

doi: 10.13241/j.cnki.pmb.2021.05.022

丙泊酚复合瑞芬太尼对高血压腹部手术患者血流动力学、炎症因子及认知功能的影响*

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摘要 目的:探讨丙泊酚复合瑞芬太尼对高血压腹部手术患者血流动力学、炎症因子及认知功能的影响。**方法:**选取 2018 年 2 月~2020 年 2 月期间我院收治的高血压行腹部手术患者 150 例,上述患者根据随机数字表法分为对照组($n=75$)和研究组($n=75$),对照组患者予以丙泊酚维持麻醉,研究组予以丙泊酚复合瑞芬太尼维持麻醉,比较两组患者围术期指标、血流动力学、炎症因子及认知功能情况。**结果:**研究组呼吸恢复时间、拔气管导管时间、苏醒时间均短于对照组($P<0.05$)。研究组手术结束(T1)~拔管后(T3)时间点心率(HR)、收缩压(SBP)、舒张压(DBP)均高于对照组($P<0.05$)。研究组术后 3d、术后 5d 白介素-1(IL-1)、白介素-6(IL-6)、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 3d、术后 5d 简易智力状态检查表(MMSE)评分均高于对照组($P<0.05$)。研究组术后 1d、术后 3d 的 POCD 发生率低于对照组($P<0.05$)。**结论:**高血压腹部手术患者麻醉维持选用瑞芬太尼复合丙泊酚方案,可维持机体血流平稳,减轻机体炎症应激及认知功能损害,具有较高的临床应用价值。

关键词:丙泊酚;瑞芬太尼;高血压;腹部手术;血流动力学;炎症因子;认知功能

中图分类号:R544.1;R656 **文献标识码:**A **文章编号:**1673-6273(2021)05-907-04

Effects of Propofol Combined with Remifentanyl on Hemodynamics, Inflammatory Factors and Cognitive Function in Patients Undergoing Abdominal Surgery for Hypertension*

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ABSTRACT Objective: To investigate the effect of propofol combined with remifentanyl on hemodynamics, inflammatory factors and cognitive function in patients with hypertension undergoing abdominal surgery. **Methods:** From February 2018 to February 2020, 150 patients who hypertension underwent abdominal surgery in our hospital were selected. The patients were divided into control group ($n=75$) and study group ($n=75$) according to the random number table method. The patients in the control group were given propofol maintenance anesthesia, while the patients in the study group were given propofol combined with remifentanyl maintenance anesthesia. The perioperative indexes, hemodynamics, inflammatory factors and cognitive function of the two groups were compared. **Results:** The respiratory recovery time, tracheal catheter extraction time and resuscitation time of the study group were shorter than those of the control group ($P<0.05$). The heart rate (HR), systolic blood pressure (SBP) and diastolic blood pressure (DBP) at the time point between end of the operation (T1) and after extubation (T3) were all higher in the study group than in the control group ($P<0.05$). Interleukin-1 (IL-1), interleukin-6 (IL-6) and tumor necrosis factor- α (TNF- α) of the study group at 1d after operation, 3d after operation, 5d after operation were lower than those of the control group ($P<0.05$). The scores of mini-mental state examination (MMSE) of the study group were higher than those of the control group ($P<0.05$). The incidence of POCD of the study group at 1d after operation, 3d after operation were lower than those of the control group ($P<0.05$). **Conclusion:** Remifentanyl for maintenance of anesthesia in patients with hypertensive abdominal surgery conforms to the propofol scheme, which can maintain the stable blood flow, reduce the body's inflammatory stress and cognitive impairment, and has high clinical application value.

Key words: Propofol; Remifentanyl; Hypertensive; Abdominal surgery; Hemodynamics; Inflammatory factors; Cognitive function

Chinese Library Classification(CLC): R544.1; R656 **Document code:** A

Article ID: 1673-6273(2021)05-907-04

* 基金项目: 国家自然科学基金面上项目(81071771);四川省卫生和计划生育委员会科研项目(150254)

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(收稿日期:2020-07-26 接受日期:2020-08-21)

前言

高血压病是临床常见的退行性疾病,以动脉血压升高为主要临床特征,好发于中老年群体^[1-3]。此类患者在接受外科手术治疗时,对麻醉药物代谢速度降低,心血管疾病的发生风险明显高于正常群体,因而对手术中的麻醉要求也随之提高^[4-6]。丙泊酚、瑞芬太尼均是目前临床上应用较为广泛的静脉麻醉药物,两种药物在多种外科手术中均有较好的疗效,均具有镇痛效果好、可控性好、作用时间短等特点^[7,8]。但有关其联合应用于高血压腹部手术患者的相关报道并不十分多见。鉴于此,本研究通过探讨丙泊酚复合瑞芬太尼对高血压腹部手术患者的影响,以期临床高血压腹部手术麻醉方法的选择提供参考。

