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托烷司琼与帕洛诺司琼用于小儿骨科术后镇痛预防恶心呕吐的效果研究 *

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摘要 目的：比较托烷司琼与帕洛诺司琼用于小儿骨科术后镇痛时预防恶心呕吐的效果。**方法：**纳入 2019 年 3 月到 2021 年 3 月在我院进行骨科手术的儿童 60 例，根据术后镇痛泵中使用止吐药物的不同分为托烷司琼组和帕洛诺司琼组，每组 30 例，比较两组患儿术前、术后的心率（HR）、平均动脉压（MAP），在术后 48 小时内，观察两组患儿恶心呕吐、头晕头痛、皮肤瘙痒以及呼吸抑制等术后并发症。视觉模拟评分法（VAS）评估患儿术后疼痛，Ramsay 量表评估患儿术后镇静效果。**结果：**托烷司琼和帕洛诺司琼组患儿在术前和术后 HR 和 MAP 比较均无显著差异（P>0.05）；托烷司琼组和帕洛诺司琼组患儿术后 VAS 评分、Ramsay 评分均随时间延长而降低，且同一时间点两组患儿 VAS 评分无显著差异（P>0.05）；帕洛诺司琼组术后 PONV 发生率（20.00 %）高于托烷司琼组（3.33 %）（P<0.05）。帕洛诺司琼组和托烷司琼组患儿出现头晕头痛、皮肤瘙痒以及呼吸抑制例数分别为 3/2 例、1/0 例和 1/0 例。两组间术后并发症发生率比较无差异（P>0.05）。**结论：**托烷司琼与帕洛诺司琼对骨科手术后儿童血流动力学、疼痛和镇静效果并无差异，但在预防术后恶心呕吐方面托烷司琼效果优于帕洛诺司琼。

关键词：托烷司琼；帕洛诺司琼；儿童；骨科；术后恶心呕吐

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Effect of Tropisetron and Palonosetron on Postoperative Analgesia and Prevention of Nausea and Vomiting in Children*

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ABSTRACT Objective: To compare the effects of tropisetron and palonosetron on prevention of nausea and vomiting in pediatric orthopedic postoperative analgesia. **Methods:** A total of 60 children undergoing orthopedic surgery in our hospital from March 2019 to March 2021 were included. According to the different antiemetic drugs used in postoperative analgesia pump, they were divided into tropisetron group and palonosetron group, with 30 patients in each group. The preoperative and postoperative heart rate (HR) and mean arterial pressure (MAP) of the two groups were compared. Postoperative complications such as nausea, vomiting, dizziness, headache, skin itching and respiratory depression were observed in the two groups. **Results:** There was no significant difference in preoperative and postoperative HR and MAP between tropisetron and palonosetron (P>0.05). Postoperative VAS scores and Ramsay scores in tropisetron group and palonosetron group decreased with time, and there was no significant difference in VAS scores between the two groups at the same time point (P>0.05). The incidence of PONV in palonosetron group (20.00 %) was higher than that in tropisetron group (3.33 %) (P>0.05). The cases of drowsiness, itchy skin and dyspnea were 3 cases, 0 cases and 1 case in palonosetron group, respectively, while there were 2 cases, 0 cases and 0case in tropansetron group, but there was no difference in postoperative complications between the two groups (P>0.05). **Conclusion:** Tropisetron and Palonosetron have no difference in hemodynamics, pain and sedation in children after orthopedic surgery, but tropisetron is better than palonosetron in preventing postoperative malignant vomiting .

Key words: Tropisetron; Palonosetron; Children; Orthopedics; Postoperative nausea and vomiting

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前言

作为手术后最常见的不良反应之一，术后恶心呕吐（Post-operative nausea and vomiting, PONV）可引起患者不适，其中术后呕吐的发生率约为 30 %，术后恶心的发生率约为 50 %，在一些高危患者中，PONV 的发生率高达 80 %[1,2]。研究发现，PONV 的发生不仅受手术类型、麻醉方式、患者精神状态和焦虑抑郁程度等影响，还与患者年龄有关。儿童和青少年 PONV 的发病

