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• 临床研究 •

丙泊酚与咪达唑仑用于全麻后苏醒室躁动疗效的比较*

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摘要 目的:比较丙泊酚及咪达唑仑用于全麻后苏醒室(post-anesthesia care unit, PACU)躁动的疗效。**方法:**本研究选取 2016 年 11 月至 2020 年 4 月全麻术后转入 PACU 后发生中、重度躁动的患者 194 例,分为丙泊酚组(P 组, n=98)、咪达唑仑组(M 组, n=96)。P 组静脉注射丙泊酚 0.5 mg/kg~1 mg/kg, M 组静脉注射咪达唑仑 0.03 mg/kg。必要时重复给药,直至患者 Riker 镇静和躁动评分在 4 分及以下。记录两组患者给药次数、药物起效时间、给药前后 Riker 评分、PACU 停留时间、给药前、末次给药后生命体征及处理方法。**结果:**首次给药后,两组患者躁动均可得到缓解, Riker 评分差异无统计学意义($P>0.05$)。P 组 48 例患者缓解后躁动再次加重,重复给药后 38 例可渐缓解,另 10 例仍需制动。M 组 12 例患者躁动缓解后再次加重,重复给药后均可渐缓解。两组患者首次给药后躁动缓解后再次加重的症状差异具有统计学意义($P<0.05$), PACU 停留时间差异无统计学意义($P>0.05$)。其中 P 组 7 例患者重复给药后呼吸抑制予托下颌面罩供氧后可快速缓解, M 组重复给药后 3 例患者呼吸抑制需放置口咽通气道。**结论:**咪达唑仑用于 PACU 躁动较丙泊酚不易反复发作,但重复给药后引起的呼吸抑制需被重视。

关键词:苏醒室;躁动;全身麻醉;咪达唑仑;丙泊酚

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Comparison of the Effects of Propofol and Midazolam on Postoperative Agitation in Post-anesthesia Care Unit*

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ABSTRACT Objective: To compare the effects of propofol and midazolam on emergence agitation in post-anesthesia care unit (PACU). **Methods:** 194 patients with moderate or severe agitation in PACU after general anesthesia from November 2016 to April 2020 were selected. The patients were divided into two groups: Group Propofol (Group P, n=98) and Group Midazolam (Group M, n=96). Patients in Group P received intravenous 0.5 mg/kg~1 mg/kg propofol and patients in Group M received intravenous 0.03 mg/kg midazolam for treatment. Repeat the medication if necessary, until the Riker score is less than or equal to 4. Administration times, efficacy time, Riker scores before and after administration, PACU residence time, vital signs before the first and after the last administration, and the treatment were recorded. **Results:** Agitation was relieved in both groups after the first administration, there was no significant difference in Riker score difference ($P>0.05$). 48 patients in Group P showed recurrence agitation and 38 patients of them required second administration, another 10 of them still needed to be bound after the last administration. 12 patients in Group M showed recurrence and were gradually relieved after repeated administration. The difference of the recurrence situation between Group M and Group P was significant ($P<0.05$), and there was no significant difference in PACU residence time ($P>0.05$). 7 patients in Group P needed jaw thrust maneuvers and oxygen masks, and 3 patients in Group M needed inserting oropharyngeal airways for respiratory depression after repeated administration. **Conclusions:** The treatment of midazolam for agitation in PACU had less recurrence than propofol, however, great importance should be attached to its respiratory depression effect.

Key words: Post-anesthesia care unit; Agitation; General anesthesia; Midazolam; Propofol

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前言

全麻后恢复期躁动是全身麻醉后常见的早期并发症,以活动亢进为主要表现,带给患者痛苦不适感,可造成患者躁动期

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间自行拔除引流管、落床、自伤、失血等严重不良后果^[1];恢复期躁动不仅对患者本身造成不利影响,对 PACU 工作人员安全亦是潜在威胁^[2];恢复期躁动与术后瞻望密切相关,可能会延长患者住院时间,增加不良反应的发生率与死亡率^[3],因此预防和缓解恢复期躁动尤为重要。研究表明恢复期躁动可能与留置导管、气管插管及患者术前精神状态有关^[4],尚无方法可完全避免非中重度疼痛引起的全麻恢复期躁动,镇静治疗对急性躁动有一定疗效。目前临床研究提示麻醉期间或麻醉结束前给予咪达唑仑、丙泊酚或右美托咪等镇静药物定可减少术后躁动的发生^[5-7]。丙泊酚是一种全麻镇静药,咪达唑仑为苯二氮、类镇静药,二者均初始分布半衰期短,可用于躁动患者短时镇静,但镇静药物的使用亦存在呼吸抑制的风险^[8,9],本研究旨在比较二者对 PACU 患者急性躁动的疗效及副作用,探索应对恢复期躁动的合理用药。