1 资料与方法

1.1 一般资料

选取2018年2月~2020年2月期间我院收治的行腹部手术的高血压患者150例,此研究已获取我院伦理学委员会批准进行。纳入标准:(1)美国麻醉协会(American Society of Anesthesiology, ASA)分级Ⅰ~Ⅱ级,收缩压(SBP)≤179 mmHg,舒张压(DBP)≤109 mmHg^[9];(2)患者及其家属知情本次研究且签署了同意书;(3)符合手术指征,对本次研究用药耐受者;(4)手术均由同一组医师完成操作。排除标准:(1)合并凝血功能障碍者;(2)合并心肝肾等脏器功能障碍者;(3)既往有腹部手术史者;(4)合并精神疾患,无法正常沟通交流者;(5)内分泌系统疾病者。上述患者根据随机数字表法分为对照组(n=75,丙泊酚维持麻醉)和研究组(n=75,丙泊酚复合瑞芬太尼维持麻醉),其中对照组男36例,女39例,年龄39~62岁,平均(50.38±4.27)岁;体质量指数20.5~26.2 kg/m²,平均(23.15±0.83) kg/m²;ASA分级Ⅰ级38例,Ⅱ级37例;腹部手术类型:其中肝脏、胆囊手术21例,胃、十二指肠手术26例,结肠手术20例,其他手术8例。研究组男34例,女41例,年龄42~65岁,平均(50.96±4.05)岁;体质量指数20.9~25.8 kg/m²,平均(23.23±0.75) kg/m²;ASA分级Ⅰ级40例,Ⅱ级35例;腹部手术类型:其中肝脏、胆囊手术23例,胃、十二指肠手术28例,结肠手术17例,其他手术7例。两组一般资料对比无统计学差异($P>0.05$)。

1.2 方法

所有患者术前均禁饮、禁食6h,入室后开放静脉通道,监测患者心电图、血压、心率(Heart rate, HR)。麻醉诱导:依次静脉滴注咪达唑仑(宜昌人福药业有限责任公司生产,国药准字H20067041,规格:2 mL:10 mg)0.05 mg/kg,丙泊酚乳状注射液(四川国瑞药业有限责任公司,国药准字H20030114,规格:50 mL:0.5 g)2 mg/kg,舒芬太尼(宜昌人福药业有限责任公司生产,国药准字H20054171,规格:1 mL:50 μg)0.5 μg/kg,顺式阿曲库铵(江苏恒瑞医药股份有限公司生产,国药准字H20060869,规格:10 mg)0.15 mg/kg,诱导成功后插入气管导管,连接麻醉机控制呼吸,呼吸12次/min,二氧化碳呼气末分压35~45 mmHg,呼吸比1:2,调节氧流量2 L/min。对照组患者仅用丙泊酚TCI:2~4 μg/mL维持麻醉,研究组则给予丙泊酚TCI:2~4 μg/mL联合注射用盐酸瑞芬太尼[宜昌人福药业有限责任公司生产,国药准字H20030197,规格:1 mg(以瑞芬太尼C₂₀H₂₈N₂O₅计)]

TCI:2~4 ng/mL维持麻醉。在术中密切监测患者的HR与血压,对于血压值超过基础值10%的患者给予硝酸甘油(河南润弘制药有限公司,国药准字H20057216,规格:1 mL:5 mg)进行降压治疗;对于HR超过100次/min的患者给予艾司洛尔(齐鲁制药有限公司,国药准字H19991059,规格:10 mL:0.1 g)进行控制心率治疗。手术缝皮时停用所有麻醉药物。

1.3 观察指标

1.3.1 围术期指标 记录两组围术期指标,包括呼吸恢复时间、苏醒时间、拔气管导管时间。

1.3.2 血流动力学指标 记录两组手术前(T₀)、手术结束(T₁)、拔管时(T₂)和拔管后(T₃)的HR、收缩压(Systolic blood pressure, SBP)和舒张压(Diastolic blood pressure, DBP)。

1.3.3 炎症因子 抽取患者T₀、术后3d、术后5d时间点的肘静脉血6 mL,经3600 r/min离心12 min,离心半径12 cm,分离上清液置于-30℃冰箱中待测。选用武汉华美生物科技有限公司试剂盒,根据试剂盒说明书步骤进行操作,采用酶联免疫吸附法检测白介素-1(Interleukin-1, IL-1)、白介素-6(Interleukin-6, IL-6)、肿瘤坏死因子-α(Tumor necrosis factor-α, TNF-α)水平。

