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复合羟考酮时依托咪酯用于老年人胃镜检查的半数有效剂量

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[摘要] 目的: 探讨复合羟考酮时依托咪酯用于老年人胃镜检查的半数有效剂量。方法: 选择2017年6月至2018年1月保定市第一中心医院行无痛胃镜检查的29例老年人, 年龄65~78岁, 体重49~66 kg, 美国麻醉医师协会(American Society of Anesthesiologists, ASA)I~III级。静脉注射羟考酮0.05 mg/kg, 2 min后静脉注射依托咪酯, 待患者睫毛反射消失, 托下颌无反应后行胃镜检查。采用序贯法确定依托咪酯剂量, 起始剂量为0.2 mg/kg, 如上1例患者在胃镜检查中出现呛咳或体动反应, 则下1例患者采用高一浓度, 反之则采用低一浓度, 相邻浓度比为1:1.2。采用概率单位法计算依托咪酯的半数有效剂量及95%CI。结果: 复合羟考酮时依托咪酯用于老年人胃镜检查的半数有效剂量为0.15 mg/kg(95% CI 0.13~0.17 mg/kg)。结论: 复合羟考酮时依托咪酯用于老年人胃镜检查的半数有效剂量为0.15 mg/kg。

[关键词] 羟考酮; 依托咪酯; 胃镜检查; 老年; 半数有效剂量

Median effective dose of etomidate for gastroscopy in elderly people when combined with oxycodone

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Abstract **Objective:** To explore the median effective dosage (ED50) of etomidate for gastroscopy in elderly people when combined with oxycodone. **Methods:** Twenty-nine elderly people underwent gastroscopy in the First Center Hospital of Baoding from June 2017 to January 2018 were included in this study. Those patients, aged 65 to 78 years, weighing 49–66 kg, with American Society of Anesthesiologists physical status I–III, were intravenously injected with oxycodone 0.05 mg/kg. After 2 min, all people were intravenously injected with etomidate. Gastroscopy was performed when the eyelash reflex disappeared. The dose of etomidate was determined by sequential method, and initial dose of etomidate was 0.2 mg/kg. The next patient used a higher level of dosage when the last patient had a cough or somatic reaction during gastroscopy, and the ratio of adjacent dosage was 1:1.2. The ED50 and 95% CI of etomidate were calculated by probability unit method. **Results:** The ED50 and 95% CI of etomidate for gastroscopy was 0.15 mg/kg (95% CI 0.13–0.17 mg/kg) in

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elderly people when combined with oxycodone. **Conclusion:** The ED₅₀ of etomidate for gastroscopy was 0.15 mg/kg in elderly people when combined with oxycodone.

Keywords oxycodone; etomidate; gastroscopy; elderly; median effective dosage

随着人口老龄化的加快及对健康重视程度的提高,越来越多的老年人注重胃肠道疾病的早期筛查。胃镜是筛查与诊断上消化道疾病的重要手段。无痛胃镜可避免清醒检查所带来的痛苦,受到患者喜爱。2014年《中国消化内镜诊疗镇静/麻醉的专家共识》^[1]推荐:老年患者,尤其是高龄患者选择依托咪酯作为麻醉镇静药物利于血流动力学稳定,但应预先静脉注射适量阿片类镇痛类药物,弥补依托咪酯镇痛不全,降低恶心、呕吐及肌阵挛发生的风险。羟考酮是目前临床上唯一的 μ 和 κ 阿片受体激动药,既可以激动中枢神经系统突触前端细胞的 μ 阿片受体来抑制躯体痛信号的转导,又可以激动胃肠平滑肌细胞的 κ 受体抑制内脏痛的转导,因此较纯 μ 阿片受体激动药(如舒芬太尼等)对胃镜检查引起的内脏痛镇痛效果更佳,且不易引起呼吸抑制及恶心、呕吐^[2-5],理论上更适合于老年人无痛胃镜检查。然而,羟考酮复合依托咪酯用于胃镜检查的效果及量效关系的相关研究鲜见报道。因此,本研究拟评估复合羟考酮时依托咪酯用于老年人胃镜检查的半数有效剂量(effective dosage in 50% patients, ED₅₀),为临床用药提供参考。

1 对象与方法

1.1 对象

本研究经保定市第一中心医院伦理委员会批准,并获患者知情同意。选取2017年6月至2018年1月保定市第一中心医院行无痛胃镜检查的老年患者29例,年龄65~78岁,体重49~66 kg,美国麻醉医师协会(American Society of Anesthesiologists, ASA)I~III级。排除标准:对试验药物过敏者;近2周内应用镇痛药物者;肝肾功能严重障碍者等。

1.2 方法

患者均未给予术前用药。采用常规监测,开放上肢液路,输注复方林格氏液维持。吸氧去氮,氧流量2 L/min。缓慢静脉注射羟考酮[萌蒂(中国)制药有限公司, BM247]0.05 mg/kg, 2 min后缓慢静脉注射依托咪酯(江苏恩华药业股份有限公司, 20161123),判断患者睫毛反射消失,托下

颌无反应后行胃镜检查。所有胃镜检查均由同一高年资内镜医师完成。采用序贯法确定依托咪酯剂量,即前1例患者麻醉效果决定其后1例患者的用量。根据参考文献[6]及预试验,选择依托咪酯的起始剂量为0.2 mg/kg。若上1例患者在胃镜检查中出现呛咳或体动反应(定义为阳性),则下1例患者采用高一等级剂量,反之则采用低一级剂量,相邻剂量比为1:1.2。为减少受试者数量又保证结果的普遍性,有连续8个上下交叉即停止试验。当胃镜检查中出现呛咳或体动反应时静脉追加依托咪酯0.05~0.1 mg/kg。发生呼吸抑制时,托起下颌开放气道,辅助呼吸,必要时退出胃镜并控制呼吸,待呼吸抑制解除后再继续进行胃镜检查。记录呼吸抑制、低血压、心动过缓、头晕、肌阵挛及恶心呕吐的发生情况。

