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布托啡诺复合瑞芬太尼对纤维支气管镜麻醉术后不良反应的影响

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[摘要] 目的: 探讨布托啡诺复合瑞芬太尼用于纤维支气管镜麻醉镇痛的有效性和安全性。方法: 选取2018年5月至2019年4月于空军军医大学第二附属医院行无痛性纤维支气管镜诊疗的患者108例, 使用随机数表法随机分为瑞芬太尼组(R组)、布托啡诺组(B组)及瑞芬太尼复合布托啡诺组(RB组)。R组、B组及RB组分别予以瑞芬太尼、布托啡诺及瑞芬太尼复合布托啡诺作为镇痛药物, 各组均使用丙泊酚镇静。比较3组患者心率(heart rate, HR)、平均动脉压(mean arterial pressure, MAP)、睫毛反射消失时间、复苏过程中Steward评分, 及术后咳嗽、恶心呕吐、寒颤、嗜睡及头晕发病率的差异。记录各组患者术中体动及术后心动过速、心动过缓、高血压、低血压及呼吸抑制发生情况。结果: 与R组比较, B组与RB组患者睫毛反射消失时间更短($P < 0.05$), 术后恶心、呕吐的发病率更低($P < 0.05$)。与B组比较, R组与RB组患者术后苏醒更迅速($P < 0.05$), 术后头晕发病率更低($P < 0.05$)。3组患者其他不良反应无明显差异($P > 0.05$)。3组患者血流动力学差异无统计学意义($P > 0.05$)。结论: 布托啡诺复合瑞芬太尼用于纤维支气管镜诊疗镇痛效果确切, 术后不良反应发病率低。

[关键词] 布托啡诺; 瑞芬太尼; 纤维支气管镜; 麻醉; 不良反应

Effect of butorphanol combined with remifentanil on adverse reactions after fiberoptic bronchoscopy

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Abstract **Objective:** To investigate the efficacy and safety of butorphanol combined with remifentanil for analgesia under fiberoptic bronchoscopy. **Methods:** A total of 108 patients who undergoing fiberoptic bronchoscopy in Second Affiliated Hospital of Air Force Medical University from May 2018 to April 2019 were randomly divided into the remifentanil group (group R), butorphanol group (group B) and remifentanil combined with butorphanol group (group RB) by the random number table method. The group R, group B and group RB were respectively given remifentanil, butorphanol and remifentanil plus remifentanil as analgesic drugs, and all three groups were combined with propofol. Heart rate (HR), mean arterial pressure (MAP), disappearance time of eyelash reflex, Steward score during resuscitation and postoperative incidence of cough, nausea, vomiting,

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chills, lethargy and dizziness of the three groups were compared. Intraoperative and postoperative tachycardia, bradycardia, high blood pressure, low blood pressure and respiratory depression in each group were recorded.

Results: Compared with patients in group R, the disappearance time of eyelash reflex in group B and group RB was shorter ($P<0.05$), and the incidence of intraoperative nausea and vomiting was lower ($P<0.05$). Compared with patients in group B, patients in group R and RB recovered more quickly after surgery ($P<0.05$), and the incidence of postoperative dizziness was lower ($P<0.05$). There was no significant difference in other adverse reactions among the three groups ($P>0.05$). No significant difference in hemodynamics between the three groups ($P>0.05$). **Conclusion:** Remifentanyl combined with butorphanol provided adequate pain relief and fewer complications when used in fiberoptic bronchoscopy.

Keywords butorphanol; remifentanyl; fiber bronchoscope; anesthesia; adverse reaction

纤维支气管镜是呼吸系统疾病诊疗的重要手段, 在气道新生物、气道狭窄及气道内异物等方面优势明显^[1]。为减轻患者不适, 提高医疗质量, 无痛纤维支气管镜常规应用于临床, 但镇痛方案仍存在不足需进一步提升。

瑞芬太尼是短效的 μ 受体激动剂, 起效时间约为1 min, 作用持续时间仅有5~10 min, 作用易控制, 但对呼吸、循环的抑制强, 术后恶心呕吐的发病率高^[2-3]。布托啡诺具有很强的镇痛作用, 并且其对循环系统影响轻微, 呼吸抑制轻, 作用时间长^[4-5], 常被用于短小手术的麻醉镇痛。本研究对比布托啡诺、瑞芬太尼及瑞芬太尼联合布托啡诺在纤维支气管镜麻醉中的临床应用, 观察3种麻醉方案对患者术后不良反应的影响。

