丙泊酚联合瑞芬太尼麻醉对直肠癌根治术患者血流动力学和 T 淋巴细胞亚群的影响 *

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摘要 目的：探讨直肠癌根治术患者采用丙泊酚联合瑞芬太尼麻醉维持的临床效果。方法：选取 2016 年 3 月~2019 年 3 月期间在我院行直肠癌根治术的患者 82 例，根据乱数表法将患者分为对照组(n=41)和研究组(n=41)，其中对照组给予七氟醚麻醉维持，研究组给予丙泊酚联合瑞芬太尼麻醉维持，比较两组患者围术期指标、血流动力学和 T 淋巴细胞亚群变化，记录两组围术期不良反应情况。结果：研究组患者的清醒时间、拔管时间均短于对照组($P<0.05$)。两组患者麻醉成功后(T_2)~ 术后 72 h(T_5)时间点心率(HR)、平均动脉压(MAP)均呈先降低后升高趋势($P<0.05$)；研究组 T_2~ 术后 24 h(T_4)时间点 HR、MAP 高于对照组($P<0.05$)。两组不良反应发生率对比无差异($P>0.05$)。两组患者 T_2~T_5 时间点 CD4$^+$、CD4$^+$/CD8$^+$ 均呈先降低后升高趋势($P<0.05$)，CD8$^+$ 呈先升高后降低趋势($P<0.05$)；研究组 T_2~T_4 时间点 CD4$^+$、CD4$^+$/CD8$^+$ 高于对照组($P<0.05$)，CD8$^+$ 低于对照组($P<0.05$)。结论：直肠癌根治术患者麻醉维持选用丙泊酚联合瑞芬太尼可减少对机体血流动力学的影响，减轻免疫抑制，改善围术期相关指标，且不增加不良反应发生率。

关键词：丙泊酚；瑞芬太尼；直肠癌根治术；血流动力学；T 淋巴细胞亚群
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Effects of Propofol Combined with Remifentanil Anesthesia on Hemodynamics and T Lymphocyte Subsets in Patients Undergoing Radical Resection of Rectal Cancer*

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ABSTRACT Objective: To investigate the effects of propofol combined with remifentanil anesthesia on hemodynamics and T lymphocyte subsets in patients undergoing radical resection of rectal cancer. **Methods:** 82 patients with rectal cancer who underwent radical operation in our hospital from March 2016 to March 2019 were selected, and they were divided into control group (n=41) and study group (n=41) according to random number table method. The control group was given sevoflurane anesthesia for maintenance, and the study group was given propofol combined with remifentanil anesthesia maintenance. Perioperative indexes, hemodynamics and T lymphocyte subsets were compared between the two groups, and adverse reactions during treatment were recorded between the two groups. **Results:** The awakening time and extubation time of the study group were shorter than those of the control group ($P<0.05$). Heart rate (HR) and central venous pressure (MAP) decreased first and then increased after successful anesthesia (T_2)~72 h after anesthesia (T_5) between the two groups ($P<0.05$). HR and MAP in the study group at T_2~24 h after anesthesia (T_4) were higher than those in the control group ($P<0.05$). There was no significant difference in the incidence of adverse reactions between the two groups ($P>0.05$). The CD4$^+$, CD4$^+$/CD8$^+$ in both groups decreased at first and then increased at T_2~T_5 time points ($P<0.05$). CD8$^+$ increased first and then decreased ($P<0.05$). CD4$^+$, CD4$^+$/CD8$^+$ in the study group at T_2~T_4 time points were higher than those in the control group ($P<0.05$), and CD8$^+$ was lower than that in the control group ($P<0.05$). **Conclusion:** Propofol combined with remifentanil anesthesia can reduce the hemodynamic effects, alleviate immune suppression, improve perioperative related indicators, and do not increase the incidence of adverse reactions in patients undergoing radical resection of rectal cancer.