1.3 统计学处理

采用概率单位法计算依托咪酯的ED₅₀及95%CI。ED₅₀的计算方法为:依托咪酯剂量的对数(x)及该剂量的患者合计数(n)、依托咪酯抑制体动及呛咳的有效率(p)、两相邻剂量对数的差值(d)。按照下列序贯法公式计算ED₅₀及其95%CI。

$$\text{ED}_{50} \text{的对数值: } \lg \text{ED}_{50} = \Sigma nx / \Sigma n。$$

$$\text{ED}_{50} \text{的标准误: } \text{SlgED}_{50} = d [\Sigma p(1-p) / (n-1)]^{1/2}。$$

$$\text{ED}_{50} \text{对数值的95\%CI: } (\lg \text{ED}_{50} - 1.96 \text{ SlgED}_{50}, \lg \text{ED}_{50} + 1.96 \text{ SlgED}_{50})。$$

各对数值取反对数即得ED₅₀及其95%CI。

采用SPSS 17.0统计软件进行分析。连续变量采用Kolmogorov-Smirnov检验评估其是否为正态分布,正态分布的计量资料以均数±标准差($\bar{x} \pm s$)表示;非正态分布的计量资料以中位数(全距)表示;计数资料以率(%)表示。

2 结果

研究共招募患者29名,男15名,女14名;年龄65~78岁;体重49~66 kg,身高153~176 cm。复合羟考酮时依托咪酯用于老年人胃镜检查的ED₅₀为0.15 mg/kg(95%CI 0.13~0.17 mg/kg,图1)。29名患者中1例出现呼吸抑制,托起下颌开放气道后,血氧逐渐恢复正常。1例患者苏醒后诉头晕,

未予处理, 逐渐恢复正常。所有患者未出现低血压、心动过缓、肌阵挛及恶心呕吐等不良反应。

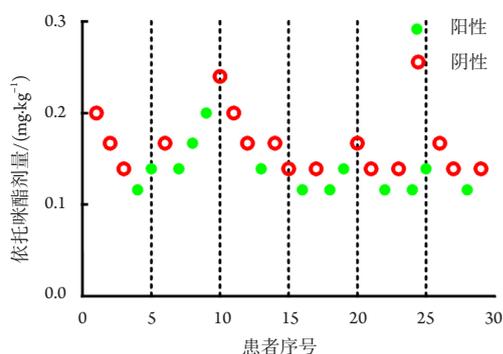


图1 依托咪酯剂量序贯图

Figure 1 Sequential diagram of dosage of etomidate

3 讨论

随着健康中国战略的提出, 人民群众对健康生活的期望与日俱增, 主动进行疾病早期筛查的人群日益增多, 尤见于老年人群。无痛胃肠镜检查以其舒适、安全、依从性高等优势, 倍受患者及内镜医师青睐。由于老年人脏器功能减退, 对麻醉药物耐受性差, 加上术前禁食水导致的血容量不足, 故要求麻醉药物既要镇痛镇静效果确切, 又要对呼吸循环影响轻微, 同时还要严格控制麻醉药物的用量。因此, 本研究以ED₅₀作为切入点研究依托咪酯复合羟考酮用于老年人胃镜检查的量效关系, 为无痛胃镜用药提供依据。

序贯法是研究药物量效关系的较经典的方法, 其可最大限度的减少研究所需的样本数量。本研究采用改良的Dixon-Mood序贯法, 按照等比级数进行序贯研究, 根据研究对象的阴性/阳性反应的结果来增加/减少下1例研究对象所需依托咪酯的剂量, 达到8个上下交叉时停止试验研究, 既减少了研究对象的样本量, 又保证了研究结果的可靠性。本研究结果显示: 复合0.05 mg/kg羟考酮时依托咪酯的ED₅₀为0.15 mg/kg。而卢盛位等^[6]研究发现联合0.3 μg/kg瑞芬太尼时依托咪酯用于老年胃镜检查的ED₅₀为0.17 mg/kg, 其剂量高于本研究结果, 分析原因可能是: 1) 瑞芬太尼作用时间短, 一次给药剂量的作用时间不足以完成胃镜检查, 故需要增加依托咪酯用量来弥补; 2) 胃镜检查过程中产生的伤害性刺激属内脏痛范畴, 瑞芬太尼为μ阿片受体激动剂, 对内脏痛镇痛效果较羟

考酮弱^[7-10], 故需增加依托咪酯的用量。林慧等^[11]研究发现复合舒芬太尼时依托咪酯用于老年胃镜检查的ED₅₀为0.118 mg/kg, 其剂量低于本研究结果, 可能与其要求达到的目标(镇静催眠)较本研究要求达到的目标(完全抑制胃镜检查过程中的体动及呛咳)的麻醉深度浅, 从而药物用量低有关。

恶心呕吐与肌阵挛是依托咪酯的主要不良反应, 发生率较高, 且与注射剂量及浓度相关^[12-14]。本研究中29名患者中除1例出现呼吸抑制, 1例患者苏醒后诉头晕外, 均未出现低血压、心动过缓、肌阵挛及恶心呕吐等不良反应。分析原因可能为: 1) 预注射阿片类药物可减少恶心呕吐及肌阵挛的发生^[14-19]; 2) 羟考酮抗伤害效应较强, 减少了依托咪酯的用量, 从而降低了恶心呕吐和呼吸抑制的发生率。

综上所述, 复合羟考酮时依托咪酯用于老年人胃镜检查的半数有效剂量为0.15 mg/kg。

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