1 资料与方法

1.1 一般资料

选择 2016 年 11 月至 2020 年 4 月,上海市同济医院全麻手术拔除气管导管后 PACU 内发生急性中、重度躁动(Riker 评分 ≥ 6 分)的成年患者 194 例:ASA 分级 I 或 II 级,年龄 22~67 岁;排除精神疾病、中枢神经系统疾病、阿片类药物成瘾或酗酒、吸毒、术中输血、缺氧或二氧化碳潴留、电解质紊乱及体温低于 36.3℃等患者。受试者根据所给药物分为两组:P 组(丙泊酚组)和 M 组(咪达唑仑组),P 组 98 例,M 组 96 例。其中 Riker 镇静和躁动评分 5 分为躁动,6 分为非常躁动/中度躁动(very agitated, VA),7 分为危险躁动/重度躁动(dangerous agitation, DA)。

1.2 方法

所有全麻患者拔除气管导管或喉罩后予鼻导管吸氧 2

L/min,入 PACU 后进行常规心电图监护。P 组给予丙泊酚 0.5 mg/kg~1 mg/kg 静脉注射^[10],M 组给予咪达唑仑 0.03 mg/kg 静脉注射^[10]镇静治疗,躁动反复发作者重复上述给药,给药次数达 3 次后不再重复给药,同时给予患者保护性制动。患者出现自主呼吸不能维持氧合者予托下颌面罩供氧,必要时放置口咽通气道。本研究采用 Riker 评分评估患者躁动、镇静情况。患者改良 Aldrete 评分(Modified Aldrete scoring system) ≥ 9 分为达到可送回病房标准,记录此时间为 PACU 停留截止时间。

1.3 监测指标

记录患者给药次数、给药后 Riker 评分、PACU 停留时间。患者 Riker 镇静和躁动评分评分 ≤ 4 分判断为药物起效。监测首次给药前(T0)、药物起效时(T1)及末次给药后 10 分钟(T10)的平均血压(MBP)、指脉氧饱和度(SpO₂)、心率(HR)。

1.4 统计分析

统计分析采用 SPSS26.0 软件,计量资料以均数 $\pm$ 标准差($\bar{x} \pm s$)描述,采用两样本独立 t 检验,计数资料比较采用 χ^2 检验及 Fisher 确切概率检验,检验标准以 $P < 0.05$ 差异具有统计学意义。用药前后两组患者血压心率的变化趋势用多组重复测量资料的方差分析,检验水准为 0.05,对应 F 界值表 $P < 0.05$ 具有统计学意义。

2 结果

2.1 两组患者 PACU 停留时间差异、性别、年龄、身高、体重、体重指数差异无统计学意义

两组患者 PACU 停留时间分别为 (58.37 $\pm$ 6.25)min、(57.65 $\pm$ 7.03)min,差异无统计学意义($P > 0.05$)。对两组患者一般情况进行评估,其性别、年龄、身高、体重、体重指数差异均无统计学意义($P > 0.05$)。就躁动严重程度而言,两组患者发生 VA 或 DA 数量差异无统计学意义($P > 0.05$)。

表 1 两组患者一般情况比较

Table 1 Comparison of general data between the two groups

Groups	n	Male/Female	Age/yo	Height/cm	Weight/kg	BMI	VA/DA
P	98	64/34	50.27 $\pm$ 13.15	167.83 $\pm$ 7.13	65.36 $\pm$ 11.88	24.02 $\pm$ 4.03	29/21
M	96	67/29 ^a	49.50 $\pm$ 10.35 ^b	165.57 $\pm$ 7.41 ^c	63.93 $\pm$ 10.40 ^d	23.97 $\pm$ 4.15 ^e	26/19 ^f

Note: $P^a > 0.05$, $P^b > 0.05$, $P^c > 0.05$, $P^d > 0.05$, $P^e > 0.05$, $P^f > 0.05$.

