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预防性应用不同剂量羟考酮对腹腔镜胆囊手术拔管期应激反应的影响

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摘要 目的:探讨预防性应用不同剂量羟考酮对腹腔镜胆囊手术(laparoscopic cholecystectomy, LC)拔管期应激反应的影响。**方法:**将 75 例接受 LC 的患者随机分为低、中、高剂量组,每组均 25 例。术毕 15 min,低、中、高剂量组分别预防性静脉注射盐酸羟考酮 0.1 mg/kg、0.15 mg/kg、0.2 mg/kg。比较各组拔管前(T₁)、拔管时(T₂)、拔管后 5 min(T₃)、拔管后 10 min(T₄)、拔管后 30 min(T₅)血流动力学改变、麻醉苏醒时间、拔管情况及不良反应的发生情况。**结果:**与 T₁ 时刻比较,各组 T₂ 时刻收缩压(systolic blood pressure, SBP)、舒张压(diastolic blood pressure, DBP)、心率(heart rate, HR)均明显升高($P<0.05$),但中、高剂量组 T₃ 时刻后 SBP、DBP、HR 均显著下降,恢复至 T₁ 时刻水平($P>0.05$),各指标水平明显低于低剂量组($P<0.05$)。中剂量组与高剂量组各指标比较差异均无统计学意义($P>0.05$)。随着剂量羟考酮的增加,患者苏醒时间、拔管时间逐渐延长($P<0.05$);中、高剂量组拔管质量评分显著低于低剂量组($P<0.05$),而中、高剂量组间拔管质量评分比较差异无显著性($P>0.05$)。高剂量组恶心呕吐、呼吸抑制的发生率明显高于低剂量组,中、高剂量组追加镇痛药物的比例明显低于低剂量组($P<0.05$)。**结论:**预防性使用羟考酮可不同程度抑制 LC 术后拔管期应激反应,0.15 mg/kg 羟考酮能够更好地维持患者血流动力学的稳定,促进患者早期苏醒,且安全性较高。

关键词:腹腔镜胆囊手术;羟考酮;剂量;拔管期;应激反应

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Effects of Preventive use of Different Doses of Oxycodone on the Stress Response during Tracheal Extubation in Laparoscopic Cholecystectomy

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ABSTRACT Objective: To explore the effects of preventive use of different dose of oxycodone on the stress response during tracheal extubation in laparoscopic cholecystectomy (LC). **Methods:** 75 patients with LC surgery were randomly divided into low, medium and high dose group, 25 cases in each group. 15 min at end of operation, low, medium and high dose group was preventively given oxycodone hydrochloride 0.1 mg/kg, 0.15 mg/kg, 0.2 mg/kg, respectively. The hemodynamic change, anesthesia waking time, tracheal extubation and the occurrence of adverse reactions among each group before extubation(T₁), during extubation(T₂), at 5 min after extubation (T₃) and 10 min after extubation (T₄) were Compared. **Results:** Compared with T₁ time point, the SBP, DBP, HR in T₂ time point were significantly increased in each group ($P<0.05$), but after T₃ time point, the SBP, DBP, HR in medium and high dose group had dropped significantly, returned to the level of T₁ time point ($P>0.05$), the level of all indexes were significantly lower than those in low dose group ($P<0.05$). There were no statistically significant difference on all indexes between medium dose group and high dose group($P>0.05$). With the increase of oxycodone dose, awakening time, extubation time is longer ($P<0.05$). The extubation quality scores in medium and high dose group were significantly lower than those in low dose group ($P<0.05$), while the high dose group had no significant difference with low dose group ($P<0.05$). The incidences of nausea and vomiting, respiratory depression in high dose group were obviously higher than those in medium and low dose group, the proportion of additional analgesic drugs in middle and high dose group was significantly lower than that in low dose group ($P<0.05$). **Conclusions:** Prophylactic use of oxycodone can restrain stress response during tracheal extubation in LC at different degree, dose of oxycodone 0.15 mg/kg can be better to maintain hemodynamic stability, promote the early awakening, reduce incidence of adverse reactions, and safe to use.