前言

直肠癌是指从齿状线至直肠乙状结肠交界处之间的癌,是消化道系统常见的恶性肿瘤之一[1]。现临床针对直肠癌的治疗主要以手术治疗为主,直肠癌根治术可有效阻止患者疾病进展,其手术的安全性及根治性也逐渐得到认可[2]。但直肠癌根治术作为有创手术,术中及麻醉刺激均可引起机体不同程度的血流动力学变化和免疫功能下降,影响患者术后恢复[3,4]。此外,由于直肠癌的多发群体为40~60岁的中老年人,此类患者身体各项技能逐渐下降,对手术和麻醉耐受性差,若处理不当,可诱发各种并发症,加重机体功能障碍[5]。不少临床实践证实[6,7],围术期中合理的麻醉方案可保证手术的顺利进行,故寻找安全、有效的麻醉方法对改善直肠癌根治术患者预后具有积极的临床意义。丙泊酚为新型的短效麻醉药,常用于全身麻醉诱导和麻醉维持中,发挥较好的镇静、镇痛作用[8]。瑞芬太尼为阿片类新型药物,具有麻醉起效快、半衰期短等优点[9]。本研究对在我院行直肠癌根治术的患者术中给予丙泊酚联合瑞芬太尼麻醉维持,效果较好,报道如下。

1 资料与方法

1.1 基线资料

选取2016年3月~2019年3月于我院行直肠癌根治术的82例患者。纳入标准:(1)均符合《直肠癌规范化诊疗指南(试行)》[10]中直肠癌的诊断标准,并经病理实验等证实;(2)均在我院择期行直肠癌根治术者;(3)美国麻醉医师协会(American Society of Anesthesiologists,ASA)分级Ⅰ~Ⅱ级者;(4)患者及其家属知情本研究且签署同意书;(5)均符合手术指征者。排除标准:(1)对本次研究用药存在禁忌症者;(2)合并其他肿瘤疾病者;(3)合并凝血功能障碍者;(4)合并心肝肾等重要脏器功能不全者;(5)合并免疫缺陷者。此次研究已获取我院伦理学委员会批准同意。根据乱数表法将患者分为对照组(n=41)和研究组(n=41),其中对照组男26例,女15例,年龄38~62岁,平均(49.82± 3.46)岁;ASA分级:Ⅰ级24例,Ⅱ级17例;病理类型:浸润型13例,隆起型14例,溃疡型14例;分化程度:低分化15例,中分化17例,高分化9例。研究组男24例,女17例,年龄36~61岁,平均(50.09± 3.62)岁;ASA分级:Ⅰ级23例,Ⅱ级18例;病理类型:浸润型13例,溃疡型12例,隆起型16

例;分化程度:低分化14例,中分化16例,高分化11例。两组一般资料比较无差异(P>0.05)。

1.2 方法

所有患者入院后行常规检查,择期行直肠癌根治术。所有患者麻醉前30 min肌注阿托品0.5 mg、咪唑安定3 mg,入室后常规监测心率(Heart rate,HR)、平均动脉压(MAP),建立静脉通路,实施面罩吸氧。两组患者均给予以下药物行麻醉诱导:舒芬太尼(国药准字H20054256,宜昌人福药业有限责任公司,规格:按舒芬太尼计5 mL:250 μg)0.4 μg/kg,咪达唑仑注射液(国药准字H20153019,江苏九旭药业有限公司,规格:3 mL:15 mg)0.1 mg/kg,顺苯磺酸阿曲库铵(国药准字H20090202,浙江仙琚制药股份有限公司,规格:5 mg (以顺阿曲库铵计))0.5 mg/kg,丙泊酚注射液(国药准字H20123318,西安力邦制药有限公司,规格:50 mL:1.0 g)4~6/mg·h,静脉注射。诱导成功后,行气管插管。对照组麻醉维持选用1-3%七氟醚静脉输注直至术毕;研究组麻醉维持:丙泊酚注射液0.5 μg/kg·min,瑞芬太尼(国药准字H20143315,江苏恩华药业股份有限公司,规格:2 mg(以瑞芬太尼计))0.1~0.25 μg/kg·min,静脉输注直至术毕。术后给予常规抗感染、镇痛处理。

1.3 观察指标

(1)记录两组患者清醒时间和拔管时间,其中清醒时间为手术结束至唤醒,拔管时间为手术结束至拔管。(2)记录两组患者麻醉前(T_1)、麻醉成功后(T_2)、术毕即刻(T_3)、术后24h(T_4)、术后72h (T_5)等时间点的血流动力学指标:HR、MAP。(3)于T_1~T_5抽取患者肘静脉血2 mL,经4600 r/min离心15 min,离心半径8 cm,取上清置于-30℃冰箱中待测。采用流式细胞仪(美国Coulter公司EPICS-XL型)检测T淋巴细胞亚群:$CD4^+$、$CD8^+$,计算$CD4^+/CD8^+$。(4)记录两组围术期不良反应。

