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不同剂量舒芬太尼对直肠癌患者全麻气管插管应激反应和血流动力学的影响 *

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摘要 目的:研究不同剂量舒芬太尼对直肠癌患者全麻气管插管应激反应和血流动力学的影响。**方法:**选择 2017 年 1 月~2019 年 12 月在我院择期进行腹腔镜直肠癌切除术患者 90 例作为研究对象,依据随机数字表法分为 A 组、B 组、C 组,每组各 30 例。A 组:0.4 $\mu\text{g/kg}$ 舒芬太尼、B 组:0.5 $\mu\text{g/kg}$ 舒芬太尼、C 组:0.6 $\mu\text{g/kg}$ 舒芬太尼,观察并比较各组气管插管应激反应,插管前后血流动力学指标,麻醉恢复指标以及不良反应的发生情况。**结果:**插管后 1 min 及 3 min,各组去甲肾上腺素(NA)、肾上腺素(AD)水平均较基础值显著上升,A 组以上指标依次高于 B 组、C 组($P<0.05$);A 组、B 组心率、平均动脉压水平均较基础值上升,A 组以上指标高于 B 组,C 组以上指标低于基础值($P<0.05$);A 组、B 组 BIS 值均较基础值下降,A 组以上指标高于 B 组、C 组($P<0.05$)。A 组、B 组自主呼吸恢复时间、呼吸睁眼时间和拔管时间比较无统计学差异($P>0.05$),但均短于 C 组($P<0.05$)。A 组呛咳率显著高于 B 组、C 组,C 组恶心呕吐率高于 A 组、B 组($P<0.05$)。**结论:**0.5 $\mu\text{g/kg}$ 舒芬太尼能够减轻直肠癌全麻气管插管应激反应,减少血流动力学波动,且无苏醒延长,不增加药物不良反应。

关键词:直肠癌;不同剂量舒芬太尼;气管插管应激反应;血流动力学

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Effects of Different Doses of Sufentanil on the Stress Response and Hemodynamics of Tracheal Intubation under General Anesthesia in the Patients with Rectal Cancer*

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ABSTRACT Objective: To study the effects of different doses of sufentanil on the stress response and hemodynamics of in rectal cancer patients undergoing tracheal intubation under general anesthesia. **Methods:** Ninety patients undergoing elective laparoscopic rectal cancer resection in our hospital from January 2017 to December 2019 were selected as research objects and divided into group A, group B and group C according to random number table method, with 30 cases in each group. Group A: 0.4 $\mu\text{g/kg}$ sufentanil; Group B: 0.5 $\mu\text{g/kg}$ sufentanil; Group C: 0.6 $\mu\text{g/kg}$ sufentanil. The stress response, hemodynamic index before and after intubation, anaesthesia recovery index and incidence of adverse reactions were observed and compared between different groups. **Results:** At 1 min and 3 min after intubation, the levels of norepinephrine (NA) and epinephrine (AD) in each group were significantly increased compared with the basal values, the above indexes in group A were successively higher than those in group B and group C ($P<0.05$). The heart rate and average arterial pressure of group A and group B were all higher than the baseline values, which were higher in group A than those of group B, while those of group C were lower than the baseline values ($P<0.05$). The BIS values of group A and group B decreased from the base values, and the above indexes of group A were higher than those of group B and group C ($P<0.05$). There was no statistically significant difference between group A and group B in the recovery time of spontaneous breathing, time of respiratory opening and time of extubation ($P>0.05$), but all of them were shorter than group C ($P<0.05$). The rate of choking in group A was significantly higher than that in group B and group C, and the rate of nausea and vomiting in group C was significantly higher than that in group A and group B ($P<0.05$). **Conclusion:** 0.5 $\mu\text{g/kg}$ sufentanil can reduce the stress response of tracheal intubation under general anesthesia in rectal cancer, reduce the fluctuation of hemodynamics, and do not prolong resuscitation and increase the adverse drug reaction.