Key words: Laparoscopic cholecystectomy; Oxycodone; Dose; Tracheal extubation; Stress response

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前言

腹腔镜胆囊切除术(laparoscopic cholecystectomy, LC)以其

创伤小、出血少、恢复快等优势已成为临床广泛应用的微创手术方法,但受二氧化碳刺激所致负面影响,机体极易出现血流动力学波动,从而产生围拔管期心血管应激反应,严重影响患

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者的术后恢复^[1-3]。目前,临床上多采用血管扩张剂、 β 受体阻滞剂等缓解拔管期反应,但效果欠佳^[4,6],而阿片类药物存在恶心呕吐、呼吸抑制、皮肤瘙痒等不良反应。

盐酸羟考酮作为一种半合成阿片受体激动剂,具有 μ 、 k 受体双重激动作用,起效快,具有良好的镇静及应激反应抑制,但其在LC术的使用剂量及量效关系尚未达成共识^[7-9]。本研究对LC术患者采用预防性使用不同剂量羟考酮,旨在探讨其对术后镇痛及拔管期应激反应的影响,现报道如下。

1 资料与方法

1.1 一般资料

选择2016年6月~2017年6月在上海同仁医院接受LC术的患者,共75例。入组标准:(1)美国麻醉师协会(ASA)分级I~III级;(2)年龄 ≤ 65 岁;(3)近3个月未镇静或镇痛药物;(4)排除认知功能障碍,明显呼吸、循环、神经系统疾病。其中男38例,女37例;年龄33~65岁,平均 (45.8 ± 4.1) 岁;体质指数(BMI) $23.8 \sim 29.1$ kg/m²,平均 (25.3 ± 2.7) kg/m²。将患者按照随机数字法随机分为低、中、高剂量三组,各25例。各组患者在年龄、性别、ASA分级、BMI等方面差异均无统计学意义($P > 0.05$)。本研究已通过我院伦理学委员会审核通过,且均获得患者或家属知情同意。

1.2 麻醉方法

术前禁食8h以上,入室后开放右侧上肢静脉通道,连接Philips MP40型心电监护仪,监测心电图(electrocardiograph, ECG)、收缩压(systolic blood pressure, SBP)、舒张压(diastolic blood pressure, DBP)、心率(heart rate, HR)及血氧饱和度(oxygen saturation, SpO₂)等血流动力学指标。麻醉诱导:静脉注射咪达唑仑0.1 mg/kg、舒芬太尼0.4 μ g/kg、顺阿曲库铵0.15 mg/kg、丙泊酚1.5~2.0 mg/kg;当意识丧失后行气管插管,连接麻醉机进行机械通气。参数设置:潮气量(tidal volume, VT)8~10 mL/kg,呼吸频率(respiratory rate, RR)10~12次/min, PetCO₂ 35~45 mmHg。麻醉维持:采用全凭静脉麻醉维持麻醉,持续静脉泵注丙泊酚4~6 mg $\cdot$ kg⁻¹ $\cdot$ h⁻¹,瑞芬太尼0.15~0.2 μ g $\cdot$ kg⁻¹ $\cdot$ min⁻¹,根据患者实际情况给予顺阿曲库铵维持肌松。

术前15 min,低、中、高剂量组分别静脉注射盐酸羟考酮(批号:AW259)0.1 mg/kg、0.15 mg/kg、0.2 mg/kg。术后待患者恢复吞咽反射,RR > 12 次/min, VT > 6 mL/kg,且意识基本恢复后拔管。所有患者的拔管操作均由同一麻醉医师完成。

1.3 观察指标

(1)血流动力学指标:采用Philips MP40型多功能心电监护仪监测并记录各组患者拔管前(T₁)、拔管时(T₂)、拔管后5 min(T₃)、拔管后10 min(T₄)、拔管后30 min(T₅)五个不同时刻的SBP、DBP、HR及SpO₂变化。

(2)拔管相关指标:记录各组患者苏醒时间(停药至呼之睁眼、意识恢复)、拔管时间(停药至拔管),并进行拔管质量评分^[10]。评分标准如下:没有咳嗽计1分,轻微咳嗽(1~2次)计2分,中度咳嗽(3~4次)计3分,严重咳嗽(5~10次)或屏气计4分,剧烈咳嗽(10次以上)或喉痉挛计5分。