1.4 统计学方法

数据分析采用SPSS25.0进行,以率表示计数资料,行χ^2检验,计量资料以($\bar{x}\pm s$)的形式表示,行t检验。检验标准设置为α=0.05。

2 结果

2.1 两组围术期指标比较

研究组患者的清醒时间、拔管时间均短于对照组(P<0.05)。详见表1。

表1 两组围术期指标比较($\bar{x}\pm s$,min)

Table 1 Comparison of perioperative indicators between two groups($\bar{x}\pm s$, min)

Groups	Awakening time	Extubation time
Control group(n=41)	11.95±1.26	18.48±1.78
Study group(n=41)	8.16±1.21	13.27±1.69
t	13.892	13.592
P	0.000	0.000

2.2 两组血流动力学指标比较

两组患者 T_1 时间点 HR、MAP 比较无差异（$P>0.05$）；与 T_1 时间点比较，两组患者 T_2~T_5 时间点 HR、MAP 均呈先降低后升高趋势（$P<0.05$）；研究组 T_2~T_4 时间点 HR、MAP 高于对照组（$P<0.05$）；详见表 2。

表 2 两组血流动力学指标比较（$\bar{x}\pm s$）

Table 2 Comparison of hemodynamic parameters between two groups（$\bar{x}\pm s$）

Groups	Time points	HR(Times/min)	MAP(mmHg)
Control group(n=41)	T_1	80.26±5.13	103.39±8.23
	T_2	64.35±6.02[a]	85.11±7.18[a]
	T_3	68.24±7.42[ab]	90.26±7.78[ab]
	T_4	73.19±6.33[abc]	94.84±7.65[abc]
	T_5	79.14±6.54[bcd]	101.18±9.95[bcd]
Study group(n=41)	T_1	80.28±7.23	104.35±7.73
	T_2	68.36±6.26[ae]	89.52±8.42[ae]
	T_3	72.67±6.87[abe]	94.83±7.31[abe]
	T_4	76.81±6.15[abce]	98.53±8.54[abce]
	T_5	79.93±6.3[bcd]	102.13±8.27[bcd]

Note: Compared with T_1 time point, [a]$P<0.05$; compared with T_2 time point, [b]$P<0.05$; compared with T_3 time point, [c]$P<0.05$; compared with T_4 time point, [d]$P<0.05$; compared with control group, [e]$P<0.05$.

2.3 两组 T 淋巴细胞亚群比较

两组患者 T1 时间点 CD4+、CD8+、CD4+/CD8+ 比较无差异（$P>0.05$）；两组患者 T_2~T_5 时间点 CD4+、CD4+/CD8+ 均呈先降低后升高趋势（$P<0.05$），CD8+ 呈先升高后降低趋势（$P<0.05$）；研究组 T_2~T_4 时间点 CD4+、CD4+/CD8+ 高于对照组（$P<0.05$），CD8+ 低于对照组（$P<0.05$）；详见表 3。

表 3 两组 T 淋巴细胞亚群比较（$\bar{x}\pm s$）

Table 3 Comparison of T lymphocyte subsets between two groups（$\bar{x}\pm s$）

Groups	Time points	CD4+	CD8+	CD4+/CD8+
Control group(n=41)	T_1	57.18±6.14	24.84±3.99	2.30±0.29
	T_2	48.91±6.05[a]	31.93±4.01[a]	1.53±0.31[a]
	T_3	45.09±6.27[ab]	35.28±2.26[ab]	1.28±0.26[ab]
	T_4	49.13±6.41[ac]	30.28±2.37[ac]	1.62±0.32[ac]
	T_5	55.42±5.58[bcd]	24.93±2.74[bcd]	2.22±0.26[bcd]
Study group(n=41)	T_1	57.22±6.47	24.97±3.82	2.29±0.27
	T_2	53.29±5.71[ae]	27.84±3.12[ae]	1.91±0.19[ae]
	T_3	48.17±6.62[abe]	31.85±3.16[abe]	1.51±0.22[abe]
	T_4	52.41±5.87[ace]	28.20±3.83[ace]	1.86±0.19[ace]
	T_5	56.96±6.02[bcd]	25.18±2.90[bcd]	2.26±0.21[bcd]

Note: Compared with T_1 time point, [a]$P<0.05$; compared with T_2 time point, [b]$P<0.05$; compared with T_3 time point, [c]$P<0.05$; compared with T_4 time point, [d]$P<0.05$; compared with control group, [e]$P<0.05$.

