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七氟醚复合瑞芬太尼静吸麻醉对急性胆囊炎腹腔镜手术患者麻醉效果、血流动力学及炎性因子的影响*

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摘要 目的:探讨七氟醚复合瑞芬太尼静吸麻醉对急性胆囊炎腹腔镜手术患者麻醉效果、血流动力学及炎性因子的影响。**方法:**选取 2018 年 1 月到 2019 年 12 月期间我院收治的 120 例急性胆囊炎腹腔镜手术患者,根据信封抽签法分为对照组 60 例(丙泊酚复合瑞芬太尼)和观察组 60 例(七氟醚复合瑞芬太尼),对比两组麻醉效果、血流动力学、炎性因子及不良反应。**结果:**观察组术毕(T5)时间点心率(HR)、平均动脉压(MAP)与麻醉前(T1)比较未见显著性差异($P>0.05$),观察组插管后 1 min(T2)~T5 时间点 HR、MAP 高于对照组($P<0.05$)。两组术后 1 d、术后 3 d 肿瘤坏死因子- α (TNF- α)、C 反应蛋白水平(CRP)、白介素-6(IL-6)均高于术前,观察组术后 1 d、术后 3 d CRP、IL-6、TNF- α 低于对照组($P<0.05$)。观察组自主呼吸恢复时间、定向力恢复时间、睁眼时间、言语应答时间均短于对照组($P<0.05$)。两组不良反应发生率组间比较无显著性差异($P>0.05$)。**结论:**急性胆囊炎腹腔镜手术患者采用七氟醚复合瑞芬太尼静吸麻醉,麻醉效果较好,可平稳患者血流动力学,减轻炎症应激且安全性较好。

关键词:七氟醚;瑞芬太尼;静吸麻醉;急性胆囊炎;腹腔镜手术;麻醉效果;血流动力学;炎性因子

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Effects of Sevoflurane Combined with Remifentanyl on Anesthesia Effects, Hemodynamics and Inflammatory Factors in Patients with Acute Cholecystitis Undergoing*

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ABSTRACT Objective: To investigate the effect of sevoflurane combined with remifentanyl on anesthesia effects, hemodynamics and inflammatory factors in patients with acute cholecystitis undergoing laparoscopic cholecystectomy. **Methods:** 120 patients with acute cholecystitis undergoing laparoscopic cholecystectomy in our hospital from January 2018 to December 2019 were selected, and randomly divided into control group of 60 cases (propofol combined with remifentanyl) and observation group of 60 cases (sevoflurane combined with remifentanyl) according to the envelope lottery. The anesthesia effect, hemodynamics, inflammatory factors and adverse reactions of the two groups were compared. **Results:** There was no significant difference in heart rate (HR) and mean arterial pressure (MAP) between end of operation (T5) and before anesthesia (T1) in the observation group ($P>0.05$), HR and MAP of the observation group at 1 min after intubation (T2)~T5 were higher than those of the control group ($P<0.05$). The levels of tumor necrosis factor- α (TNF- α), C-reactive protein (CRP) and interleukin-6 (IL-6) of both groups from 1 d after operation to 3 d after operation in the two groups were higher than those before operation, and CRP, IL-6 and TNF- α of the observation group at 1 d after operation and 3 d after operation were lower than those of the control group ($P<0.05$). The speech response time, eye opening time, directional force recovery time and spontaneous breathing recovery time of the observation group were shorter than those of the control group ($P<0.05$). There was no significant difference in the incidence of adverse reactions between the two groups ($P>0.05$). **Conclusion:** Sevoflurane combined with remifentanyl for acute cholecystitis patients undergoing laparoscopic surgery has good anesthetic effect, can stabilize the hemodynamics of patients, reduce inflammatory stress and it has good safety.

Key words: Sevoflurane; Remifentanyl; Intravenous anesthesia; Acute cholecystitis; Laparoscopic surgery; Anesthetic effect; Hemodynamics; Inflammatory factors

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前言

急性胆囊炎是临床常见急腹症,主要是由细菌侵袭以及胆管阻塞所引起^[1]。该病以女性较为多见,约有95%可伴有结石,其典型临床特征为右上腹阵发性绞痛,伴有明显的腹肌强直和触痛,若未能予以及时治疗,可危及患者生命^[2-4]。腹腔镜胆囊切除术是治疗急性胆囊炎的常用方法,其优点为手术用时短、创伤小等^[5,6]。因该手术需术中建立人工气腹,易干扰呼吸系统、循环系统,麻醉要求高^[7,8]。目前临床腹腔镜胆囊切除术中常用的麻醉药物有瑞芬太尼^[9]、丙泊酚^[10],两种麻醉药物均具有起效迅速、消除快等特点,但丙泊酚的镇痛效果相对较弱。七氟醚为卤素类吸入麻醉药,起效快,对呼吸系统刺激较小^[11]。本研究通过探讨急性胆囊炎腹腔镜手术患者应用七氟醚复合瑞芬太尼静吸麻醉效果、血流动力学及炎症因子的影响,以期急性胆囊炎腹腔镜手术的麻醉方案选择提供参考。

