laparoscopic radical resection of rectal cancer in our hospital from June 2015 to August 2017 were selected as research object, and they were randomly divided into the observation group and the control group according to the random number table method, 55 cases in each group. The observation group was anaesthetized by propofol intravenous general anesthesia, the control group was anaesthetized by sevoflurane inhalation general anesthesia. The average arterial pressure (MAP) and heart rate (HR) were observed at different time points in the two groups. The cognitive function, T lymphocyte levels, liver function indexes before and after operation and adverse reaction of the two groups were compared. **Results:** There was no significant difference in MAP and HR between the two groups at different time points($P>0.05$). The scores of mini-mental state examination (MMSE) at 6 h and 12 h after operation in the observation group were lower than those before operation, and the MMSE scores in the control group at 6 h, 12 h and 24 h after operation were lower than those before operation and in the observation group ($P<0.05$). The levels of $CD3^+$, $CD4^+$ and $CD4^+/CD8^+$ in two groups at 3d after operation were decreased, and the level of $CD8^+$ were increased, the levels of $CD3^+$, $CD4^+$ and $CD4^+/CD8^+$ in the observation group were higher than those in the control group, and the level of $CD8^+$ was lower than that in the control group ($P<0.05$). The levels of alanine aminotransferase (ALT), aspartate aminotransferase (AST), total bilirubin (TBIL), direct bilirubin (DBIL) of patients in two groups at 3 d after operation were increased, but the indexes levels of the patients in the observation group was lower than that of the control group ($P<0.05$). The incidence of adverse reactions in the observation group was 12.73%, and there was no significant difference compared with the 7.27% of the control group ($P>0.05$). **Conclusions:** The anesthetic effect of sevoflurane and propofol in laparoscopic radical resection of rectal cancer is the same,

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and there is no serious adverse reaction. However, the effect of propofol on the postoperative cognitive function, T lymphocyte and liver function indexes is less, which is worthy of clinical application.

Key words: Sevoflurane; Propofol; Laparoscope; Radical resection of rectal cancer; Cognitive function; T lymphocyte; Liver function

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前言

直肠癌是消化道系统常见的恶性肿瘤之一,易出现在直肠及乙状结肠的交界处,对患者的消化系统及全身功能均有着严重的威胁^[1-3]。直肠癌早期通常无明显症状易导致漏诊,当确诊时多处于中晚期,此时手术切除是最为有效的治疗方式^[4-6]。腹腔镜下直肠癌根治术由于手术创伤性小、术后恢复快、术后并发症发生率低,已成为直肠癌病灶切除的首选手术方法。而麻醉是外科手术必不可少的过程,近些年有临床报道显示,麻醉方式的不同及麻醉药物的选择对于手术的麻醉效果、患者术后的精神状态、免疫功能及肝功能等均有不同的影响,从而影响患者的手术效果及术后的康复情况^[7-9]。因此,对于麻醉过程中的药物种类、给药方式应慎重合理选择,使得手术能够更为顺利进行,从而获得更好的手术效果及预后。静脉全麻和吸入全麻是两种常用的手术麻醉方案,应用于各种外科手术中^[10-12]。为了进一步探讨不同麻醉药物及给药方式对于手术过程及术后患者各项指标的影响,本研究以腹腔镜直肠癌根治术患者为对

象,分别采用丙泊酚静脉全麻和七氟烷吸入全麻进行手术麻醉,以期腹腔镜直肠癌根治术麻醉方式的选择提供参考,现报道如下。

1 资料与方法

1.1 一般资料

选择我院于2015年6月至2017年8月期间110例行腹腔镜直肠癌根治术的患者为研究对象,纳入标准^[13]:(1)患者经CT、MRI、组织病理学检查确诊为直肠癌;(2)患者均有直肠癌根治术的手术指征;(3)患者能够耐受本研究的手术治疗方式;(4)患者对本研究的麻醉药物无严重过敏反应;(5)患者或家属知情同意并签署知情同意书。排除标准:(1)合并严重的心肝肾功能不全、凝血障碍者;(2)患者精神状态异常,术后无法配合完成问卷调查者;(3)患者术前1周内服用过影响认知功能的相关药物者。将上述患者按随机数字表法分为观察组(n=55)和对照组(n=55)。两组患者的基础资料比较无差异(P>0.05),可进行组间比较,见表1。本研究方案经医院伦理委员会批准。

