

doi: 10.13241/j.cnki.pmb.2022.10.023

右美托咪定联合七氟醚对老年腹腔镜胃肠肿瘤切除术患者 应激反应和脑氧代谢的影响 *

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摘要 目的:观察老年腹腔镜胃肠肿瘤切除术患者使用七氟醚联合右美托咪定复合麻醉后,机体应激反应和脑氧代谢的变化情况。**方法:**将我院 2020 年 1 月至 2020 年 12 月期间收治的 100 例老年腹腔镜胃肠肿瘤切除术患者根据随机数字表法分为对照组(n=50,七氟醚麻醉)和研究组(n=50,右美托咪定联合七氟醚麻醉)。观察两组血流动力学、应激反应、脑氧代谢、认知功能和不良反应。**结果:**两组手术 60 min(T1)~术后 30 min(T3)时间点较麻醉诱导前(T0)时间点心率(HR)先下降后升高,平均动脉压(MAP)先升高后下降($P<0.05$)。研究组 T1~T3 时间点 HR 及 MAP 低于对照组($P<0.05$)。两组术后 3 d 多巴胺(DA)、肾上腺素(AD)、去甲肾上腺素(NE)水平升高,但研究组低于对照组($P<0.05$)。两组术后 3 d 血氧含量差(DajvO₂)和脑氧摄取率(CERO₂)下降,且研究组低于对照组($P<0.05$)。研究组术后 6 h、术后 1 d、术后 3 d 简易精神状态检查量表(MMSE)评分高于对照组($P<0.05$)。两组不良反应发生率,对比无显著性差异($P>0.05$)。**结论:**七氟醚联合右美托咪定应用于老年腹腔镜胃肠肿瘤切除术患者,可有效减轻机体应激反应,减轻机体认知功能损伤,维持血流动力学稳定和脑氧代谢。

关键词:右美托咪定;七氟醚;老年;腹腔镜;胃肠肿瘤切除术;脑氧代谢

中图分类号:R735 **文献标识码:**A **文章编号:**1673-6273(2022)10-1909-05

Effects of Dexmedetomidine Combined with Sevoflurane on Stress Response and Cerebral Oxygen Metabolism in Elderly Patients Undergoing Laparoscopic Gastrointestinal Tumor Resection*

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ABSTRACT Objective: To observe the effects of dexmedetomidine combined with sevoflurane on cerebral oxygen metabolism and stress response in elderly patients undergoing laparoscopic gastrointestinal tumor resection. **Methods:** 100 elderly patients undergoing laparoscopic gastrointestinal tumor resection who were treated in our hospital from January 2020 to December 2020 were divided into control group (n=50, sevoflurane anesthesia) and study group (n=50, dexmedetomidine combined with sevoflurane anesthesia) by random number table method. Hemodynamics, stress response, cerebral oxygen metabolism, cognitive function and adverse reactions of two groups were observed. **Results:** 60 min (T1) to 30 min (T3) after operation, The heart rate (HR) of the two groups first decreased and then increased compared with the time point before induction of anesthesia (T0), and the mean arterial pressure (MAP) first increased and then decreased ($P<0.05$). HR at T1~T3 time points in the study group were lower than those in the control group ($P<0.05$). The dopamine (DA), epinephrine (AD) and norepinephrine (NE) levels in two groups at 3 d after operation were increased, but the study group was lower than the control group ($P<0.05$). The difference of blood oxygen content (DajvO₂) and cerebral oxygen uptake rate (CERO₂) in both groups at 3d after operation decreased, but the study group was lower than the control group ($P<0.05$). The scores of mini mental state examination scale (MMSE) in the study group at 6h, 1d and 3d after operation 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 ($P>0.05$). **Conclusion:** Sevoflurane combined with dexmedetomidine in elderly patients undergoing laparoscopic gastrointestinal tumor resection can effectively reduce the body's stress response, reduce the damage of cognitive function, and maintain hemodynamic stability and cerebral oxygen metabolism.

Key words: Dexmedetomidine; Sevoflurane; Elderly; Laparoscopic; Gastrointestinal tumor resection; Cerebral oxygen metabolism

* 基金项目:江苏省自然科学基金青年基金项目(BK2017447)

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(收稿日期:2021-11-20 接受日期:2021-12-14)