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率远高于成年人,且发病率随年龄增长而降低[3,4]。PONV 不仅延长患者住院时间,增加诊治医疗费用,且可能引起患者水电解质失衡、伤口开裂、误吸和吸入性肺炎,严重者可能影响生命安全[5,6]。5- 羟色胺受体拮抗剂是目前临床应用最广泛的治疗恶心呕吐的药物,其代表药物主要有多拉司琼、托烷司琼和帕洛诺司琼等[7,8]。帕洛诺司琼是一种长效且高选择性的 5- 羟色胺 3 受体(5- hydroxytryptamine 3, 5-HT3)拮抗剂,临床上被批准用于中度致呕性化疗药物引起的延迟性恶心、呕吐的预防药物[9-11]。托烷司琼是一种高效的选择性 5-HT3 受体拮抗剂,临床上主要被用于治疗和预防化疗引起的恶心呕吐。临床研究发现,托烷司琼在治疗和预防化疗引起的恶心呕吐上临床疗效优于帕洛诺司琼等其他 5- 羟色胺受体拮抗剂[12,13]。然而,鲜有研究比较儿童骨科手术后应用镇痛泵时,托烷司琼与帕洛诺司琼对 PONV 发生率的临床效果影响。本研究拟比较两种药物对儿童骨科手术后应用镇痛泵时 PONV 的预防效果。

1 材料与方法

1.1 研究对象与分组

研究选取 2019 年 3 月到 2021 年 3 月在我院进行骨科手术的儿童 60 例,根据术后镇痛泵中添加的止吐药物分为托烷司琼组和帕洛诺司组,每组各 30 例。

纳入标准:年龄 <18 周岁;ASAI-II 级,单独骨科手术,术后需应用镇痛泵;患儿监护人对本次研究知情,签订知情同意书自愿加入本次研究;本研究经我院伦理委员会批准。

排除标准:智力低下和精神障碍;先天性心脏病或其他先天性疾病;同时进行其他手术治疗;慢性传染性疾病;术前恶心呕吐病史、酗酒史;严重心肝肾肺疾病;术前 24 h 内未服用促吐药。

1.2 药物干预方法

所有患儿术前均未使用地塞米松或其他止吐药物治疗,术后均使用镇痛泵,帕洛诺司组配方为舒芬太尼 2.5 μg/kg+ 帕洛诺司琼(正大天晴药物集团,5 μg/kg),托烷司琼组配方为舒芬太尼 2.5 μg/kg+ 托烷司琼(江苏恒瑞医药股份有限公司,0.2 mg/kg)治疗。两组患儿术后镇痛泵均配至 100 mL,泵注持续速度 2 mL/h,间隔 15 min,单次追加 1 mL。

1.3 观察指标

1.3.1 围术期指标 首先,记录两组患儿的手术时间和麻醉时间。此外术前、术后测量并记录患儿心率(Heart rate, HR)和平均动脉压(Mean arterial pressure, MAP)。

1.3.2 疼痛与镇静 在术后 4 h、24 h 和 48 h,通过视觉模拟评分法(Visual analogue scale, VAS)评估患儿术后疼痛情况,通过 Ramsay 量表评估术后镇静效果[14]。VAS 评分:0 分:无疼痛感;不影响睡眠、活动、起床,但伴有轻微疼痛,为 1~3 分;起床时疼痛加剧,卧床伴有疼痛感,为 4~6 分;患儿难以睡眠,卧床时伴有剧烈疼痛感,为 7~9 分;有严重疼痛感为 10 分。Ramsay 量表:情绪为躁动、激动、焦虑等,为 1 分;存在定向力且能平静配合医护人员工作,为 2 分;指令发出时有反应,有嗜睡现象,为 3 分;处于睡眠状态时进行大声呼唤或轻叩眉间反应较为迅速,为 4 分;处于睡眠状态进行大声呼唤或轻叩眉间反应较为迟钝为 5 分;刺激无反应,处于麻醉深睡眠状态为 6 分。

1.3.3 术后并发症 在术后 48 小时内,观察两组患儿恶心呕吐、皮肤瘙痒、头晕头痛以及呼吸抑制等术后并发症情况。

1.4 统计学分析方法

采用软件 SPSS 24.0 进行数据分析,计数资料以(n/%)表示,对比为 χ^2 检验;计量资料以($\bar{x}\pm s$)表示,对比为 t 检验,检验水准为 α=0.05。