表1 两组患者基础资料比较

Table 1 Comparison of the basic data of two groups of patients

Groups	n	Gender		Age (year)	Tumor classification			ASA classification	
		Male	Female		Adenocarcinoma	Mucous carcinoma	Undifferentiated carcinoma	I grade	II grade
Observation group	55	29	26	58.75± 12.98	28	16	11	27	28
Control group	55	32	23	56.10± 11.35	25	17	13	21	34
t/x ²	-	0.331		1.140		0.367		1.331	
P	-	0.565		0.257		0.832		0.249	

1.2 治疗方法

两组患者进入手术室后均建立静脉通路,并监测患者的心率、血压、呼吸等基础生理指标,所有患者的麻醉诱导均采用0.05 mg/kg的咪达唑仑(江苏恩华药业有限公司,国药准字H20031037,规格:2 mL:2 mg)、3 μg/kg的枸橼酸芬太尼(宜昌人福药业有限责任公司,国药准字H42022076,规格:2 mL:0.1 mg)、2 mg/kg的丙泊酚(AstraZeneca UK Limited,国药准字H20130535,规格:20 mL:200 mg)、0.15 mg/kg的阿曲库铵(浙江仙琚制药股份有限公司,国药准字H20090202,规格:5 mg/瓶)。然后对患者进行气管插管后行机械通气,氧气流量为1.5 L/min,潮气量为8-10 mL/kg。观察组患者麻醉维持采用丙泊酚靶控输注的方式给药,靶浓度为2-4 μg/mL,对照组患者采用七氟烷(上海恒瑞医药有限公司,国药准字H20070172,规格:120 mL/瓶)吸入进行麻醉维持,吸入浓度为1.0%-3.0%,两组患者均进行腹腔镜下直肠癌根治术治疗。术后两组患者均给予抗感染治疗和镇痛治疗。

1.3 评价方法

对两组患者手术过程中的麻醉效果进行观察比较,具体监测两组患者术前(T₀)、麻醉诱导后(T₁)、气腹建立即刻(T₂)、病灶切除时(T₃)、手术完成时(T₄)的平均动脉压(Mean arterial pressure, MAP)、心率(Heart rate, HR)。采用简易智力状态量表(Mini-mental State Examination, MMSE)对两组患者手术前1 h、术后6 h、术后12 h、术后24 h、术后48 h的认知功能进行评价比较,该量表满分为30分,得分越高表明患者的认知功能越好。分别在患者手术前1 d和术后3 d采集患者的空腹静脉血5 mL,加入枸橼酸钠抗凝处理后,采用TGL-20KR型高速离心机(上海安亭科学仪器厂)进行离心,3000 r/min,10 min后分离得到CD3⁺、CD4⁺、CD8⁺水平,并计算CD4⁺/CD8⁺的比值。采用AU5800型全自动生化分析仪(美国贝克曼库尔特公司)检测两组患者术前及术后3 d的肝功能,检测指标包括谷丙转氨酶(Alanine transaminase, ALT)、谷草转氨酶(Aspartate aminotransferase, AST)、总胆红素(Total bilirubin, TBILI)、直接胆红

素(Direct bilirubin, DBILI),所有检测操作均严格按照说明书进行,各检测试剂盒均购置于赛默飞世尔科技有限公司。

1.4 统计学方法

采用 SPSS 21.0 进行数据处理,计量资料以($\bar{x} \pm s$)表示,实施 t 检验,组内不同时间点比较采用 F 检验,计数资料以[n(%)]表示,实施 χ^2 检验,检验标准设置为 $\alpha=0.05$ 。

2 结果

2.1 两组患者不同时间点 MAP、HR 比较

观察组与对照组不同时间点 MAP、HR 组内比较差异无统计学意义($P>0.05$),两组患者不同时间点 MAP、HR 组间比较差异无统计学意义($P>0.05$),见表 2。

表 2 两组患者不同时间点 MAP、HR 比较($\bar{x} \pm s$)

Table 2 Comparison of MAP and HR in two groups of patients at different time points($\bar{x} \pm s$)

Groups	Indexes	T ₀	T ₁	T ₂	T ₃	T ₄	F	P
Observation group(n=55)	MAP(mmHg)	90.12± 10.29	100.38± 12.22	96.09± 9.37	98.21± 10.09	95.41± 9.89	1.231	0.213
	HR(time/min)	75.38± 8.87	79.89± 10.28	76.12± 9.90	73.09± 8.91	72.19± 8.08	0.982	0.302
Control group (n=55)	MAP(mmHg)	89.01± 11.23	98.32± 11.82	95.72± 10.08	99.20± 10.72	96.68± 9.90	1.349	0.201
	HR(time/min)	73.18± 8.81	80.34± 11.09	77.47± 10.02	74.80± 8.67	73.82± 8.34	0.693	0.452