Key words: Rectal Cancer; Different doses of sufentanil; Stress reaction of tracheal intubation; Hemodynamics

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前言

直肠癌为消化道最常见的恶性肿瘤之一,目前其治疗以外科手术为主。近年来,腹腔镜直肠癌手术已成为首选治疗术式,较传统开腹直肠癌术具有明显优势^[1,2]。但全麻气管插管机械刺激可经神经内分泌作用机制导致机体发生强烈的应激反应,能够增加肺血管阻力和平均肺动脉压力,引起血流动力学变化^[3,4]。临床报道^[5,6]全麻气管插管时给予阿片类药物能够减少或避免机体的应激反应,但其一般具有多种药理作用。舒芬太尼为阿片类的代表药物,具有易透过血脑屏障、和阿片受体亲和力强、镇痛作用强等特点,现已广泛用于麻醉诱导及辅助麻醉。但有研究显示^[7,8]舒芬太尼的药理作用有一定的剂量依赖性,其安全剂量和效果尚未达成共识。本研究主要分析不同剂量舒芬太尼对直肠癌患者全麻气管插管应激反应和血流动力学影响,结果报道如下。

1 资料与方法

1.1 一般资料

选择 90 例腹腔镜直肠癌切除术患者为研究对象,纳入标准^[9]:TNM 分期:Ⅰ~Ⅱ期;美国麻醉师协会(asa class asa, ASA):Ⅰ~Ⅱ级;凝血功能正常;无全麻禁忌证;患者知情同意本研究;年龄 31~86 岁。排除标准:预计气管插管或拔管困难;长期阿片类药物和其他镇痛药物史;酒精、药物滥用史;严重心、肝肾等疾病;妊娠或哺乳期妇女。所有患者依据随机数字表法分为 A 组、B 组、C 组,每组各 30 例。A 组男 17 例,女 13 例;年龄(57.18±6.44)岁;体质指数(22.86±1.41)kg/m²;TNM 分期:Ⅰ期 24 例、Ⅱ期 6 例;ASA 分级:Ⅰ级 22 例、Ⅱ级 8 例。B 组男 20 例,女 10 例;年龄(56.94±7.01)岁;体质指数(22.71±1.53)kg/m²;TNM 分期:Ⅰ期 19 例、Ⅱ期 11 例;ASA 分级:Ⅰ级 18 例、Ⅱ级 12 例。C 组男 18 例,女 12 例;年龄(57.33±5.91)岁;体质指数(22.62±1.47)kg/m²;TNM 分期:Ⅰ期 19 例、Ⅱ期 11 例;ASA 分级:Ⅰ级 21 例、Ⅱ级 9 例。各组基线资料比较无统计学差异($P>0.05$),具有可比性。

1.2 麻醉方法

所有患者均予以经口气管插管全凭静脉麻醉,术前 30 min 肌肉注射 0.01 mg/kg 阿托品和 0.1~0.2 mg/kg 安定。进入麻醉室后予以面罩吸氧,取监护仪监测脉搏血氧饱和度、无创动脉血压和心电图等,开放静脉,取 0.08 mg/kg 安定,局麻下予以桡动脉穿刺置管测压,取 10 min 后稳定的心率和平均动脉压为基础值。麻醉诱导:A 组:0.4 μg/kg 舒芬太尼、B 组:0.5 μg/kg 舒芬太尼、C 组:0.6 μg/kg 舒芬太尼,各组均给予 0.12 mg/kg 维库溴铵,1.5 mg/kg 丙泊酚。通过面罩纯氧通气 3 min 后予以气管插管,并接通麻醉机进行机械通气,设定相应参数。麻醉维持:微泵输注 0.05~0.2 mg/kg·min 丙泊酚,A 组微泵持续注入 0.4 μg/kg·h 舒芬太尼、B 组:0.5 μg/kg·h 舒芬太尼、C 组:0.6 μg/kg·h 舒芬太尼,并给予维库溴铵维持肌松。各组手术结束前 30~45 min 均停止舒芬太尼或芬太尼输注,关腹后停止异丙酚输注,术毕送入麻醉后恢复室,查看患者自主呼吸恢复时间、呼吸睁眼时间和拔管时间。

1.3 观察指标

于麻醉诱导前、插管后 1 min、3 min 采集患者静脉血 4 mL,用高效液相色谱-电化学法检测血浆去甲肾上腺素(Norepinephrine, NA)、肾上腺素(Adrenaline, AD)值。记录麻醉诱导前、插管后 1 min、3 min 心率、平均动脉压和脑电双频指数(bispectral index, BIS)值。观察并记录患者呛咳、恶心呕吐等不良反应的发生情况。