Chinese Library Classification(CLC): R735 Document code: A

Article ID: 1673-6273(2022)10-1909-05

前言

胃肠肿瘤的临床症状主要表现为腹部疼痛、肠道出血等,腹腔镜手术是早期胃肠肿瘤的主要治疗方案,创伤小、安全性高,患者接受度较高^[1]。随着人口老龄化的加剧,老年胃肠肿瘤发病率逐年递增^[2]。患者随着年龄的增加身体机能退化,手术耐力差,术后应激反应强烈,导致患者术后发生较多的并发症,影响患者术后恢复^[3,4]。而合理的麻醉药物则有利于手术的顺利进行,并可帮助患者尽早恢复。七氟醚是临床常用的麻醉药物,具有肌松药用量小、术后苏醒快等优点,但其对部分患者可能存在肾毒性作用^[5]。右美托咪定是近年来临床上愈发受重视的麻醉药物,起效快,作用时间短,具有镇痛、镇静、抗焦虑作用^[6]。本次研究以老年腹腔镜胃肠肿瘤切除术患者作为观察对象,探讨七氟醚联合右美托咪定的临床应用价值,以期为此类患者临床麻醉方案的选择提供参考依据。

1 资料与方法

1.1 临床资料

选取2020年1月至2020年12月期间我院收治的老年腹腔镜胃肠肿瘤切除术患者100例。本研究获本院医学伦理委员会批准。纳入标准:(1)年龄 ≥ 60 岁;(2)签署同意书;(3)美国麻醉医师协会(ASA)分级II-III级者^[7];(4)患者具备手术指征;(5)对本次研究药物无过敏。排除标准:(1)严重心肝肾功能障碍患者;(2)术前接受放化疗;(3)精神疾病或服用精神类药物;(4)术前进行过镇痛治疗;(5)酒精、药物成瘾。采用随机数字表法分为对照组和研究组。研究组50例中,女性20例,男性30例;胃癌15例,结肠癌12例,直肠癌17例,胃间质瘤及其它6例;合并基础疾病:糖尿病、高血压、高血脂各为7例、13例、6例;年龄61~75岁,平均 (70.36 ± 2.08) 岁;ASA分级:II级、III级各为29例、21例;BMI $21 \sim 31 \text{ kg/m}^2$,平均 $(26.37 \pm 1.14) \text{ kg/m}^2$ 。对照组50例中,女性17例,男性33例;胃癌17例,结肠癌10例,直肠癌16例,胃间质瘤及其它7例;合并基础疾病:糖尿病、高血压、高血脂各为8例、12例、7例;年龄60~76岁,平均 (70.94 ± 2.37) 岁;ASA分级:II级、III级各为31例、19例;体质指数(BMI) $22 \sim 31 \text{ kg/m}^2$,平均 $(26.83 \pm 1.09) \text{ kg/m}^2$ 。两组一般资料及肿瘤分布对比无差异($P > 0.05$),可比性佳。

1.2 方法

术前8h禁食禁药,术前6h禁水。入室后连接美国惠普公司生产的78352C型心电监护仪,开放上肢静脉通路。两组麻醉诱导药物:咪达唑仑注射液(江苏九旭药业有限公司,规格:3 mL:15 mg,国药准字H20153019)0.03 mg/kg、枸橼酸舒芬太尼注射液(国药集团工业有限公司廊坊分公司,规格:按 $\text{C}_{22}\text{H}_{30}\text{N}_2\text{O}_5\text{S}$ 计1 mL:50 μg ,国药准字H20203712)0.5 $\mu\text{g/kg}$ 、丙泊酚乳状注射液(广东嘉博制药有限公司,规格:50 mL:1 g,国药准字H20143369)1~1.5 mg/kg、注射用维库溴铵(晋城海斯制药有限公司,规格:4 mg,国药准字H20084542)0.1 mg/kg。手术期间对照组采用1%~2%七氟醚吸入浓度维持麻醉,研究组

在对照组基础上加用盐酸右美托咪定注射液[江苏恩华药业股份有限公司,规格:1 mL:0.1 mg(按右美托咪定计),国药准字H20133331]维持麻醉,10 min内以 $(4 \mu\text{g} \cdot \text{mL}^{-1})1 \mu\text{g} \cdot \text{kg}^{-1}$ 泵入,随后以 $0.5 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$ 维持至术毕前10 min,麻醉过程中视患者具体情况调整剂量。术后,待患者自主呼吸恢复,拔除气管导管,送至麻醉恢复室。

1.3 观察指标

(1)监测两组麻醉诱导前(T0)、手术60 min(T1)、手术结束时(T2)、手术后30 min(T3)的平均动脉压(MAP)、心率(HR)。(2)分别于术前、术后3 d抽取患者静脉血4 mL,采用酶联免疫吸附试验检测多巴胺(DA)、肾上腺素(AD)、去甲肾上腺素(NE)水平,严格参考试剂盒(上海酶研生物科技有限公司)说明书步骤进行操作。(3)分别于术前、术后3 d采集血样行血气分析,测量动脉血氧含量(CaO_2)、颈内静脉血氧含量(CjvO_2),根据Fick公式^[8]计算脑氧摄取率(CERO_2)和动脉颈内静脉血氧含量差(DajvO_2)。其中 $\text{CERO}_2 = (\text{CaO}_2 - \text{CjvO}_2) / \text{CaO}_2 \times 100\%$; $\text{DajvO}_2 = \text{CaO}_2 - \text{CjvO}_2$ 。(4)对患者进行简易精神状态检查量表(MMSE)^[9]评分,MMSE总分30分,分数越高,认知功能越高。评估时间:术前、术后6 h、术后1 d、术后3 d。(5)记录麻醉期间不良反应发生情况。