(3)不良反应:比较两组患者镇痛期间的不良反应发生情况,包括恶心呕吐、呛咳、呼吸抑制的发生率,及术后追加镇痛

药物的比例等。

1.4 统计学分析

采用SPSS18.0版软件包进行统计分析,计数资料比较采用 χ^2 检验,计量资料比较采用成组t检验,以 $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 各组不同时刻的血流动力学变化的比较

T₁时刻,各组SBP、DBP、HR、MAP比较差异均无统计学意义($P > 0.05$)。与T₁时刻比较,各组T₂时刻SBP、DBP、HR均明显升高($P < 0.05$),但中、高剂量组T₃时刻后SBP、DBP、HR均显著下降,恢复至T₁时刻水平($P > 0.05$),各指标水平明显低于低剂量组,差异均有统计学意义($P < 0.05$)。中剂量组与高剂量组各指标比较以及各组不同时刻的SpO₂比较差异均无统计学意义($P > 0.05$)。见表1。

2.2 各组拔管相关指标比较

随着羟考酮剂量的增加,患者苏醒时间、拔管时间逐渐延长,差异有统计学意义($P < 0.05$);中、高剂量组拔管质量评分显著低于低剂量组,差异有统计学意义($P < 0.05$),而中、高剂量组间拔管质量评分比较差异无显著性($P > 0.05$)。见表2。

2.3 各组不良反应发生情况的比较

高剂量组恶心呕吐、呼吸抑制的发生率明显高于低剂量组,中、高剂量组追加镇痛药物的比例明显低于低剂量组,差异均有统计学意义($P < 0.05$)。各组呛咳的发生率比较,差异均无统计学意义($P > 0.05$)。见表3。

3 讨论

研究表明适度的应激反应对机体具有保护作用,可改善术后功能,但过度应激反应则容易导致交感或副交感神经系统异常兴奋以及全身炎症反应综合征等一系列不良效应,严重者可出现多器官功能衰竭^[11-14]。LC术属于微创手术,对机体内环境的影响较小,但CO₂气腹可直接影响术中血流动力学稳定,且咽部吸痰、拔除气管导管等刺激下可造成肾素-血管紧张素-醛固酮系统(RAAS)、皮质醇、儿茶酚胺等物质分泌增多,增强患者的应激反应^[15,16]。此外,切口疼痛与内脏痛是LC术后麻醉苏醒期的主要疼痛来源,而术后疼痛是导致患者围拔管期心血管应激反应的一个重要因素^[17,18]。临床上多通过使用硝酸酯类及 β 受体阻滞剂等药物缓解拔管期间的应激反应,但其效果均为一过性改善血压升高和心动过速,无法从根本上减轻术后疼痛及苏醒期躁动^[19,20]。

羟考酮属于半合成的阿片受体激动剂,2~3 min起效,半衰期段,镇痛作用与同剂量吗啡相当,且无封顶效应,其在临床上应用多年,广泛地用于术后中重度急性疼痛、癌痛和内脏痛等^[21-23]。临床研究显示羟考酮有效地用于手术患者术后自控镇痛,且药物不良反应的发生率较低,无成瘾性,且能够从整体改善心理功能状态^[24-26]。但羟考酮也存在剂量依赖性呼吸抑制,迄今为止其最佳剂量尚未明确。本研究结果显示与T₁时刻比较,各组T₂时刻SBP、DBP、HR均明显升高,但中、高剂量组T₃时刻后SBP、DBP、HR均显著下降,恢复至T₁时刻水平,与邵娴等^[27]研究结果一致,提示中、高剂量(0.15 mg/kg、0.2 mg/kg)对拔

表 1 各组围拔管期不同时刻血流动力学比较($\bar{x} \pm s$)Table 1 Comparison of the haemodynamics during periextubation at different time points among different groups($\bar{x} \pm s$)

