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丙泊酚联合依托咪酯麻醉诱导对腹腔镜胆囊切除术患者血流动力学、炎性因子和认知功能的影响 *

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摘要 目的:探讨丙泊酚联合依托咪酯麻醉诱导对腹腔镜胆囊切除术(LC)患者血流动力学、炎性因子和认知功能的影响。**方法:**选取2018年6月~2019年9月期间我院收治的行LC治疗的患者90例,随机将患者分为对照组(n=45)和研究组(n=45),对照组患者给予丙泊酚麻醉诱导,研究组采用丙泊酚联合依托咪酯麻醉诱导,比较两组围术期指标、血流动力学、炎性因子、认知功能及不良反应发生率。**结果:**研究组诱导插管时、气腹后5 min、手术结束时的心率(HR)、平均动脉压(MAP)高于对照组($P<0.05$)。研究组术后1 d、术后3 d白介素-6(IL-6)、C反应蛋白(CRP)和肿瘤坏死因子- α (TNF- α)均低于对照组($P<0.05$)。研究组睁眼时间、拔管时间、定向力恢复时间短于对照组($P<0.05$)。两组术前1 h~术后48 h简易智力状态检查表(MMSE)评分呈先下降后升高趋势,但研究组术后2 h、术后24 h、术后48 h MMSE 评分高于对照组($P<0.05$)。两组患者不良反应总发生率比较无差异($P>0.05$)。**结论:**LC患者给予丙泊酚联合依托咪酯麻醉诱导,可有效减轻血流动力学波动及炎性应激,降低术后认知功能损害,且安全性较好。

关键词:依托咪酯;丙泊酚;腹腔镜胆囊切除术;血流动力学;炎性因子;认知功能

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Effects of Propofol Combined with Etomidate on Hemodynamics, Inflammatory Factors and Cognitive Function in Patients Undergoing Laparoscopic Cholecystectomy*

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ABSTRACT Objective: To investigate the effects of propofol combined with etomidate induction on hemodynamics, inflammatory factors and cognitive function in patients undergoing laparoscopic cholecystectomy (LC). **Methods:** From June 2018 to September 2019, 90 patients with LC in our hospital were selected. Patients were randomly divided into control group (n=45) and study group (n=45). Patients in control group were induced by propofol. The study group was induced by propofol and etomidate. The perioperative indexes, hemodynamics, inflammatory factors, cognitive function and incidence of adverse reactions were compared. **Results:** The heart rate (HR) and mean arterial pressure (MAP) in study group were higher than those in control group at the induction intubation time, 5 minutes after pneumoperitoneum and the end of operation time ($P<0.05$). The levels of interleukin-6 (IL-6), C-reactive protein (CRP), and tumor necrosis factor- α (TNF- α) in the study group at 1d after operation and 3 d after operation were lower than those in the control group ($P<0.05$). The eye opening time, extubation time and directional force recovery time in the study group were shorter than those in the control group ($P<0.05$). The scores of mini-mental state examination (MMSE) in the two groups decreased first and then increased at 1 h before operation~48 h after operation, but the scores of MMSE in the study group at 2 h after operation, 24 h after operation, 48 h after operation were higher than those in the control group ($P<0.05$). There was no significant difference in the total incidence of adverse reactions between the two groups ($P>0.05$). **Conclusion:** Propofol combined with etomidate induction the patients with LC, it can effectively reduce the hemodynamic fluctuation and inflammatory stress, reduce the postoperative cognitive impairment, and which has a good safety.

Key words: Etomidate; Propofol; Laparoscopic cholecystectomy; Hemodynamics; Inflammatory factors; Cognitive function

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前言

腹腔镜胆囊切除术(Laparoscopic cholecystectomy, LC)是胆道外科的常用术式,具有创伤小、术后恢复快等优势^[1,2]。虽然

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LC 为微创术式,但是术中二氧化碳气腹以及游离胆囊床的应激反应仍可能引起患者血流波动,部分患者甚至产生术后认知功能障碍,不利于患者术后尽快苏醒和早期活动^[3-5]。因此,合理的麻醉方案以减轻术中刺激对于改善 LC 术后患者的预后具有积极的促进作用。既往 LC 常用的麻醉诱导药物为丙泊酚或依托咪酯,丙泊酚为短效静脉类麻醉药,诱导平稳且迅速,但部分患者循环系统会受到不同程度的抑制^[6,7]。依托咪酯是咪唑类衍生物,具有作用时间短、起效快、对循环系统和呼吸系统影响较小等多种优势^[8,9]。鉴于此,本研究通过探讨丙泊酚联合依托咪酯麻醉诱导对 LC 患者血流动力学、炎症因子和认知功能的影响,以期临床 LC 术中麻醉选择提供参考。