1 对象与方法

1.1 对象

选择2018年5月至2019年4月于空军军医大学第二附属医院行无痛性纤维支气管镜穿刺活检或镜下治疗患者, 年龄45~65岁, 体重指数(body mass index, BMI) 18.5~30.0 kg/m², 美国麻醉师协会(American Society of Anesthesiologists, ASA)分级I~II。排除标准: 严重的心血管系统疾病; 严重的肝肾功能不全; 凝血功能异常; 哮喘或慢性阻塞性肺疾病病史; 妊娠患者; 对布托啡诺、丙泊酚、瑞芬太尼有过敏史或无法耐受者; 免疫功能缺陷者; 入选前3个月内参加过其他临床试验者。采用随机数表法将入选患者随机分为3组: 布托啡诺组(B组)、瑞芬太尼组(R组)与布托啡诺复合瑞芬太尼组(BR组)。本试验采用双盲的方式, 分配方案采用不透明的信封隐藏传递。本研究经空军军医大学第二附属

医院医学伦理委员会审核批准, 患者均知情同意。

1.2 麻醉方法

所有患者术前禁食禁饮, 入室后建立静脉通路, 常规检测血压(blood pressure, BP)、HR、脉搏血氧饱和度(pulse oxygen saturation, SpO₂)和心电图。B组、BR组及R组患者分别于麻醉诱导前5 min给予布托啡诺15 μ g/kg, 7 μ g/kg或等量生理盐水, 药物由同一麻醉护士准备。

麻醉诱导使用丙泊酚2 mg/kg在相同静脉通路进行, 诱导后用面罩吸氧去氮, 置入喉罩。此后以丙泊酚60 μ g/(kg·min)维持, R组与BR组患者于诱导时给予瑞芬太尼, 负荷量1 μ g/kg, 然后以0.15 μ g/(kg·min)持续泵注维持, B组患者以相同方式输入生理盐水。RB组瑞芬太尼停药时间为麻醉诱导后15 min, 其余用药均维持至手术结束(图1)。

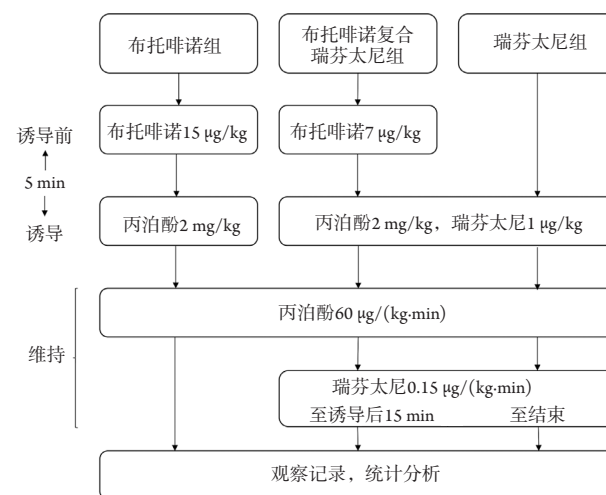


图1 流程图

Figure 1 Flow chart

1.3 观察指标

记录睫毛反射消失时间;入室后静卧10 min (T0)、麻醉诱导后(T1)、诱导后10 min (T2)、20 min (T3)及术后20 min (T4)患者的心率(heart rate, HR)、平均动脉压(mean arterial pressure, MAP);术后5, 10, 15, 20 min各时刻患者的Steward评分及术后患者咳嗽、恶心、呕吐、寒颤、嗜睡与头晕的发生情况。记录各组患者术中体动及术后心动过速、心动过缓、高血压、低血压及呼吸抑制发生情况。

1.4 统计学处理

采用SPSS统计软件分析数据。正态分布计数资料组间比较采用卡方检验,例数较少选用Fisher检验并以例数或率(%)表示;计量资料采用单因素方差分析,以均数±标准差($\bar{x} \pm s$)表示;等级资料采用Wilcoxon秩和检验并以构成比(%)表示。 $P < 0.05$ 为差异有统计学意义。

2 结果

本研究共纳入108例患者,其中R组36例,B组35例, RB组患者33例,4例患者由于诊疗方案改变无法继续行原方案麻醉被剔除。各组患者性别、年龄、BMI、ASA分级、丙泊酚用量无统计学意义($P > 0.05$,表1)。3组患者镜下检查或治疗方式无统计学意义($P > 0.05$,表2)。

与R组相比,B组及BR组患者睫毛反射消失时间明显缩短($P < 0.05$,图2);与B组相比,R组及BR组患者术后各时刻的Steward评分明显升高,患者复苏速度更快($P < 0.05$)。BR组与R组诱导及苏醒速度的差异无统计学意义($P > 0.05$,图3)。在血流动力学方面,3组患者各时间点的MAP,HR的差异无统计学意义($P > 0.05$,表3)。