1 资料与方法

1.1 临床资料

选取2018年1月到2019年12月期间我院收治的急性胆囊炎腹腔镜手术患者120例,纳入标准:(1)急性胆囊炎诊断标准参考《实用外科学》^[12];(2)美国麻醉医师协会分级(ASA)^[13]均为I~III级;(3)签署知情同意书;(4)均符合手术指征,择期行腹腔镜胆囊切除术;(5)手术均由同一组医师完成。排除标准:(1)合并肝肾功能不全者;(2)凝血功能障碍者;(3)伴有呼吸系统疾病者;(4)合并精神异常,无法正常沟通者;(5)长期服用阿片类药物者;(6)对研究所用麻醉药物过敏者。根据信封抽签法将患者分为观察组60例和对照组60例,其中对照组女33例,男27例,年龄34~67岁,平均 (49.52 ± 3.86) 岁;ASA分级:I级25例、II级18例、III级17例;体质量指数 $20 \sim 26 \text{ kg/m}^2$,平均 $(23.17 \pm 0.84) \text{ kg/m}^2$ 。观察组女35例,男25例,年龄32~69岁,平均 (49.14 ± 4.29) 岁;ASA分级:I级27例、II级20例、III级13例;体质量指数 $20 \sim 27 \text{ kg/m}^2$,平均 $(23.24 \pm 0.79) \text{ kg/m}^2$ 。两组年龄、体质量指数、性别等一般资料均衡可比($P > 0.05$)。本研究经我院伦理学委员会批准。

1.2 方法

两组均行腹腔镜胆囊切除术,术前禁水6h,禁食8h,麻醉前30min肌注阿托品(东北制药集团沈阳第一制药有限公司,国药准字H21021924,规格:盐酸吗啡10mg,硫酸阿托品0.5mg)0.5mg、苯巴比妥钠(重庆药友制药有限责任公司,国药准字H50021537,规格:2mL:0.2g)0.1g,入室后开放上肢静脉,常规监测心率(HR)、平均动脉压(MAP)等生命体征。对照组面罩吸氧,给予丙泊酚(广东嘉博制药有限公司,国药准字H20133360,规格:50mL:500mg)2mg/kg复合瑞芬太尼[国药集团工业有限公司廊坊分公司,国药准字H20123421,规格:2mg(以瑞芬太尼C20H28N2O5计)]200 μg 麻醉诱导,患者意识消失后静注维库溴铵(扬子江药业集团有限公司,国药准字H20066941,规格:4mg)0.1mg/kg,5min后行气管插管,机械通气,潮气量 $8 \sim 12 \text{ mL/kg}$,丙泊酚维持麻醉 $0.2 \text{ mg/kg} \cdot \text{min}$,术毕即可停用麻醉药物。观察组面罩吸氧,靶控输注瑞芬太尼 3 ng/mL ,开启七氟醚(河北一品制药股份有限公司,国药准字

H20173156,规格:250mL)挥发罐,氧流量 4 L/min ,从0.5%浓度开始吸入,每呼吸2~3次增加0.5%至4%,患者意识消失后静注维库溴铵 0.1 mg/kg ,5min后行气管插管,机械通气,潮气量 $8 \sim 12 \text{ mL/kg}$,持续吸入2%七氟醚,术毕即可停用麻醉药物。

1.3 评价指标

(1)对比两组麻醉前(T1)、插管后1min(T2)、切皮时(T3)、气腹5min后(T4)及术毕(T5)的HR、MAP。(2)记录两组围术期不良反应。(3)记录两组言语应答时间、睁眼时间、自主呼吸恢复时间及定向力恢复时间。(4)采集两组患者术前、术后1d、术后3d的空腹肘静脉血4mL,经离心处理(离心半径8cm,3400r/min离心12min)分离上清液,采用双抗体夹心酶联免疫吸附法检测肿瘤坏死因子- α (TNF- α)、C反应蛋白(CRP)及白介素-6(IL-6)水平。

1.4 统计学方法

以SPSS23.0软件进行数据分析。呈正态分布的计量资料以 $\text{MEAN} \pm \text{SD}$ 表示,组间比较采用t检验,计数资料以n(%)表示,组间比较采用卡方检验。重复测量资料采用重复测量方差分析,两组间比较采用LSD-t检验,组内比较采用差值t检验。使用Bonferroni校正法对时间维度多次比较的检验水准进行调整,检验水准为 $\alpha = 0.05$ 。