2 结果

2.1 一般资料

托烷司琼组和帕洛诺司琼组患儿一般资料对比无差异,(P>0.05),如表 1 所示。

2.2 围术期血流动力学

托烷司琼和帕洛诺司琼患儿在术前和术后 HR 和 MAP 比较均无显著差异(P>0.05),如表 2 所示。

表 1 一般资料比较($\bar{x}\pm s$)

Table 1 Comparison of general information ($\bar{x}\pm s$)

Groups	n	Gender(male (%))	Age(years)	Weight(kg)	Operation time (min)	Anesthesia time (min)
Palonosetron	30	17 (56.67)	10.61±4.04	39.29±15.79	165.80±77.11	196.72±69.71
Tropisetron	30	16 (53.33)	9.38±4.32	39.12±18.54	166.80±68.49	198.92±78.59

表 2 围术期 HR 和 MAP 比较($\bar{x}\pm s$)

Table 2 Comparison of HR and MAP in the perioperative period ($\bar{x}\pm s$)

Groups	n	HR (times/min)		MAP (mmHg)	
		Preoperative	Postoperative	Preoperative	Postoperative
Palonosetron	30	85.18±19.36	96.36±14.38	70.62±11.25	73.93±10.52
Tropisetron	30	85.68±18.26	97.38±15.63	70.56±15.62	75.23±12.54

2.3 术后镇痛、镇静效果

托烷司琼组和帕洛诺司琼组患儿术后 VAS 评分、Ramsay 评分均随时间延长而降低,且同一时间点两组患儿 VAS 评分无显著差异(P>0.05)。具体如表 3 所示。

2.4 患儿术后 PONV 情况

6 例帕洛诺司琼组患儿术后发生 PONV，高于托烷司琼组（1 例），帕洛诺司琼组术后 PONV 发生率（20.00 %）高于托烷司琼组（3.33 %）（P<0.05）。

表 3 术后不同时间 VAS 评分比较（$\bar{x}\pm s$）

Table 3 Comparison of VAS scores at different time after surgery ($\bar{x}\pm s$)

Groups	n	VAS			Ramsay		
		4 h	24 h	48 h	4 h	24 h	48 h
Palonosetron	30	3.23±0.54	2.53±0.71	1.75±0.62	2.65±0.38	2.13±0.62	1.64±0.79
Tropisetron	30	3.24±0.62	2.49±0.73	1.76±0.71	2.72±0.42	2.24±0.68	1.66±0.81

2.5 患儿术后其他并发症情况

帕洛诺司琼组患儿出现头晕头痛、皮肤瘙痒以及呼吸抑制例数分别为 3 例、1 例和 1 例，而托烷司琼组患儿出现头晕头痛、皮肤瘙痒及呼吸抑制例数分别为 2 例，0 例和 0 例。但两组间术后并发症发生率比较无差异（P>0.05）。

表 4 术后其他并发症发生率比较（n(%)）

Table 4 Incidence of other postoperative complications (n(%))

Groups	n	Complications		
		Lethargy	Itchy skin	Poor breathing
Palonosetron	30	3 (9.99%)	1 (3.33%)	1 (3.33%)
Tropisetron	30	2 (6.67%)	0 (0.00%)	0 (0.00%)
t		0.351	1.017	1.017
P		0.554	0.313	0.313