1.3.4 认知功能 于术前、术后1d、术后3d、术后5d采用简易智力状态检查表(Mini-mental state examination, MMSE)^[10]评分评价患者认知功能状况。MMSE评分主要包括定向力检测、记忆力检测、注意力检测、语言功能检测、计算力检测、空间位置觉检测等,总分30分,分数越高,认知功能越好。统计两组患者术后认知功能障碍(Postoperative cognitive dysfunction, 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SPSS20.0进行数据分析。计量资料采用平均值±标准差来表示,采用t检验。计数资料采用%表示,通过χ²检验,检验水准为α=0.05。

2 结果

2.1 两组围术期指标比较

研究组呼吸恢复时间、苏醒时间、拔气管导管时间均短于对照组($P<0.05$);详见表1。

2.2 两组血流动力学指标比较

两组T₀时间点HR、SBP、DBP比较无差异($P>0.05$);两组T₀~T₃时间点HR、SBP、DBP呈先降低后升高趋势($P<0.05$);研究组T₁~T₃时间点HR、SBP、DBP均高于对照组($P<0.05$);详见表2。

2.3 两组炎症因子比较

两组T₀时间点IL-1、IL-6、TNF-α比较无差异($P>0.05$);两组T₀~术后5dIL-1、IL-6、TNF-α呈先升高后降低趋势($P<0.05$);研究组术后3d、术后5dIL-1、IL-6、TNF-α低于对照组($P<0.05$);详见表3。

2.4 两组MMSE评分比较

两组术前MMSE评分比较无差异($P>0.05$);两组术前~术后5dMMSE评分呈下降后升高趋势($P<0.05$);研究组术后1d、术后3d、术后5dMMSE评分均高于对照组($P<0.05$);详见表4。

表 1 两组围术期指标比较($\bar{x} \pm s, \text{min}$)Table 1 Comparison of perioperative indicators between the two groups($\bar{x} \pm s, \text{min}$)

Groups	Respiratory recovery time	Resuscitation time	Tracheal catheter extraction time
Control group(n=75)	8.62±1.21	18.87±2.35	22.24±2.78
Study group(n=75)	4.97±0.96	13.22±2.86	15.96±2.35
t	20.465	13.219	14.941
P	0.000	0.000	0.000

表 2 两组血流动力学指标比较($\bar{x} \pm s$)Table 2 Comparison of hemodynamic indexes between the two groups($\bar{x} \pm s$)

Groups	Time point	HR(beats/min)	SBP(mmHg)	DBP(mmHg)
Control group(n=75)	T0	82.41±6.45	150.85±8.33	99.48±7.36
	T1	63.35±6.19 ^a	87.19±7.25 ^a	78.04±7.52 ^a
	T2	69.21±5.27 ^{ab}	94.01±9.20 ^{ab}	85.68±6.97 ^{ab}
	T3	75.88±6.49 ^{abc}	101.78±7.33 ^{abc}	91.74±7.21 ^{abc}
Study group(n=75)	T0	82.28±7.33	149.33±7.13	98.53±8.09
	T1	69.41±6.94 ^{ad}	94.36±7.18 ^{ad}	82.35±7.36 ^{ad}
	T2	75.95±5.84 ^{abd}	101.39±8.39 ^{abd}	90.46±6.41 ^{abd}
	T3	80.15±6.48 ^{bcd}	107.57±8.11 ^{bcd}	97.19±7.59 ^{bcd}

Notes: compared with T0 time point, ^a $P<0.05$; compared with T1 time point, ^b $P<0.05$; compared with T2 time point, ^c $P<0.05$; compared with the control group, ^d $P<0.05$.

表 3 两组炎症因子水平比较($\bar{x} \pm s$)Table 3 Comparison of levels of inflammatory factors between the two groups($\bar{x} \pm s$)

Groups	Time point	IL-1(pg/mL)	IL-6(pg/mL)	TNF- α (ng/mL)
Control group(n=75)	T0	54.41±8.26	85.86±6.36	72.36±6.35
	3d after operation	82.33±9.23 ^a	112.31±7.57 ^a	95.39±6.41 ^a
	5d after operation	69.25±7.89 ^{ab}	101.59±8.21 ^{ab}	86.25±7.74 ^{ab}
Study group(n=75)	T0	53.23±9.78	85.62±6.10	71.97±7.46
	3d after operation	73.94±7.19 ^{ac}	102.94±6.89 ^{ac}	86.72±8.44 ^{ac}
	5d after operation	62.03±8.01 ^{abc}	93.41±7.73 ^{abc}	79.76±7.52 ^{abc}