2.2 两组躁动患者首次给药后均能达缓解,Riker 评分变化无统计学意义($P > 0.05$)

P 组 98 例患者、M 组 96 例患者首次给药后躁动全部缓

解,首次给药后 Riker 评分差异分别为 (2.57 $\pm$ 0.73)、(2.81 $\pm$ 0.76),差异无统计学意义($P > 0.05$)。

表 2 两组患者用药前后 Riker 评分比较

Table 2 Comparison of Riker Scales between the two groups before and after treatment

Groups	n	Riker score before treatment	Riker score after first dosing	Score difference after first dosing
P	98	6.13 $\pm$ 0.43	3.56 $\pm$ 0.76	2.57 $\pm$ 0.73
M	96	6.22 $\pm$ 0.42	3.41 $\pm$ 0.71	2.81 $\pm$ 0.76

Note: $P > 0.05$.

2.3 两组患者首次给药后 P 组发生再次躁动患者人数较多,重复给药后 M 组患者呼吸抑制较为严重,差异有统计学意义

($P < 0.05$)。

P 组首次给药后 98 例患者躁动全部缓解,其中 48 例患者躁动缓解后再次出现躁动加重,需重复给药,重复给药后 38 例可渐缓解,仍有 10 例给药次数达 3 次后躁动仍再次加重试图拔除尿管,需维持保护性制动。47 例重复给药患者中 7 例患者重复给药后出现指脉氧饱和度下降至 90%,予托下颌面罩供氧后均迅速缓解。M 组首次给药后 96 例患者躁动全部缓解,其中 12 例患者躁动缓解后再次出现躁动加重需重复给药。重复给药后 10 例患者持续镇静,其中 2 例无需特殊处理自主呼吸

可维持氧合,5 例患者出现呼吸抑制,托下颌后迅速缓解,另有 3 例患者表现为严重 / 持续呼吸抑制,需放置口咽通气道以维持氧合,缓解后拔出口咽通气道持续镇静。两组患者首次给药后均有部分患者发生再次躁动,P 组患者数量较多,差异有统计学意义($P < 0.05$)。两组患者重复给药后均有患者出现不同程度呼吸抑制,但 M 组患者呼吸抑制较为严重,需放置口咽通气道自主呼吸维持氧合,两组比较差异具有统计学意义($P < 0.05$)。无患者出现窦性心动过缓(见表 3)。

表 3 两组患者给药后躁动反复情况及不良反应比较

Table 3 Comparison of recurrence and adverse reactions after treatment between the two groups

Adverse Reactions	Recurrence	Continuous Sedation	Respiratory Inhibition	Severe Respiratory Inhibition	Bradycardia
Group P	48/98	0/98	7/98	0/98	0/98
Group M	12/96 ^a	10/96 ^b	5/96 ^c	3/96 ^d	0/96

Note: $P^a < 0.05$, $P^c > 0.05$; $P^b < 0.05$, $P^d < 0.05$.

2.4 两组患者手术前平均血压、心率均值比较无统计学意义($P > 0.05$)

患者全麻恢复期出现急性躁动后(T0),两组用药后药物起

效时(T1)、末次给药后第 10 分钟(T10)血压心率均有不同程度下降,差异具有统计学意义,但两组间比较差异不具有统计学意义($P > 0.05$)(见表 4)。

表 4 两组患者治疗前后血压心率比较

Table 4 Comparison of MBP and HR before and after treatment between the two groups

	Groups	Pre-operation	T0	T1	T10
MBP/mmHg	P	92.30± 3.77	100.50± 5.27	85.47± 5.71	89.73± 6.50
	M	91.57± 4.31	99.73± 6.41	90.55± 5.35	93.20± 6.87
HR/bpm	P	75.50± 13.31	99.12± 20.10	83.45± 18.33	85.28± 15.21
	M	78.15± 11.25	97.83± 19.43	95.41± 17.50	93.15± 18.17

3 讨论

全麻后苏醒期躁动发生机制目前尚不完全明确,研究发现其发生可能与年龄、性别、麻醉用药、手术方式、手术时长、术后疼痛、代谢紊乱、导尿管刺激等有关^[1]。既往前瞻性观察研究表明,恢复期躁动发生率约为 4.7%^[11]~19%^[12]。恢复期躁动多为一过性,PACU 医生需要及时处理患者躁动。去除诱发躁动的因素为主要治疗手段,因非疼痛因素引起的躁动,包括因留置导管等因素在患者处于 PACU 阶段常不能去除,常需应用镇静药物快速缓解,以防发生不良事件。