3 讨论

人的呕吐神经中枢位于第四脑室的腹侧面极后区化学触发带和孤束核后方，分为神经反应中枢和化学感受器触发带。神经反应中枢接受来自视觉、味觉、触觉以及来自咽喉、胃部、肠道、内耳庭、化学触发带等传入的刺激。而化学触发带主要包含各种与恶心呕吐相关受体的集合，包括 5-HT3-6、阿片受体（μ、δ、κ、σ 四种）、大麻受体以及多巴胺受体等[15,16]。因此，抗呕吐药的作用部位主要是神经反应中枢和化学触发带，有作用于大脑皮层的苯二氮卓类以及作用于化学触发带中的各类受体拮抗剂药物，包括 5- 羟色胺受体拮抗剂、抗组胺类药物以及阿片类受体拮抗剂药物。其中 5-HT3 受体拮抗剂药物是治疗和预防 PONV 最常用的药物[17,18]。目前，临床上被广泛应用的 5-HT3 受体拮抗剂药物主要有昂丹司琼、格拉司琼、帕洛诺司琼以及托烷司琼等[19,20]。尽管 5-HT3 受体拮抗剂被广泛应用于预防和治疗 PONV 的发生，但关于不同 5-HT3 受体拮抗剂药物在儿童骨科术后应用中的效果比较中的报道较少。

本研究发现，两组患儿的手术时间和麻醉时间无差异，且围术期心率和平均动脉压比较也无显著差异。这一结果与 Choudhary J[21]、闫堃[22]等人结果具有一致性。经分析发现，静脉注射帕洛诺司琼或托烷司琼不会影响患者血流动力学的稳定。帕洛诺司琼和托烷司琼的主要机制是通过结合外周胃肠嗜铬细胞和中枢 5-HT 受体，5-HT 释放受到抑制，并将向呕吐中枢冲动传入阻断，进而达到预防治疗恶心呕吐的效果[23]。此外，由于帕洛诺司琼和托烷司琼均为术后镇痛泵持续泵注，其对患者术后镇痛及镇静的影响也需考虑[24]。儿童骨科手术后由于创伤较大会发生强烈的疼痛感，对后期恢复影响较大，围术期合理用药以帮助有效的镇痛和镇静对加速患儿早期康复锻炼以及减少术后并发症的发生意义重大。本研究发现，术后使用帕洛诺司琼和托烷司琼的两组患儿，术后各时间点 VAS 评分和 Ramsay 评分均无显著差异。这一结果与 Cho E 等人[25]的报道具有一致性。结合本研究分析可知，帕洛诺司琼和托烷司琼这两种药物对儿童骨科手术术后镇痛镇静的影响效果是类似的，即这两种药物不作用于患儿的镇痛镇静。

因儿童部分骨科手术创伤较大，会发生强烈的疼痛感，影响患儿术后恢复，因此使用舒芬太尼的镇痛泵以帮助有效镇痛，然而镇痛泵的使用可能增加 PONV 的发生率，故加入帕洛诺司琼或托烷司琼预防恶心呕吐的发生[26,27]。本研究发现，使用帕洛诺司琼的儿童 PONV 的发生率高于使用托烷司琼的患儿，其他并发症的发生率与托烷司琼组的患儿无显著差异，这与 Yang Y 等人[28]的报道相反。Yang Y 的报道显示，帕洛诺司琼是一种高选择性的预防药物，与托烷司琼相比，其效果可能更好。分析其原因，纳入患者的年龄可能是引起研究结论相反的主要原因，这也表明帕洛诺司琼和托烷司琼在儿童中的使用效果是有别于成年人的，次要原因是帕洛诺司琼的剂量使用范围很广，5 μg/kg 可能是较小的剂量，需要进一步的实验研究剂量分组来探讨是否增加剂量可有效降低儿童术后镇痛泵应用时的恶心呕吐发生率 [3,4]。虽然帕洛诺司琼和托烷司琼均为 5-HT3 拮抗剂受体类药物，其预防和治疗恶心呕吐的机制是一致的，并且在最新版《成人术后恶心呕吐防治指南》中也指出 5-HT3 受体拮抗剂之间在治疗和预防恶心呕吐的效果无差异，但缺乏大样本量临床数据支撑 [29]。但因不同 5-HT3 受体拮抗剂与 5-HT3 受体结合强度以及在体内的代谢半衰期不同可能会造成其在治疗和预防不同类型、不同手术和麻醉类型患者时预防

PONV 的效果差异[30]。需指出的是,本研究纳入样本量有限,研究结果还需要进一步大样本量研究证实。

综上所述,托烷司琼与帕洛诺司琼对骨科手术后儿童血流动力学、疼痛和镇静效果并无差异,但在预防术后恶心呕吐方面托烷司琼效果优于帕洛诺司琼。

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