B组与RB组患者恶心呕吐发生率明显低于R组($P < 0.05$)。B组患者术后头晕发生率明显高于其余两组($P < 0.05$)。在咳嗽、嗜睡寒颤方面,3组差异无统计学意义($P > 0.05$,表4)。

表1 3组患者一般情况比较

Table 1 Comparison of basic data among the three groups

| 组别 | <i>n</i> | 性别(男/女)/例 | 年龄/岁 | BMI/($\text{kg} \cdot \text{m}^{-2}$) | 丙泊酚用量/mg | ASA(I/II)/例 |
|-----|----------|-----------|------------|---|----------------|-------------|
| R组 | 36 | 20/16 | 58.1 ± 5.8 | 21.90 ± 2.78 | 209.46 ± 35.58 | 5/31 |
| B组 | 35 | 21/14 | 54.3 ± 5.6 | 23.39 ± 3.19 | 233.04 ± 46.45 | 5/30 |
| RB组 | 33 | 18/15 | 56.3 ± 4.9 | 22.76 ± 3.04 | 227.46 ± 41.94 | 4/29 |

表2 3组患者检查或治疗方法比较

Table 2 Comparison of examination or treatment among the three groups

| 组别 | <i>n</i> | 检查/治疗方法 | | | | |
|-----|----------|-----------|-----------|----|-------|-----|
| | | 超声引导下穿刺活检 | 氩气刀/电刀+冰冻 | 冰冻 | 扩张支气管 | 取异物 |
| R组 | 36 | 19 | 14 | 1 | 1 | 1 |
| B组 | 35 | 17 | 13 | 1 | 2 | 2 |
| RB组 | 33 | 17 | 12 | 2 | 2 | 0 |

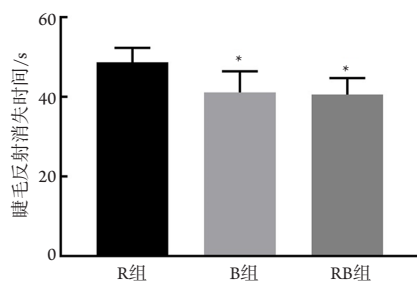


图2 3组患者睫毛反射消失时间

Figure 2 Comparison of the time period from anesthetic induction to the disappearance of eyelash reflex among the three groups

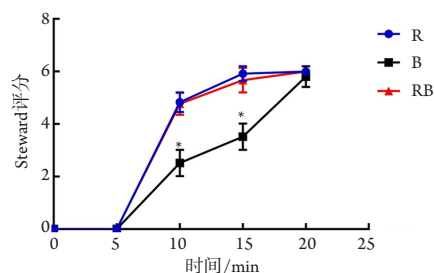
与R组相比, * $P < 0.05$ 。Compare with group R, * $P < 0.05$.

图3 3组患者术后Steward评分比较

Figure 3 Comparison of the Steward score from the end of operation among the three groups

与R组相比, * $P < 0.05$ 。Compare with group R, * $P < 0.05$.

表3 3组患者血流动力学比较

Table 3 Comparison of hemodynamic among the three groups

| 组别 | n | HR/min ⁻¹ | | | | | MAP/mmHg | | | | |
|-----|----|----------------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|------------|-------------|
| | | T0 | T1 | T2 | T3 | T4 | T0 | T1 | T2 | T3 | T4 |
| R组 | 36 | 84.5 ± 11.9 | 71.6 ± 11.0 | 77.7 ± 12.4 | 77.4 ± 8.5 | 85.6 ± 11.2 | 88.9 ± 10.0 | 77.8 ± 8.8 | 85.7 ± 10.8 | 85.1 ± 9.5 | 89.1 ± 10.3 |
| B组 | 35 | 83.6 ± 13.9 | 74.5 ± 10.2 | 75.2 ± 9.6 | 75.4 ± 11.7 | 82.1 ± 12.4 | 87.3 ± 12.1 | 80.4 ± 10.0 | 83.9 ± 13.1 | 83.3 ± 8.6 | 86.7 ± 10.5 |
| RB组 | 33 | 84.1 ± 13.1 | 71.7 ± 10.6 | 77.6 ± 11.0 | 76.7 ± 7.8 | 85.5 ± 9.7 | 91.2 ± 11.5 | 81.1 ± 10.0 | 87.1 ± 12.4 | 86.4 ± 9.3 | 90.3 ± 9.3 |

1 mmHg=0.133 kPa.