1.4 统计学分析

数据处理选用 SPSS18.0 软件包,计量资料用($\bar{x} \pm s$)表示,组间比较选用 t 检验,不同时间点采用方差分析,计数资料用[例(%)]表示,组间比较用 χ^2 检验比较,以 $P<0.05$ 表示差异有统计学意义。

2 结果

2.1 各组全麻气管插管前后血浆 NA、AD 水平的比较

各组基础血浆 NA、AD 水平比较无统计学差异($P>0.05$);插管后 1 min 及 3 min, 各组血浆 NA、AD 水平均较基础值上升, A 组以上指标依次高于 B 组、C 组, 差异有统计学意义($P<0.05$),见表 1。

表 1 各组气管插管前后血浆 NA、AD 水平的比较($\bar{x} \pm s$)

Table 1 Comparison of the plasma NA and AD levels before and after tracheal intubation between different groups($\bar{x} \pm s$)

Groups	n	Time	NA(pg/mL)	AD(pg/mL)
Group A	30	Base value	152.29±20.19	93.74±12.18
		At 1min after intubation	216.44±27.65 ^d	144.25±16.71 ^d
		At 3min after intubation	211.05±28.97 ^d	140.08±15.95 ^d
Group B	30	Base value	154.20±19.61	93.75±12.55
		At 1min after intubation	183.03±23.08 ^{ad}	126.22±14.01 ^{ad}
		At 3min after intubation	181.01±24.95 ^{ad}	122.61±13.88 ^{ad}
Group C	30	Base value	153.71±20.08	92.56±11.84
		At 1min after intubation	171.12±21.07 ^{abd}	110.05±12.16 ^{abd}
		At 3min after intubation	171.94±22.85 ^{abd}	107.94±14.27 ^{abd}

Note: Compared with group A, ^a $P<0.05$; Compared with group B, ^b $P<0.05$; Compared with the basic values of same group, ^d $P<0.05$.

2.2 各组全麻气管插管前后血流动力学指标的比较

各组基础心率、平均动脉压及 BIS 值比较无统计学差异 ($P>0.05$); 插管后 1 min 及 3 min, A 组、B 组心率、平均动脉压

水平均较基础值上升, A 组以上指标高于 B 组、C 组, C 组以上指标低于基础值 ($P<0.05$); A 组、B 组 BIS 值均较基础值下降, A 组以上指标高于 B 组、C 组 ($P<0.05$), 见表 2。

表 2 各组全麻气管插管前后血流动力学指标的比较($\bar{x} \pm s$)

Table 2 Comparison of the hemodynamic indexes before and after tracheal intubation between different groups($\bar{x} \pm s$)

Groups	n	Time	Heart rate(times/min)	Mean arterial pressure(mmHg)	BIS
Group A	30	Base value	74.09 $\pm$ 8.63	84.11 $\pm$ 9.66	98.71 $\pm$ 13.86
		At 1min after intubation	104.27 $\pm$ 12.14 ^d	106.32 $\pm$ 12.17 ^d	56.84 $\pm$ 7.55 ^d
		At 3min after intubation	98.33 $\pm$ 13.26 ^d	101.29 $\pm$ 13.18 ^d	55.91 $\pm$ 6.94 ^d
Group B	30	Base value	75.42 $\pm$ 8.51	83.53 $\pm$ 10.16	96.74 $\pm$ 15.01
		At 1min after intubation	94.27 $\pm$ 14.19 ^{ad}	95.27 $\pm$ 12.59 ^{ad}	48.11 $\pm$ 6.71 ^{ad}
		At 3min after intubation	91.33 $\pm$ 13.45 ^{ad}	92.66 $\pm$ 13.01 ^{ad}	47.75 $\pm$ 7.03 ^{ad}
Group C	30	Base value	74.81 $\pm$ 9.75	82.95 $\pm$ 11.21	97.52 $\pm$ 14.29
		At 1min after intubation	62.72 $\pm$ 9.13 ^{abd}	73.81 $\pm$ 8.75 ^{abd}	41.07 $\pm$ 6.03 ^{abd}
		At 3min after intubation	65.75 $\pm$ 8.71 ^{abd}	74.73 $\pm$ 9.61 ^{abd}	42.63 $\pm$ 6.77 ^{abd}

Note: Compared with group A, ^a $P<0.05$; Compared with group B, ^b $P<0.05$; Compared with the same group of basic values, ^d $P<0.05$.