1 资料与方法

1.1 一般资料

纳入标准:(1)符合 LC 手术指征者,均于我院择期行 LC 术者;(2)美国麻醉医师协会(American Society of Anesthesiologists, ASA)II 或 III 级^[10];(3)手术均由同一组医师进行;(4)对本次研究用药无过敏者;(5)患者及其家属知情,并已签署同意书。排除标准:(1)合并血液系统疾病者;(2)既往有腹部手术史者;(3)肝肾等重要脏器功能障碍者;(4)妊娠或哺乳期妇女;(5)伴有全身感染性疾病者;(6)长期使用糖皮质激素者以及术前使用甾体类药物者。选取 2018 年 6 月~2019 年 9 月期间我院收治的行 LC 治疗的患者 90 例。随机将患者分为对照组(n=45)和研究组(n=45),其中对照组男 20 例,女 25 例,年龄 42~68 岁,平均(55.69±4.27)岁;体质指数 20.3~26.9 kg/m²,平均(24.18±0.83)kg/m²;疾病类型:胆囊息肉 17 例,胆囊腺肌症 20 例,胆囊结石 8 例;ASA 分级:II 级 26 例,III 级 19 例。研究组男 18 例,女 27 例,年龄 41~70 岁,平均(56.24±5.36)岁;体质指数 20.8~27.6 kg/m²,平均(24.35±0.96)kg/m²;疾病类型:胆囊息肉 15 例,胆囊腺肌症 19 例,胆囊结石 11 例;ASA 分级:II 级 24 例,III 级 21 例。两组患者一般资料比较无差异($P>0.05$)。医院伦理委员会已批准本研究。

1.2 方法

入院后患者行常规检查,择期行 LC 手术。术前常规禁饮禁食,入室后开放静脉通道,常规监测患者心率(Heart rate, HR)、脉搏氧饱和度(Pulse oxygen saturation, SpO₂)、平均动脉压(Mean arterial pressure, MAP)、脑电双频指数(Bispectral index, BIS)等。麻醉诱导:两组患者均依次静脉注射舒芬太尼[宜昌人福药业有限责任公司,国药准字 H20054171,规格:1 mL:1:50 μg(以舒芬太尼计)]0.5 μg/kg、顺式阿曲库铵[浙江仙琚制药股份有限公司,国药准字 H20090202,规格:5 mg(以顺阿曲库铵计)]0.2 mg/kg,随后对照组患者静脉注射丙泊酚(广东嘉博制药有限公司,国药准字 H20051842,规格:20 mL:200 mg)2 mg/kg,研究组采用丙泊酚 1 mg/kg 联合依托咪酯(江苏恒瑞医药股份有限公司,国药准字 H32022379,规格:10 mL:20 mg)0.1 mg/kg。30 s 内完成所有诱导过程。面罩给氧去氮 3 min 后,气管插管,连接麻醉机,调整好呼吸参数,呼吸频率 12~16 次/min,潮气量 7 mL/kg,呼气末二氧化碳分压维持在 35~45 mmHg,吸呼比 1:2。麻醉维持泵注丙泊酚 3~4 mg/kg·h,维持镇静

(BIS45~60),泵注瑞芬太尼[宜昌人福药业有限责任公司,国药准字 H20030197,规格:1 mg(以瑞芬太尼 C₂₀H₂₈N₂O₃计)]0.1~0.2 μg/kg·min,维持镇痛,间断静注顺阿曲库铵维持肌肉松弛。术后观察患者麻醉恢复效果,待患者循环稳定、意识清醒后拔管。观察后无异常送回病房。

1.3 观察指标

(1)记录两组患者睁眼时间、拔管时间以及定向力恢复时间。(2)记录两组术中不良反应发生情况。(3)记录两组患者麻醉诱导前、诱导插管时、气腹后 5 min 以及手术结束时的 HR、MAP。于术前、术后 1 d、术后 3 d 采集患者晨时空腹肘静脉血 4 mL,3600 r/min 离心 12 min,离心半径 9 cm,取上清液置于 -80℃ 冰箱中待测。采用酶联免疫吸附实验检测白介素-6(Interleukin-6, IL-6)、C 反应蛋白(C-reactive protein, CRP)和肿瘤坏死因子-α(Tumor necrosis factor-α, TNF-α),试剂盒均来源于武汉博士德生物科技有限公司。(4)于术前 1 h、术后 2 h、术后 24 h、术后 48 h 采用简易智力状态检查表(Mini-mental state examination, MMSE)^[11] 评分评估患者认知功能状况。MMSE 评分主要包括定向力、计算能力、注意力、语言即刻回忆、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。