Indexes	Group(n=25)	T ₁	T ₂	T ₃	T ₄	T ₅
SBP (mmHg)	Low dose group	139.1± 15.1	163.6± 20.8*	155.7± 15.9	157.4± 15.1	140.7± 18.4
	Medium dose group	139.4± 15.8	149.4± 16.7* [#]	141.6± 14.7* [#]	140.6± 14.6* [#]	137.7± 19.2* [#]
	High dose group	138.4± 15.3	146.2± 18.7* [#]	138.1± 13.2* [#]	137.4± 12.3* [#]	125.4± 12.1* [#]
DBP (mmHg)	Low dose group	84.8± 12.6	96.7± 12.1*	94.5± 12.0	95.6± 13.7	88.7± 10.1
	Medium dose group	83.1± 11.3	88.6± 11.5* [#]	84.4± 10.8* [#]	85.4± 10.7* [#]	83.4± 8.6* [#]
	High dose group	84.6± 10.3	87.4± 10.1* [#]	85.9± 9.6* [#]	84.8± 9.5* [#]	83.8± 8.4* [#]
HR (time/min)	Low dose group	85.8± 9.5	93.6± 12.7*	90.2± 12.6	90.6± 12.3	89.2± 10.5
	Medium dose group	84.2± 9.1	89.4± 9.4* [#]	86.7± 11.9* [#]	84.7± 11.4* [#]	84.1± 8. * [#]
	High dose group	83.2± 9.4	87.4± 8.4* [#]	85.7± 8.4* [#]	84.5± 10.2* [#]	82.1± 7.4* [#]
SpO ₂ (%)	Low dose group	97.7± 1.9	97.5± 1.4	98.4± 1.4	98.2± 1.7	98.1± 1.7
	Medium dose group	97.6± 1.3	97.4± 1.1	98.4± 1.5	97.9± 1.6	97.8± 1.5
	High dose group	98.7± 1.9	98.5± 1.4	98.2± 1.7	97.1± 1.3	98.5± 1.2

Note: Compared with T1 time point, * $P < 0.05$; Compared with low dose group, [#] $P < 0.05$.

表 2 各组拔管相关指标比较($\bar{x} \pm s$)Table 2 Comparison of the extubation related indicators between different groups($\bar{x} \pm s$)

Group	n	Wake-up time(min)	Extubation time(min)	Extubation quality scores(score)
Low dose group	25	5.16± 0.92	8.06± 1.23	3.16± 0.93
Medium dose group	25	6.84± 1.15*	9.12± 1.31*	1.79± 0.81* [#]
High dose group	25	10.28± 1.80* [#]	14.19± 1.91* [#]	1.66± 0.69*

Note: Compared with low dose group, * $P < 0.05$; Compared with medium dose group, [#] $P < 0.05$.

表 3 各组术后不良反应发生情况的比较[例(%)]

Table 3 Comparison of the incidence of postoperative complications between different groups[n(%)]

Groups	n	Bucking	Nausea and vomiting	Respiratory depression	Additional analgesic drugs
Low dose group	25	4(16.0)	2(8.0)	0(0)	10(40.0)
Medium dose group	25	2(8.0)	5(20.0)	2(8.0)	3(12.0)*
High dose group	25	1(4.0)	11(44.0)	7(28.0)*	2(8.0)*

Note: Compared with low dose group, * $P < 0.05$; compared with medium dose group, [#] $P < 0.05$.

管时的应激反应具有明显的缓解作用,且二者作用相当,有助于维持血流动力学的稳定。

此外,随着羟考酮剂量的增加,患者术后苏醒时间、拔管时间逐渐延长,拔管质量评分明显增加,而中、高剂量组间拔管质量评分比较差异无显著性。由此可见,术毕前预防性 0.15 mg/kg 羟考酮剂量已可达到对拔管应激反应的良好抑制作用,再增加剂量并不能进一步改善其抑制效果,反而可能出现过度镇静而影响术后恢复。本研究中、高剂量组追加镇痛药物的比例明显降低,且未见严重不良反应,但高剂量组恶心呕吐、呼吸抑制的发生率明显升高,提示适当降低羟考酮的剂量既可保证良好的镇痛效果,还可减少麻醉所致不良反应^[28-30]。

综上所述,LC 术中预防性使用羟考酮可不同程度抑制拔管时的应激反应,呈一定剂量依赖性,0.15 mg/kg 剂量能够更好地维持血流动力学稳定,促进早期苏醒,且安全性高。

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