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

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

Groups	Before operation	1d after operation	3d after operation	5d after operation
Control group(n=75)	29.23±0.27	25.25±0.38 ^a	27.76±0.23 ^{ab}	28.04±0.21 ^{abc}
Study group(n=75)	29.18±0.28	26.81±0.26 ^a	28.02±0.22 ^{ab}	29.12±0.24 ^{bc}
t	1.113	29.342	7.075	29.329
P	0.267	0.000	0.000	0.000

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

2.5 两组 POCD 发生情况比较

研究组术后 1d、术后 3dPOCD 发生率低于对照组($P<0.05$); 两组术后 5dPOCD 发生率比较差异无统计学意义($P>0.05$);详见表 5。

3 讨论

高血压是指静息状态下动脉 SBP $\geq 140\text{mmHg}$ 和 (或) DBP $\geq 90\text{mmHg}$, 多发于中老年群体, 并伴有脂代谢、糖代谢紊乱现象^[11,12]。近年来, 随着人们生活结构的改变, 以及人口老龄化的加剧, 高血压的发病率呈不断升高趋势^[13]。近年来需要行腹部外科手术的高血压患者人数不断增加, 由于高血压患者泵血功能和心脏储血功能降低^[14,15]。加之高血压患者多伴有不同

表 5 两组术后 POCD 发生情况比较例(%)
Table 5 Comparison of postoperative POCD in the two groups n(%)

Groups	1d after operation	3d after operation	5d after operation
Control group(n=75)	36(48.00)	25(33.33)	9(12.00)
Study group(n=75)	24(32.00)	11(14.67)	3(4.00)
χ^2	4.000	7.164	3.265
P	0.046	0.007	0.071

程度的并发症,易导致患者术中血流波动过大,术后苏醒时间延长,在接受麻醉手术时风险明显增加^[16]。此外,不同麻醉药物对患者脑氧代谢的影响不同,对此其造成的脑神经损伤程度也有区别,不少患者术后可出现 POCD 现象^[17]。丙泊酚是一种新型静脉麻醉药物,具有起效迅速、苏醒迅速的特点。但既往有报道表明^[18],丙泊酚在麻醉维持期有抑制患者呼吸、影响患者血压等不良作用。瑞芬太尼是一种新型 μ 型阿片受体激动剂,其镇痛效果显著,在体内的代谢清除过程不受麻醉诱导剂量的影响,常用于麻醉诱导和麻醉维持镇痛^[19]。

本次研究结果显示,两组患者术中均出现不同程度的血流波动,但研究组的血流波动程度明显更轻。分析其原因,丙泊酚亲脂性高,进入人体后可迅速分布至中枢神经系统和周围组织^[20]。而瑞芬太尼可以剂量依赖性地降低血压和 HR,可通过舒张血管平滑肌进而抑制儿茶酚胺的释放,有效抑制气管插管和手术应激时的高血压反应^[21,22]。当瑞芬太尼与丙泊酚联合用药时,产生协同作用,进一步维持血流动力学稳定^[23]。而研究组呼吸恢复时间、苏醒时间、拔气管导管时间均短于对照组,提示两种药物联合使用可促进患者快速苏醒。究其原因可能在于瑞芬太尼血气分配系数低,对机体的循环系统影响较小。手术创伤作为一种特殊的创伤形式可激活机体炎症因子,IL-1、IL-6、TNF- α 均是急性炎症期反应的重要指标,可评估患者术后创伤严重程度^[24,25]。本次研究中两组患者均存在炎症应激,但丙泊酚复合瑞芬太尼方案者的炎症应激反应程度更轻。其可能机制在于:复合用药可减少丙泊酚的使用剂量,进而减轻丙泊酚带来的呼吸系统和心血管系统的抑制;加之瑞芬太尼还可抑制淋巴细胞增殖,减轻炎症应激反应^[26,27]。研究中丙泊酚复合瑞芬太尼方案还可保护患者认知功能,减少 POCD 发生率。这可能是因为瑞芬太尼起效迅速,在人体 1 min 左右内即可达到血-脑平衡,维持脑氧正常代谢,不受血浆胆碱酯酶的影响,且排泄速度快,易于从人体消除,减少对人体神经中枢的损害,从而提高手术麻醉的质量。

综上所述,高血压腹部手术患者麻醉维持选用丙泊酚复合瑞芬太尼方案,可维持机体血流平稳,减轻机体炎症应激及认知功能损害,具有较高的临床应用价值。

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