2.4 不良反应比较

对照组围术期出现躁动、寒战、恶心呕吐、低血压各 1 例，心动过缓 2 例，不良反应发生率为 14.63%（6/41），研究组围术期出现心动过缓、躁动、低血压各 2 例，寒战、恶心呕吐各 1 例，不良反应发生率为 19.51%（8/41），经比较两组不良反应发生率无差异（$\chi^2=0.345$，$P=0.557$）。

3 讨论

直肠癌发病率较高，在我国其发病率仅次于胃癌[11]。近年来随着人们生活水平的改善，饮食结构不断发生变化，致使直肠癌的发病率呈逐年递增趋势，已成为危害人类生命健康的主要疾病之一[12]。直肠癌根治术是治疗直肠癌的主要方式，该术式手术成功率高、术后恢复快，可有效阻止直肠癌病情进展[13]。但该术式作为有创术式，由于手术创伤、术中刺激以及术后疼痛可使机体产生强烈的应激反应，造成机体血流波动，导致患者免疫功能降低，术后感染发生风险增加[14,15]，其具体的手术效

果很大程度上受麻醉方法的影响,故寻找一种科学、安全的麻醉方法尤为必要。丙泊酚静脉注射后可保护机体各组织器官、调节免疫、镇静、抑制血小板聚集、止痛,且具有苏醒时间短、控制性强、危害小等优势,然而单一的药物镇痛存在较多不足,剂量过少难以达到镇痛效果,剂量过多又易增加呼吸抑制等不良反应发生风险[16,17]。现临床多主张多模式镇痛以达到最佳的麻醉效果。瑞芬太尼为阿片类新型药物,静脉滴注后可迅速达到有效药物浓度,发挥镇静、镇痛的效果[18,19]。

本次研究结果显示,两组患者不同时间点 HR、MAP 均呈先降低后升高趋势,研究组不同时间点 HR、MAP 高于对照组,可见两种麻醉方式均可引起患者的血流波动,但丙泊酚联合瑞芬太尼麻醉者的血流波动可明显减轻,分析其原因,丙泊酚进入机体后,主要作用于 γ- 氨基丁酸受体复合物,产生较好的麻醉效果[20],而瑞芬太尼衍生于芬太尼,相较于芬太尼,瑞芬太尼效用较强,可有效抑制机体应激反应,减轻手术对患者呼吸、循环系统、压力感受器功能的影响,对 HR 影响较轻,同时瑞芬太尼还可作用于冠状血管,促进其扩张,改善 MAP[21,22]。因此,瑞芬太尼联合丙泊酚使用可在药代动力学方面发挥协同效果,增强药效,提高麻醉效果,起到稳定 HR、MAP 的作用。细胞免疫在机体抗肿瘤免疫效应中作用显著,T 淋巴细胞亚群为关键性免疫活性细胞,其中 CD8+ 可抑制 T 细胞增生和抗体分泌,CD4+ 主要表达于抑制细胞核杀伤性 T 细胞表面,可辅助 B 细胞分化产生抗体[23,24]。而 CD4+/CD8+ 的比值降低则预示着机体免疫功能的下降。本次研究结果中,两组患者围术期间免疫功能均有不同程度的下降,但研究组免疫功能下降的程度更轻,表明丙泊酚联合瑞芬太尼麻醉可有效缓解免疫抑制。丙泊酚静脉注射后本身就具有调节免疫的作用,且瑞芬太尼可削弱 μ 受体对 T 淋巴细胞的抑制,同时还可通过刺激 K 受体,抑制神经递质,减轻机体创伤刺激,保护机体免疫功能[25-27]。此外研究组患者的清醒时间、拔管时间均短于对照组,这可能是因为瑞芬太尼对机体呼吸的抑制较为缓和,患者术后可尽早恢复,同时联合丙泊酚用药,具有可控性高、反复给药无蓄积等优势[28]。两组不良反应发生率对比未见显著差异,可见本次联合麻醉用药安全性较好,不会增加不良反应发生率,这可能是因为瑞芬太尼的代谢几乎不受患者肝肾功能影响,药物残留少[29],而丙泊酚则具有保护机体各组织器官的药效作用,安全性较好[30]。

综上所述,直肠癌根治术患者选用丙泊酚联合瑞芬太尼麻醉维持,可减轻免疫抑制,减少对机体血流动力学的影响,改善围术期指标,临床应用价值较高。

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