2.2 两组患者手术前后 MMSE 评分比较

术前、术后 48 h 两组患者 MMSE 评分比较差异无统计学意义($P>0.05$),术后 6 h、12 h 观察组 MMSE 评分低于术前,术

后 6 h、12 h、24 h 对照组 MMSE 评分低于术前和观察组($P<0.05$),见表 3。

表 3 两组患者手术前后 MMSE 评分比较(分, $\bar{x} \pm s$)

Table 3 Comparison of MMSE scores in two groups of patients before and after operation(points, $\bar{x} \pm s$)

Groups	n	Before operation	6 h after operation	12 h after operation	24 h after operation	48 h after operation
Observation group	55	25.89± 3.54	19.78± 5.61*	22.91± 3.97*	24.93± 3.01	26.08± 3.58
Control group	55	26.34± 3.21	15.34± 5.21*	19.30± 3.69*	22.02± 2.89*	25.67± 3.66
t	-	0.698	4.301	4.940	5.172	0.594
P	-	0.486	0.000	0.000	0.000	0.554

Note: Compared with before operation, * $P<0.05$.

2.3 两组患者手术前后 T 淋巴细胞水平比较

两组患者术前 CD3⁺、CD4⁺、CD8⁺、CD4⁺/CD8⁺ 水平比较无统计学差异 ($P>0.05$), 术后 3 d 两组患者 CD3⁺、CD4⁺、

CD4⁺/CD8⁺ 水平均降低,CD8⁺ 水平均升高,且观察组 CD3⁺、CD4⁺、CD4⁺/CD8⁺ 水平高于对照组,CD8⁺ 水平低于对照组 ($P<0.05$),见表 4。

表 4 两组患者手术前后 T 淋巴细胞水平比较($\bar{x} \pm s$)

Table 4 Comparison of the level of T lymphocyte in two groups of patients before and after operation($\bar{x} \pm s$)

Groups	n	CD3 ⁺ (%)		CD4 ⁺ (%)		CD8 ⁺ (%)		CD4 ⁺ /CD8 ⁺	
		Before operation	3 d after operation	Before operation	3 d after operation	Before operation	3 d after operation	Before operation	3 d after operation
Observation group	55	56.72± 5.82	52.22± 6.09*	50.09± 6.34	47.78± 5.25*	27.67± 4.89	30.12± 3.39*	1.84± 0.15	1.63± 0.19*
Control group	55	57.23± 5.34	46.34± 6.56*	50.87± 6.23	41.74± 5.02*	28.21± 4.51	33.43± 3.87*	1.83± 0.19	1.29± 0.18*
t		0.296	3.010	0.402	3.810	0.372	2.948	0.189	9.634
P		0.769	0.004	0.690	0.000	0.712	0.005	0.851	0.000

Note: Compared with before operation, * $P<0.05$.

2.4 两组患者手术前后肝功能指标比较

两组患者术前 ALT、AST、TBILI、DBILI 水平比较无统计学差异 ($P>0.05$), 术后 3d 两组患者 ALT、AST、TBILI、DBILI 水平均升高,但观察组患者各项指标水平低于对照组($P<0.05$),见表 5。

2.5 两组患者不良反应发生率比较

观察组不良反应发生率为 12.73%,与对照组的 7.27%比较差异无统计学意义($P>0.05$),见表 6。

3 讨论

直肠癌是临床高发的极具危害性的恶性消化道肿瘤疾病,目前对其发病原因尚无统一说法,根据流行病学调查显示直肠癌的发生与生活环境、饮食习惯、遗传因素、肠道疾病等因素有关^[4-16]。随着人们生活水平的提高及饮食习惯的改变,直肠癌的发病率逐渐升高,对人类的危害性进一步增大。麻醉则是手术环节中重要的一环,麻醉效果的好坏直接关系到手术过程的顺利与否,并且还可能对患者术后精神状态的恢复产生一定的影响^[17]。对于大型的外科手术来说,通常采用的是全身麻醉,常用的是静脉注射全身麻醉和吸入性全身麻醉。临床报道显示^[18,19],

两组不同的全麻维持方式均有着较好的麻醉效果。七氟烷是一种卤代吸入性全身麻醉剂,不易燃,不易爆,安全性较好^[20,21]。丙

泊酚注射液适用于诱导和维持全身麻醉,也用于加强监护病人接受机械通气时的镇静^[22,23]。

表 5 两组患者手术前后肝功能指标比较($\bar{x} \pm s$)