表4 3组患者术后不良反应比较

Table 4 Comparison of postoperative adverse reaction among the three groups

| 组别 | n | 咳嗽/[例(%)] | 恶心、呕吐/[例(%)] | 寒颤/[例(%)] | 头晕/[例(%)] | 嗜睡/[例(%)] |
|-----|----|-----------|--------------|-----------|----------------------|-----------|
| R组 | 36 | 5 (13.9) | 8 (22.2) | 0 (0.0) | 0 (0.0) [#] | 0 (0.0) |
| B组 | 35 | 2 (5.7) | 1 (2.9)* | 2 (5.7) | 6 (17.1) | 2 (5.7) |
| RB组 | 33 | 3 (9.1) | 1 (3.0)* | 1 (3.0) | 0 (0.0) [#] | 0 (0.0) |

与R组相比, * $P < 0.05$; 与B组相比, [#] $P < 0.05$ 。Compare with group R, * $P < 0.05$; Compare with group B, [#] $P < 0.05$.

3组患者均未发生术中体动及术后心动过速、心动过缓、高血压、低血压及呼吸抑制等不良反应。

3 讨论

本研究结果显示:布托啡诺复合瑞芬太尼可以达到纤维支气管镜诊疗麻醉所需镇痛水平,且安全性较好;布托啡诺复合瑞芬太尼不影响患者术后苏醒;布托啡诺与瑞芬太尼复合使用

相比两者单独使用患者术后头晕、恶心呕吐的发生率更低。

目前国际上的指南推荐对行纤维支气管镜诊疗的患者实施麻醉^[6-7]。但麻醉本身也会给患者带来很多负面影响。理想的麻醉应具有起效快、深度足、易于控制、认知恢复迅速且良好、苏醒后麻醉相关不良反应少等特点^[8-9]。瑞芬太尼作为芬太尼衍生物,具有代谢快、易控制的特点,常规应用于手术麻醉镇痛。但作为纯 μ 受体激动剂,瑞芬太尼能够引起呼吸循环抑制、恶心呕吐等不良

反应^[10], 并且其快代谢会使患者在术后很快失去镇痛。纤维支气管镜的穿刺检查或者镜下治疗刺激较强^[11]。由于诊疗操作的刺激及麻醉药物的影响, 患者常会出现术后恶心、呕吐、咳嗽及咽喉部不适感等不良反应^[9]。恶心、呕吐是常见的麻醉后不良反应可引起反流误吸, 特别对于存在创伤的气道而言, 后果可能更加严重^[12]。咳嗽是机体对呼吸道的一种保护动作^[13], 在纤维支气管镜有创诊疗后, 剧烈的咳嗽有造成气道损伤的可能^[14]。如果处理不当, 剧烈的咳嗽可能会给患者的预后造成不良影响^[15]。由于人体的呼吸道对外界刺激比较敏感^[16], 使得无痛纤维支气管镜诊疗对麻醉镇静镇痛的要求更高。

布托啡诺是吗啡南的衍生物, 主要通过激动 κ 受体发挥镇痛作用^[4]。自国内上市以来, 布托啡诺常被用于短小手术的麻醉镇痛。在本研究中, 布托啡诺用于无痛纤维支气管镜诊疗可以满足其镇痛要求。与瑞芬太尼对比, 布托啡诺明显降低了患者术后恶心呕吐的发生。但需注意的是, 布托啡诺会引起患者术后头晕发生率明显增加, 并且会引起患者术后苏醒时间延长。而布托啡诺复合瑞芬太尼作为麻醉镇痛方案在保障麻醉镇痛水平的同时, 在一定程度上也可以减少上述不良反应的发生率。推测其可能的原因为: 1) 瑞芬太尼起效迅速, 可以一定程度上覆盖布托啡诺由于起效较慢而引起的手术前期镇痛不足; 2) 复合用药中两种药物各自的用量减少, 可以一定程度上的减少相应不良反应的发生。在麻醉诱导速度方面, 布托啡诺的应用缩短了诱导时间可能与其镇静作用有关。但本研究3组患者的术后咳嗽并没有明显差异, 布托啡诺的应用未能减少纤维支气管镜治疗后患者的咳嗽, 因此还需进一步实验探究减轻患者术后咳嗽的麻醉方案。

综上所述, 布托啡诺联合瑞芬太尼作为镇痛方案复合丙泊酚用于无痛纤维支气管镜兼具两者单独使用的优点。此方案术后恶心呕吐、头晕发生率较低, 不影响患者术后复苏, 且不增加其他术后不良反应的发生率。

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