2 结果

2.1 两组血流动力学指标比较

两组血流动力学指标数据列于下表,整体比较可知:各指标组间差异、组内(时间维度)差异及交互作用均有显著性意义($P < 0.05$)。两组T1时间点HR、MAP比较无差异($P > 0.05$),两组T2~T4时间点HR、MAP较T1下降($P < 0.05$),对照组T5时间点HR、MAP与T1比较有差异($P < 0.05$),观察组T5时间点HR、MAP与T1比较未见显著性差异($P > 0.05$),但观察组T2~T5时间点HR、MAP高于对照组($P < 0.05$),数据及详细的比较结果参见表1。

2.2 两组炎症因子比较

整体比较,各指标组间差异、组内(时间维度)差异及交互作用均有显著性意义($P < 0.05$)。两组术前CRP、IL-6、TNF- α 比较无差异($P > 0.05$),两组术后1d、术后3dCRP、IL-6、TNF- α 均高于术前,但是观察组术后1d、术后3dCRP、IL-6、TNF- α 低于对照组($P < 0.05$),详见表2。

2.3 两组麻醉效果比较

观察组定向力恢复时间、自主呼吸恢复时间、睁眼时间及言语应答时间均短于对照组($P < 0.05$),详见表3。

2.4 两组不良反应发生情况比较

两组不良反应发生率比较无差异($P > 0.05$),详见表4。

3 讨论

急性胆囊炎的主要生理病理表现为细菌入侵胆管,引起粘膜充血水肿,导致化脓性胆囊炎的发生,伴随胆管梗阻、胆汁淤积等基础病变的进一步发展,胆囊内压力增加,胆囊壁血管血供不足,最终导致胆囊坏死、穿孔的发生,此时的病情进展迅速,短时间内即可出现感染性休克或多脏器功能损害,危及患者生命^[14-16]。腹腔镜胆囊切除术是目前治疗急性胆囊炎的常

表 1 两组血流动力学指标比较($\bar{x} \pm s$)Table 1 Comparison of hemodynamic indexes between the two groups($\bar{x} \pm s$)

Time points	HR(beats/min)		MAP(mmHg)	
	Control group (n=60)	Observation group (n=60)	Control group (n=60)	Observation group (n=60)
T1	86.04± 7.52	85.96± 6.65	103.79± 8.74	103.84± 7.37
T2	70.17± 6.75 ^a	73.79± 6.74 ^{ac}	85.81± 7.63 ^a	90.16± 6.92 ^{ac}
T3	73.52± 7.17 ^{ab}	77.83± 7.32 ^{abc}	89.58± 8.63 ^{ab}	94.14± 7.87 ^{abc}
T4	77.81± 5.24 ^{abc}	81.35± 7.66 ^{abce}	94.52± 7.71 ^{abc}	98.26± 7.64 ^{abce}
T5	81.14± 6.76 ^{abcd}	84.96± 6.41 ^{bcd}	98.53± 6.92 ^{abcd}	102.96± 8.52 ^{bcd}
Overall analysis	HF coefficient		0.9979	
Comparison between groups	F, P		69.238, 0.000	
Intra group comparison	F, P		174.674, 0.000	
Interaction	F, P		3.284, 0.005	

Note: compared with T1 time point, ^a $P<0.05$; compared with T2 time point, ^b $P<0.05$; compared with T3 time point, ^c $P<0.05$; compared with T4 time point, ^d $P<0.05$; compared with control group, ^e $P<0.05$.

表 2 两组炎症因子比较($\bar{x} \pm s$)Table 2 Comparison of inflammatory factors between the two groups($\bar{x} \pm s$)

Time points	CRP(mg/L)		IL-6(μ g/L)		TNF- α (μ g/L)	
	Control group (n=60)	Observation group (n=60)	Control group (n=60)	Observation group (n=60)	Control group (n=60)	Observation group (n=60)
Before operation	27.39± 3.23	27.31± 4.09	36.24± 4.42	36.39± 5.72	36.88± 6.78	36.56± 5.01
1 d after operation	56.11± 5.18 ^a	45.36± 6.26 ^{ac}	69.53± 5.33 ^a	57.52± 6.42 ^{ac}	68.24± 5.65 ^a	58.16± 6.15 ^{ac}
3 d after operation	42.34± 6.54 ^{ab}	36.74± 4.87 ^{abc}	55.18± 4.95 ^{ab}	42.83± 4.31 ^{abc}	53.54± 6.32 ^{ab}	42.93± 5.36 ^{abc}
Overall analysis	HF coefficient		0.9950		0.9747	
Comparison between groups	F, P		409.032, 0.000		214.145, 0.000	
Intra group comparison	F, P		1,109.820, 0.000		1,069.784, 0.000	
Interaction	F, P		108.571, 0.000		54.096, 0.000	