1.4 统计学方法

使用SPSS23.0进行研究资料分析。HR、MMSE、MAP、 CjvO_2 等计量数据以 $(\bar{x} \pm s)$ 描述,组内前后比较为配对t检验,组间比较为成组t检验或校正t'检验,重复观测资料行重复测量方差分析。计数资料以例数及率描述,比较为卡方检验。统计检验水准 $\alpha = 0.05$,均为双侧检验。

2 结果

2.1 血流动力学指标对比

两组T1~T3时间点较T0时间点HR先下降后升高,MAP先升高后下降($P < 0.05$)。研究组T1~T3时间点HR及MAP低于对照组($P < 0.05$)。见表1。

2.2 应激反应指标对比

两组术后3 d DA、AD、NE水平升高,但研究组低于对照组($P < 0.05$),见表2。

2.3 脑氧代谢指标对比

两组术后3 d DajvO_2 、 CERO_2 下降,且研究组低于对照组($P < 0.05$),见表3。

2.4 认知功能指标对比

两组术后6 h、术后1 d、术后3 d的MMSE评分较术前先降低后升高($P < 0.05$),但研究组上述时间点的MMSE评分均高于对照组($P < 0.05$),见表4。

2.5 不良反应发生率对比

两组不良反应发生率,对比无差异($P > 0.05$),见表5。

3 讨论

胃肠肿瘤切除术术式现今已较为成熟,但手术中的牵拉刺

表 1 血流动力学指标对比($\bar{x} \pm s$)
Table 1 Comparison of hemodynamic indexes($\bar{x} \pm s$)

Groups	Time points	HR(beats/min)	MAP(mmHg)
Control group(n=50)	T0	75.54±5.62	94.76±6.51
	T1	64.62±5.39 ^a	114.63±5.48 ^a
	T2	67.99±6.28 ^a	109.83±6.21 ^a
	T3	72.08±5.54 ^a	105.48±7.66 ^a
Study group(n=50)	T0	75.87±6.49	94.39±5.29
	T1	60.59±5.45 ^{at}	108.90±6.50 ^{at}
	T2	64.34±5.53 ^{at}	103.94±5.63 ^{at}
	T3	68.62±5.65 ^{at}	99.66±7.60 ^{at}
Overall analysis	HF coefficient	0.9669	1.0126
Group comparison	F, P	37.517, 0.000	56.871, 0.000
Intra group comparison	F, P	83.816, 0.000	121.848, 0.000
Interaction	F, P	1.662, 0.175	3.474, 0.008

Note: significance marker a was compared with the two groups $P < 0.05$. The precise comparison in time and latitude was difference t-test, and the significance marker t was compared with the first time point in the group $P < 0.05$.

表 2 应激反应指标对比($\bar{x} \pm s$, ng/L)
Table 2 Comparison of stress response indexes($\bar{x} \pm s$, ng/L)

Groups	Time points	DA	AD	NE
Control group n=50	Before operation	81.96±5.23	103.59±12.31	516.08±54.05
	3 d after operation	93.45±5.38	162.84±15.88	682.06±69.37
	t	11.300	16.785	10.350
	P	0.000	0.000	0.000
Study group n=50	Before operation	81.52±6.17	103.18±11.24	517.11±52.79
	3 d after operation	88.23±6.40	131.07±14.86	561.75±48.62
	t	4.014	16.034	3.121
	P	0.000	0.000	0.003
Comparison of two groups (t, P)	Before operation	0.385, 0.701	0.174, 0.862	0.096, 0.924
	3 d after operation	4.415, 0.000	10.329, 0.000	10.043, 0.000

表 3 脑氧代谢指标对比($\bar{x} \pm s$)
Table 3 Comparison of cerebral oxygen metabolism indexes($\bar{x} \pm s$)

Groups	Time points	DajvO ₂ (ml/L)	CERO ₂ (%)
Control group n=50	Before operation	55.13±6.34	37.13±4.25
	3 d after operation	48.52±8.47	31.93±4.21
	t	17.705	5.426
	P	0.000	0.000
Study group n=50	Before operation	55.62±7.21	37.62±5.73
	3 d after operation	41.97±5.26	25.18±5.25
	t	8.331	12.969
	P	0.000	0.000
Comparison of two groups (t, P)	Before operation	0.361, 0.719	0.486, 0.628
	3 d after operation	3.865, 0.000	3.415, 0.001