Table 5 Comparison of liver function indexes between the two groups of patients before and after operation($\bar{x} \pm s$)

Groups	n	ALT(U/L)		AST(U/L)		TBILI(μ mol/L)		DBILI(μ mol/L)	
		Before	3 d after	Before	3 d after	Before	3 d after	Before	3 d after
		operation	operation	operation	operation	operation	operation	operation	operation
Observation group	55	44.91 $\pm$ 8.10	73.23 $\pm$ 11.02*	52.39 $\pm$ 10.26	88.31 $\pm$ 15.21*	19.34 $\pm$ 6.49	30.91 $\pm$ 7.09*	6.45 $\pm$ 3.12	10.60 $\pm$ 4.16*
Control group	55	46.69 $\pm$ 8.31	97.33 $\pm$ 19.79*	51.98 $\pm$ 9.23	101.92 $\pm$ 18.02*	20.67 $\pm$ 5.71	43.87 $\pm$ 7.49*	6.80 $\pm$ 3.18	19.29 $\pm$ 5.15*
t	-	1.128	7.590	0.228	4.280	1.141	9.319	0.583	9.735
P	-	0.258	0.000	0.826	0.000	0.256	0.000	0.561	0.000

Note: Compared with before operation, *P<0.05.

表 6 两组患者不良反应发生率比较[n(%)]

Table 6 Comparison of the incidence rate of adverse reactions between the two groups[n(%)]

Groups	n	Nausea and vomiting	Dizzy	Hypotension	Fever	Spasm	Total incidence rate
Observation group	55	1(1.82)	2(3.64)	1(1.82)	1(1.82)	2(3.64)	7(12.73)
Control group	55	1(1.82)	1(1.82)	0(0.00)	1(1.82)	1(1.82)	4(7.27)
χ^2							0.909
P							0.340

在本研究中, 两组患者不同时间点 MAP、HR 比较差异无统计学意义(P>0.05), 表明丙泊酚和七氟烷的麻醉效果相当。在术后认知功能评价方面, 观察组患者在术后 6 h、12 h、24 h 的 MMSE 评分均高于对照组(P<0.05), 表明应用丙泊酚进行麻醉维持可降低对患者认知功能的损伤, 而七氟烷吸入麻醉维持则会对患者术后的认知功能、精神状态造成较大的影响, 这是因为七氟烷吸入后会对患者的突触后膜的乙酰胆碱受体产生较强的抑制作用, 并且在阻断痛觉信号向中枢传导的过程中还降低了中枢神经递质中乙酰胆碱在突触间隙的传递, 从而使得患者出现认知、意识功能障碍^[24,25]。丙泊酚则是通过节突触前膜递质的释放而发挥麻醉作用, 对中枢神经系统的抑制作用较弱, 对患者术后认知功能的影响较小^[26]。本研究结果还显示, 观察组术后 CD3⁺、CD4⁺、CD4⁺/CD8⁺ 水平均高于对照组, 而 CD8⁺ 水平低于对照组(P<0.05), 表明丙泊酚静脉全麻对患者术后免疫功能的影响较小, 这是因为丙泊酚在体内能够快速代谢消除, 减少对机体免疫功能的抑制作用, 从而对于 T 淋巴细胞各亚型的影响较小^[27]。而七氟烷吸入给药对患者的气道及其他组织器官会产生一定的刺激作用, 导致机体出现应激反应, 从而对机体的免疫功能产生一定的影响^[28]。在术后肝功能的比较方面, 观察组患者 ALT、AST、TBILI、DBILI 水平均低于对照组, 表明丙泊酚对于肝功能的影响较小, 这是因为七氟烷吸入麻醉通过对机体的刺激产生的免疫介导反应, 这种全身的免疫介导反应对患者的肝功能也会产生较大影响。而丙泊酚在作用过程中可扩张患者的内脏血管并增加肝脏的血流量, 从而减少肝脏的直接损伤^[29,30]。在不良反应发生率方面, 两组患者不良反应均较低, 提示两种麻醉方式安全性均较好。

综上所述, 在腹腔镜直肠癌根治术中采用七氟烷与丙泊酚进行麻醉维持能够获得相似的麻醉效果, 术中及术后不良反应

发生率低, 用药安全性均良好。但与七氟烷相比, 丙泊酚对患者术后的认知功能、免疫功能及肝功能的影响较小。

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