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 两组麻醉效果比较($\bar{x} \pm s, \text{min}$)Table 3 Comparison of anesthetic effect between the two groups($\bar{x} \pm s, \text{min}$)

Groups	n	Spontaneous Breathing recovery time	Eye Opening time	Directional Force recovery time	Speech response time
Control group	60	8.53± 0.64	13.02± 1.58	16.46± 1.26	19.48± 1.37
Observation group	60	6.13± 0.57	9.34± 1.73	12.83± 1.71	15.47± 1.44
t		21.692	12.166	13.238	15.628
P		0.000	0.000	0.000	0.000

表 4 两组不良反应发生率比较 例(%)

Table 4 Comparison of the incidence of adverse reactions between the two groups [n(%)]

Groups	n	Fidgety	Pain	Nausea and vomiting	Coughing	Total incidence rate
Control group	60	2(3.33)	0(0.00)	3(5.00)	1(1.67)	6(10.00)
Observation group	60	1(1.33)	0(0.00)	2(2.00)	1(1.67)	4(6.67)
χ^2						0.436
P						0.509

用术式,临床技术已较为成熟,可有效阻止疾病进展,促进临床转归^[17,18],但由于腹腔镜胆囊切除术为了扩大腹壁与内脏的空间,通常需建立人工气腹以提供宽阔的视野^[19]。人工气腹中使用的二氧化碳气体进入腹腔后可影响胸廓扩张,造成通气血流比障碍,引发交感神经兴奋和机体防御性反射,导致机体血流动力学紊乱,易出现心律失常、心肌缺氧及心脑血管意外,同时术中麻醉诱导、气管插管拔管也可导致血压剧烈波动、苏醒延迟、炎性应激等情况^[20-22]。因此,这就导致腹腔镜胆囊切除术需要一个安全有效的麻醉环境,以促进手术顺利进行。

瑞芬太尼是短效阿片受体激动剂,在麻醉中常以持续输注的形式给药,因为该药进入人体后1 min内就能达到血-脑平衡,只是维持的时间比较短暂^[23]。丙泊酚是一种烷基酚类短效静脉麻醉药,起效迅速、无蓄积,但丙泊酚诱导时会引起心肌氧供减少、血压下降,出现血流波动^[24]。七氟醚是一种新型吸入麻醉药,近年来应用广泛,其浓度易调控,组织血液中溶解度低,血气分配系数低^[25]。但七氟醚或丙泊酚单独使用时均易出现并发症,且苏醒时间较长,降低麻醉效果,故常与其他麻醉药物联合使用^[26]。临床对比七氟醚、丙泊酚分别复合瑞芬太尼的效果,本研究发现七氟醚复合瑞芬太尼静吸麻醉的患者其血流动力学波动更小,术后炎症应激反应更轻。瑞芬太尼除了可迅速达到血-脑平衡,起效迅速外,同时具有在体内可被快速清除,并对机体肝肾功能影响较轻等优势^[27]。七氟醚作为吸入性麻醉药物,本身即具备扩张外周血管,减少心排出量,降低血压及心率的作用,可使术中血流动力学稳定,减弱应激反应对心肌影响^[28]。瑞芬太尼与吸入性麻醉药合用可发挥协同作用,发挥良好的镇静镇痛效果,利于手术顺利进行^[29]。进一步研究发现,观察组自主呼吸恢复时间、定向力恢复时间、睁眼时间、言语应答时间均较对照组短,证实了七氟醚复合瑞芬太尼静吸麻醉的麻醉效果更为显著。既往研究显示七氟醚麻醉具有较低的血气分配系数,利于麻醉师控制麻醉深度,因此,颅内压可维持相对稳定,麻醉诱导及苏醒的时间较短,降低脑组织的代谢水平,神经系统影响小,减少神经细胞凋亡,有效提高神经系统的功能,从而促进患者术后恢复^[30,31]。另本研究中两组不良反应发生率组间比较差异无统计学意义,表明七氟醚复合瑞芬太尼静吸麻醉应用于急性胆囊炎腹腔镜手术患者安全性较好。

综上所述,急性胆囊炎腹腔镜手术患者采用七氟醚复合瑞芬太尼静吸麻醉,麻醉效果较好,可平稳患者血流动力学,减轻炎症应激且安全性较好。

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(上接第 518 页)

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