2.3 各组麻醉恢复指标比较

A 组、B 组自主呼吸恢复时间、呼吸睁眼时间和拔管时间

比较无统计学差异 ($P>0.05$), A 组、B 组自主呼吸恢复时间、呼吸睁眼时间和拔管时间均少于 C 组 ($P<0.05$), 见表 3。

表 3 各组麻醉恢复指标的比较(例, %)

Table 3 Comparison of the anaesthesia recovery indexes between different groups(n, %)

Groups	n	Recovery time of spontaneous respiration(min)	Opening time of respiration (min)	Extubation time(min)
Group A	30	3.16 $\pm$ 0.42	6.04 $\pm$ 0.84	8.09 $\pm$ 1.22
Group B	30	3.30 $\pm$ 0.33	6.35 $\pm$ 0.75	8.53 $\pm$ 1.02
Group C	30	6.19 $\pm$ 0.82 ^a	10.85 $\pm$ 1.29 ^a	14.27 $\pm$ 1.49 ^a

Note: Compared with group A, ^a $P<0.05$.

2.4 各组不良反应发生情况的比较

A 组呛咳率高于 B 组、C 组, C 组恶心呕吐率高于 A 组、B

组 ($P<0.05$), 见表 4。

表 4 各组不良反应发生情况的比较(例, %)

Table 4 Comparison of the incidence of adverse reactions between different groups(n, %)

Groups	n	Cough	Nausea and vomiting
Group A	30	4(13.33)	0(0.00)
Group B	30	0(0.00) ^a	1(3.33)
Group C	30	0(0.00) ^a	6(20.00) ^a

Note: Compared with group A, ^a $P<0.05$.

3 讨论

腹腔镜直肠癌切除术是直肠癌的主要术式, 气管插管作为一种伤害性刺激原能够导致气管内积咽喉部产生机械牵张刺激, 增加交感-肾上腺素系统活性, 引起神经内分泌反应^[10,11]。阿片类药物能够直接作用于应激激素前受体, 抑制应激激素释放, 且可扩张外周小血管, 抑制副交感神经的兴奋性及儿茶酚胺释放, 还可直接阻断伤害性刺激的传入^[12]。舒芬太尼作为 μ

阿片受体高选择性的激动药, 具有高受体选择性、高脂溶性等特点, 其镇痛作用明显强于芬太尼, 且安全范围宽^[13,14]。舒芬太尼有较独特的作用机理和药理学特点, 其可透过血脑屏障, 于短时间内在脑部起到有效的血药浓度, 因此其起效快速, 作用较芬太尼平稳^[15,16]。舒芬太尼能够减轻迷走神经反应, 减少突出释放, 增加迷走神经的紧张性, 其又可抑制甲状腺素和肾上腺素的分泌, 抑制应激反应及代谢^[17,18]。同时, 舒芬太尼可阻断气管插管时的机械刺激, 从而减轻气管插管所致的血流学波动,

保持平稳的生命体征^[19,20]。

既往研究报道^[21,22]小剂量阿片类药物对应激反应的控制效果欠佳,足量虽可有效抑制插管应激反应,但可能引起苏醒延迟、恶心呕吐等不良反应。加上患者个体差异性大,药物剂量对药物效应有一定影响,因此需明确最佳的给药剂量,从而在发挥良好作用的同时最大程度的降低对呼吸的影响^[23,24]。Narimani Zamanabadi M^[25]等研究表明小剂量舒芬太尼无法有效抑制插管反应,可能引起部分对抗反应,且需通过追加镇痛药达到手术镇痛作用。机体发生应激反应时可刺激儿茶酚胺的分泌,其中 NA 及 ND 变化较明显^[26]。本研究结果显示各组气管插管 1 min 及 3 min 后血浆 NA 及 AD 水平均增加,以 0.4 $\mu\text{g/kg}$ 舒芬太尼组变化更明显,提示增加舒芬太尼剂量更能明显减轻全麻气管插管时的应激反应。