表 4 认知功能指标对比($\bar{x} \pm s$, 分)
Table 4 Comparison of cognitive function indexes($\bar{x} \pm s$, scores)

Groups	Time points	MMSE score
Control group(n=50)	Before operation	26.12±0.26
	6 h after operation	23.85±0.74 ^t
	1 d after operation	24.18±0.62 ^t
	3 d after operation	25.21±0.31 ^t
Study group(n=50)	Before operation	26.07±0.28 ^a
	6 h after operation	24.45±0.82 ^{at}
	1 d after operation	25.03±0.57 ^{at}
	3 d after operation	25.87±0.38 ^{at}
Overall analysis	HF coefficient	0.8667
Group comparison	F, P	417.455, 0.000
Intra group comparison	F, P	1,402.461, 0.000
Interaction	F, P	42.012, 0.000

Note: significance marker a was compared with the two groups $P < 0.05$. The precise comparison in time and latitude was difference t-test, and the significance marker t was compared with the first time point in the group $P < 0.05$.

表 5 不良反应发生率对比[例(%)]
Table 5 Comparison of adverse reaction rates[n(%)]

Groups	Nausea and vomiting	Restlessness	Hypertension	Bradycardia	Total incidence rate
Control group(n=50)	2(4.00)	1(2.00)	1(2.00)	2(4.00)	6(12.00)
Study group(n=50)	2(4.00)	2(4.00)	2(4.00)	2(4.00)	8(16.00)
χ^2					0.332
P					0.564

激、麻醉刺激可使机体产生一系列的生理病理变化,如血流动力学波动、应激反应、术后并发症等,一定程度上影响患者术后康复^[10,11]。尤其针对老年腹腔镜胃肠肿瘤切除术患者,其应激反应相对年轻群体更强烈,且当其血流波动明显时,还可对机体心脑血管产生不良影响^[12,13]。所以选择一种合理的麻醉方案十分关键。七氟醚溶解度较低,可快速吸收和清除,在维持期间也可快速达到所需的效应浓度,故被认为是重要的挥发性麻醉药之一^[14]。但也有不少研究认为七氟醚会增加术后谵妄的发生风险^[15,16],具体表现为:七氟醚可能破坏神经突触结构,阻碍突触传递过程,从而导致认知功能下降。有研究发现^[17],应用右美托咪定可减少麻醉药物使用量,且具有一定脑保护与神经保护作用。

本次观察结果显示,复合麻醉的老年患者围术期间血流动力学较为稳定。究其原因,右美托咪定是一种肾上腺素受体激动剂,可作用于 α_2 肾上腺素能受体,促进钾离子通道开放,发挥良好的镇静、镇痛、抗焦虑及抗交感等多种效应,促使患者体内血流动力学保持稳定^[18,19]。以往 Bala R 等^[20]学者的研究也发现右美托咪定具有较好的稳定血流动力学作用,效果确切。研究显示,术中缺血再灌注损伤、外界毒素干预等均可激活炎症反应,炎症因子通过与血脑屏障中内皮细胞的表面受体结合,激活中枢炎症反应通路,导致氧化应激反应,造成神经细胞

损伤,甚至死亡^[21]。应激指标如 DA、AD、NE 等能导致一系列内分泌反应,如儿茶酚胺过度分泌,产生细胞毒性。观察结果显示七氟醚联合右美托咪定可有效减轻机体应激反应^[22]。其机制可能为右美托咪定选择性兴奋中枢孤束核突出后 α_2 受体,抑制儿茶酚胺释放,减轻机体应激反应^[23,24]。正常情况下,脑血流量是与脑氧代谢率变化同步相关的,过度缺乏的脑血流量会引起脑继发性损害^[25]。本次研究中,两组患者均存在脑氧代谢失衡情况,但复合麻醉的患者其脑氧代谢失衡程度较轻。这可能与右美托咪定可通过抑制儿茶酚胺及细胞因子的释放,从而起到脑保护作用,有效调节机体脑氧代谢有关^[26-28]。一项 meta 分析研究结果显示右美托咪定可以缩短患者 ICU 停留时间,减少认知功能障碍的发生风险^[29]。本次研究中,复合麻醉的老年患者其认知功能损伤程度更轻。这主要是因为右美托咪定可抑制 NE 的释放及降低血浆中儿茶酚胺浓度,同时右美托咪定还可减轻脑缺血再灌注损伤,有效保护人体神经功能^[30]。此外,两组不良反应发生率,对比无显著性差异,提示右美托咪定联合七氟醚较为安全,是一种可靠的麻醉方案。

综上所述,七氟醚联合右美托咪定应用于老年腹腔镜胃肠肿瘤切除术患者,可有效减轻机体应激反应,减轻机体认知功能损伤,维持血流动力学稳定和脑氧代谢。

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