1.4 统计学方法

采用 SPSS21.0 统计学软件处理数据,计数资料以率的形式表示,采用 χ^2 检验,计量资料以($\bar{x} \pm s$)的形式表示,采用 t 检验,检验标准设置为 $\alpha=0.05$ 。

2 结果

2.1 不同时间点血流动力学指标比较

两组患者诱导前 HR、MAP 比较差异无统计学意义($P>0.05$);两组患者诱导前~手术结束时 HR、MAP 呈先下降后升高趋势($P<0.05$);研究组诱导插管时、气腹后 5 min、手术结束时的 HR、MAP 高于对照组($P<0.05$);详见表 1。

2.2 不同时间点炎症因子水平比较

两组患者术前 IL-6、CRP、TNF-α 比较差异无统计学意义($P>0.05$);两组患者术前~术后 3 d 的 IL-6、CRP、TNF-α 呈升高后降低趋势($P<0.05$);研究组术后 1 d、术后 3 d 的 IL-6、CRP、TNF-α 均低于对照组($P<0.05$);详见表 2。

2.3 两组患者围术期指标比较

研究组睁眼时间、拔管时间、定向力恢复时间较对照组短($P<0.05$);详见表 3。

2.4 两组患者认知功能比较

两组术前 1 h 的 MMSE 评分比较差异无统计学意义($P>0.05$);两组术前 1 h~术后 48 h 的 MMSE 评分呈先下降后升高趋势,但研究组术后 2 h、术后 24 h、术后 48 h MMSE 评分高于对照组($P<0.05$);详见表 4。

2.5 两组不良反应发生率比较

对照组患者出现 1 例呕吐、2 例低血压、1 例注射痛,不良反应发生率为 8.89%(4/45);研究组患者出现 1 例肌阵挛、2 例呕吐、2 例躁动现象,不良反应发生率为 11.11%(5/45);两组患者不良反应总发生率比较未见统计学差异($\chi^2=0.123, P=0.725$)。

表 1 不同时间点血流动力学指标比较($\bar{x} \pm s$)Table 1 Comparison of hemodynamic indexes at different time points($\bar{x} \pm s$)

Groups	Time	HR(beats/min)	MAP(mmHg)
Control group(n=45)	Before the induction	83.48± 8.32	86.35± 8.04
	Induction intubation time	67.30± 7.95 ^a	69.09± 9.52 ^a
	5 minutes after pneumoperitoneum	72.18± 8.65 ^{ab}	74.91± 7.86 ^{ab}
	End of operation time	77.90± 9.42 ^{abc}	79.11± 9.62 ^{abc}
Study group(n=45)	Before the induction	83.75± 8.55	85.92± 8.26
	Induction intubation time	72.34± 9.04 ^{ad}	74.31± 9.79 ^{ad}
	5 minutes after pneumoperitoneum	76.98± 9.13 ^{abd}	78.93± 7.09 ^{abd}
	End of operation time	82.85± 10.12 ^{bcd}	84.56± 8.72 ^{bcd}

Note: comparison with before induction, ^a $P<0.05$; comparison with induction intubation time, ^b $P<0.05$; comparison with 5 minutes after pneumoperitoneum, ^c $P<0.05$; comparison with control group, ^d $P<0.05$.

表 2 不同时间点炎症因子水平比较($\bar{x} \pm s$)Table 2 Comparison of inflammatory factors at different time points($\bar{x} \pm s$)

Groups	Time points	IL-6(pg/mg)	CRP(mg/L)	TNF- α (ng/ml)
Control group(n=45)	Before operation	13.21± 2.25	28.56± 3.48	1.93± 0.29
	1 d after operation	37.63± 3.12 ^a	57.56± 7.15 ^a	4.23± 0.25 ^a
	3 d after operation	25.12± 3.16 ^{ab}	42.29± 6.17 ^{ab}	3.27± 0.18 ^{ab}
Study group(n=45)	Before operation	12.97± 3.12	28.88± 4.24	2.01± 0.22
	1 d after operation	26.95± 3.16 ^{ac}	43.43± 4.15 ^{ac}	3.57± 0.18 ^{ac}
	3 d after operation	18.13± 2.51 ^{abc}	36.94± 3.97 ^{abc}	2.73± 0.23 ^{abc}

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

表 3 两组患者围术期指标比较($\bar{x} \pm s$, min)Table 3 Comparison of perioperative indexes between the two groups($\bar{x} \pm s$, min)

Groups	Eye opening time	Extubation time	Directional force recovery time
Control group(n=45)	9.47± 1.25	12.90± 2.39	32.02± 3.50
Study group(n=45)	7.29± 1.17	8.46± 1.85	24.38± 3.01
t	8.541	9.855	11.102
P	0.000	0.000	0.000