咪达唑仑为苯二氮卓类镇静药物,是中枢神经系统 γ -氨基丁酸(GABA)受体激动剂,具有抗焦虑、遗忘、镇静、催眠和抗惊厥等作用^[13]。该药物相起效快、持续时间相对短、血浆清除率较高,可用于躁动患者的镇静治疗^[14]。有研究提示儿童术前单次给予咪达唑仑因药物半衰期短,不能减少患者苏醒期躁动^[15],但手术结束时给予咪达唑仑可减少全麻术后躁动的发生^[16]。应用咪达唑仑后患者血流动力学稳定,故咪达唑仑常被用于 ICU 患者镇静治疗^[17],且近年来的研究表明,苯二氮卓类药物容易引起蓄积、代谢较慢、增加镇静深度,从而进一步延长机械通气时

间及 ICU 停留时间^[18-21];目前有关咪达唑仑用于 PACU 躁动快速治疗的有效性及安全性的研究较少,但有回顾性研究表明在使用抗精神病药物的 ICU 患者中,苯二氮卓类药物应用可能是导致躁动的独立危险因素^[22]。本研究结果提示咪达唑仑可应用于 PACU 躁动的快速治疗,并未导致 PACU 停留时间延长,同时由于初始分布半衰期短,患者可较快恢复意识。此结果可能与本研究排除了存在精神类疾病、中枢神经系统疾病、吸毒、酒精或药物成瘾的患者有关,也可能与苏醒室内发生躁动多为一过性,药物短期应用及患者病情优于 ICU 患者有关^[23]。

丙泊酚也是常用的镇静药物之一,其特点是起效快、作用时间短、撤药后能快速清醒、且镇静深度呈剂量依赖性^[24],亦可产生遗忘作用和抗惊厥作用^[25]。丙泊酚单次注射时可出现暂时性呼吸抑制和血压下降、心动过缓,尤见于心脏储备功能差、低血容量的患者^[26]。研究表明丙泊酚可安全用于儿童恢复期躁动,特别是使用七氟烷麻醉的患儿^[27]。另有研究表明接受腺样体切除术的患儿,使用氯胺酮 / 丙泊酚混合液(氯胺酮:丙泊酚=1:3,mg/kg)可有效应对其恢复期躁动^[28]。本研究提示丙泊酚可快速镇静躁动患者,且以 0.5 mg/kg~1 mg/kg 静脉推注并未引起严重的血压下降,但其复发率较高,重复给药后会引起短时

呼吸抑制,予托下颌后均可缓解,因此给药后需密切监护。

PACU 躁动患者临床上需要严密监测血压、心率、氧饱和度等生命体征变化;药物作用使临床测量血压、心率所得结果波动较大,尤其是在用药早期差别尤为明显,躁动缓解后两组患者血压心率均明显下降。两组患者用药后血压虽下降,但仍未达低血压诊断标准,不需要特殊处理,表明咪达唑仑或丙泊酚处理 PACU 躁动具有安全性。

本研究结果显示,对于已发生躁动且无法去除躁动因素的患者静脉注射咪达唑仑治疗 PACU 急性躁动不易引起躁动反复发作,但有少数患者出现长时间镇静,需密切监测患者呼吸等生命体征;丙泊酚小剂量单次给药后躁动易反复发作,但其引起的呼吸抑制可很快恢复,两组患者血流动力学均相对稳定。综上所述,丙泊酚及咪达唑仑均可用于无精神疾病、无中枢神经系统疾病的患者 PACU 躁动的快速处理。重复给药后,丙泊酚及咪达唑仑均可能会引起呼吸抑制,丙泊酚呼吸抑制可快速缓解,咪达唑仑引起的镇静时间较长,呼吸抑制程度较重,需加强呼吸监测或采取相应措施。本研究中患者入 PACU 后由护士迅速进行心电监护、体温测量,两组患者给药后, Riker 评分 4-5 分时由研究者评估 VAS 评分均 ≤ 3 分,结合患者面部表情、肌张力等(参考行为疼痛量表^[29])综合评价方法,临床判断患者躁动由疼痛导致可能性小。但患者处于镇静状态及躁动时 VAS 评分或行为疼痛量表等评价方法均不准确^[30],故此评价仅作参考,不对该研究核心指标 Riker 评分产生影响。该研究中咪达唑仑及丙泊酚均无明显镇痛作用,但患者镇静后对疼痛刺激反应强度有所降低,故该项研究中两种药物对疼痛因素导致的躁动是否有效尚需进一步深入研究。

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