全麻气管插管时可引起血流动力学波动,加重心肌耗氧量,增加心律失常及心肌缺血等风险^[27]。心率及血压是评价机体血流动力学的重要指标,其中心率能够客观反映循环系统紧张程度。本研究数据显示各组基础值心率、平均动脉压无显著差异,气管插管 1 min 及 3min 后各组心率及平均动脉压均上升,但 0.5 $\mu\text{g/kg}$ 舒芬太尼组上升幅度较小,0.6 $\mu\text{g/kg}$ 舒芬太尼组心率及平均动脉压则明显低于基础值,提示小剂量舒芬太尼可能引起全麻气管插管期血流动力学波动,考虑与小剂量舒芬太尼对血管的收缩作用、镇静作用不明显,从而无法保持血流动力学平稳,但大剂量舒芬太尼则可能导致心血管抑制,对患者产生不良影响,应用 0.5 $\mu\text{g/kg}$ 舒芬太尼组血流动力学无明显波动。

应激反应能够增加机体兴奋性,出现觉醒反应,BIS 可自动分析及分级处理麻醉状态下患者的脑电图波形,以数字形式反映麻醉镇静深度,又可准确评价皮层功能状态和意识抑制程度,其结果准确可靠,现已广泛用于临床麻醉深度的监测。但既往研究报道麻醉状态下,麻醉深度和心率、血压等无明显相关性。临床为避免麻醉诱导时麻醉镇静程度过深或过浅,用 BIS 进行监测,本研究显示气管插管后 1 min、3 min,常规芬太尼对照组 BIS 明显高于不同剂量舒芬太尼组,0.4 $\mu\text{g/kg}$ 舒芬太尼组 BIS 值又高于 0.5 $\mu\text{g/kg}$ 及 0.6 $\mu\text{g/kg}$ 舒芬太尼组,0.6 $\mu\text{g/kg}$ 舒芬太尼组 BIS 值相对较低,提示 0.5 $\mu\text{g/kg}$ 舒芬太尼的麻醉深度适当,可有效抑制气管插管引起的应激反应,大剂量舒芬太尼可能引起麻醉加深。有关研究显示随着舒芬太尼用量的增加,能够导致苏醒延迟和呼吸抑制,延迟术后拔管时间,增加全身麻醉后并发症风险。本研究结果显示 0.6 $\mu\text{g/kg}$ 舒芬太尼组自主呼吸恢复时间、呼吸睁眼时间和拔管时间较 0.4 $\mu\text{g/kg}$ 及 0.5 $\mu\text{g/kg}$ 组多,0.4 $\mu\text{g/kg}$ 和 0.4 $\mu\text{g/kg}$ 舒芬太尼组相似,说明此剂量的舒芬太尼未影响患者苏醒期恢复,安全性较高,0.6 $\mu\text{g/kg}$ 舒芬太尼能够延长患者恢复时间。

药理学研究表明舒芬太尼的分布容积小,可快速经过血流屏障及神经细胞膜,加快在体外的效应,缩短终末消除期和体内消除期。但有研究显示部分患者予以舒芬太尼后可能发生麻醉恢复不及时,导致呼吸抑制^[28]。本研究结果显示 0.4 $\mu\text{g/kg}$ 舒芬太尼组呛咳发生率相对较高,0.6 $\mu\text{g/kg}$ 舒芬太尼组恶心呕吐率则又高于其他剂量舒芬太尼组,可能与拔管、吸痰等刺激增强机体交感神经系统活性,从而引起血流动力学波动,增加呛

咳几率,尽管呛咳反应多呈一过性及短暂性,但剧烈咳嗽可能增加腹内压、眼内压和颅内压,引起严重并发症,增加围术期风险,大剂量舒芬太尼则增加药物不良反应可能性,引起恶心呕吐等不适。

综上所述,0.5 $\mu\text{g/kg}$ 舒芬太尼能够减轻直肠癌全麻气管插管应激反应,减少血流动力学波动,且无苏醒延长,不增加药物不良反应的发生。

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