表 4 两组患者认知功能比较($\bar{x} \pm s$, 分)Table 4 Comparison of cognitive function between the two groups($\bar{x} \pm s$, scores)

Groups	1 h before operation	2 h after operation	24 h after operation	48 h after operation
Control group(n=45)	29.29± 0.27	25.37± 0.24 ^a	26.95± 0.31 ^{ab}	27.83± 0.27 ^{abc}
Study group(n=45)	29.33± 0.29	26.76± 0.21 ^a	27.87± 0.22 ^{ab}	28.62± 0.22 ^{abc}
t	0.677	29.239	16.235	15.216
P	0.500	0.000	0.000	0.000

Note: compared with 1H before operation, ^a $P<0.05$; compared with 2 h after operation, ^b $P<0.05$; compared with 24h after operation, ^c $P<0.05$.

3 讨论

近年来,随着人们生活方式、饮食结构的改变,我国居民胆囊息肉、胆囊结石等疾病发病率渐增^[12,13]。LC 是目前开展范围较广的治疗该病的方法,可有效阻止病情进展,获得良好的预

后^[14]。LC 术中需给予二氧化碳气腹,此类操作不可避免的可造成循环系统干扰,且随着气腹压力的增加,循环系统干扰的影响程度也愈发显著,对手术的顺利操作可造成一定影响^[15,16]。此外,认知功能障碍是部分患者术后常见的并发症,越来越多的研究显示^[17,18],全身麻醉药物的在中枢神经中的作用可能会导

致认知功能障碍发生。这就对麻醉医师提出了较高要求,在确保手术顺利进行的前提下,尽可能减轻手术对患者的刺激。现临床在 LC 术中多选用气管内插管或喉罩全身麻醉,全麻诱导通常选用丙泊酚或依托咪酯+舒芬太尼+顺式阿曲库铵的方案实施,其中丙泊酚具有起效快、作用时间短等特点,适合短小手术^[19,20]。但具有剂量和注射速度等因素导致的呼吸、循环抑制为其不足之处。依托咪酯起效快,安全界限大,且对机体呼吸无明显抑制作用,同时其不影响交感神经的张力,诱导时可为患者提供充分的镇静深度和稳定的血流动力学^[21,22]。鉴于此,本研究通过设置对照组,以探讨丙泊酚联合依托咪酯麻醉诱导的有效性和安全性。

本次研究结果显示,两种麻醉方式均可引起不同程度的血流波动,其中丙泊酚联合依托咪酯诱导者的血流波动明显更小,分析其具体作用机制,丙泊酚可通过扩张血管,减少外周血管阻力,继而导致降低血压、抑制心肌收缩及减慢心率,单独应用可影响机体血流动力学^[23,24]。联合依托咪酯后,由于依托咪酯较小影响机体交感、副交感神经形成的反射,可一定程度上降低丙泊酚剂量相关呼吸和循环系统的抑制作用,从而可以发挥更好的麻醉诱导效果^[25-27]。同时研究组在气腹后 5 min、手术结束时的 HR、MAP 亦高于对照组这可能与诱导时丙泊酚用量及手术时间短有关。此外,两组患者均存在炎性损伤,由于术中创伤、血细胞的破坏等导致补体激活,产生大量炎性细胞因子(IL-6、CRP、TNF- α 等),它们既参与机体免疫防御功能,也参与机体的损伤、炎症反应、休克等过程^[28]。但研究组的炎性损伤明显更轻,这可能与依托咪酯具有麻醉、清除氧自由基、抗氧化、抑制中性粒细胞的功能及抑制炎症细胞因子的释放等作用有关^[29]。既往有研究表明丙泊酚或依托咪酯对机体的认知功能都有一定的损害,但也是短暂、可逆的,麻醉停止后可恢复^[30],我们的结果也显示两组患者 MMSE 评分有不同程度的降低,并在术后 48 h 逐步恢复,与以往观点一致,但研究组术后 MMSE 评分高于对照组,这可能与不同麻醉药的不同使用剂量相关。本研究中研究组睁眼时间、拔管时间、定向力恢复时间短于对照组,可见丙泊酚联合依托咪酯麻醉诱导可发挥良好的麻醉诱导效果,既可保证诱导顺利进行,又有利于患者术后恢复,同时本研究两组不良反应发生率对比未见显著差异,也说明丙泊酚联合依托咪酯麻醉诱导的安全性较好。

综上所述,LC 患者给予丙泊酚联合依托咪酯麻醉诱导的麻醉效果良好,可有效减轻血流动力学波动及炎性应激,降低术后认知功能损害,且安全性较好,具有较好的临床应用价值。

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