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帕瑞昔布钠超前镇痛对妇科腹腔镜手术全凭静脉麻醉效果的影响

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摘要 目的:评价帕瑞昔布钠超前镇痛对妇科腹腔镜手术异丙酚 - 芬太尼静脉麻醉效果的影响。**方法:**选择在我院行妇科腹腔镜手术的患者 60 例,ASA 分级为Ⅰ级或Ⅱ级,年龄分布在 21-53 岁,体重为 41-72 kg。将所有患者随机分为帕瑞昔布钠组(P 组)和生理盐水组(NS 组),每组各 30 例。在麻醉诱导前 15 min,对 P 组患者采取静脉注射帕瑞昔布钠 40 mg,NS 组患者则采取静脉注射等容积的生理盐水。两组麻醉诱导方法相同,术中以脑电双频指数(bispectral index,BIS)为麻醉深度指标,根据 BIS 值调节异丙酚血浆靶浓度以维持麻醉。记录拔管期间患者的心率(HR),平均动脉压(MAP)变化情况,苏醒时间,拔管时间,苏醒期不良反应及拔管后 5 min 疼痛 VRS 评分。**结果:**①两组患者血流动力学平稳,P 组在 T3 至 T6 各时点的 MAP 和 T3 至 T5 各时点的 HR 均明显低于 NS 组,差异有统计学意义(P<0.05);②两组苏醒时间和拔管时间无明显差别(P>0.05);P 组苏醒期躁动发生率为 10%,明显低于 NS 组的 26.7%,差异有统计学意义(P<0.05);③P 组拔管后 5 min 疼痛 VRS 评分为 2.0,明显低于 NS 组的 3.6,差异有统计学意义(P<0.05)。**结论:**帕瑞昔布钠超前镇痛能减轻异丙酚 - 芬太尼静脉麻醉下妇科腹腔镜手术过程中血流动力学波动,减少苏醒期躁动的发生和疼痛 VRS 评分。

关键词:帕瑞昔布钠;超前镇痛;腹腔镜手术;全凭静麻;血流动力学

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The Effect of Parecoxib Sodium on the Intravenous Anesthesia with Propofol-fentanyl of Gynecological Laparoscopic Surgery

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ABSTRACT Objective: To evaluate the effect of parecoxib on intravenous anesthesia with propofol-fentanyl of patients undergoing gynecological laparoscopic surgery. **Methods:** Sixty patients (ASA Ⅰ orⅡ, 21053 years old, 41-72kg) who were undergoing gynecological laparoscopic surgery were selected and randomly divided into two groups: parecoxib group (group P) who were received intravenous parecoxib sodium and group NS who were received normal 0 mL before anesthesia induction for 15 min, 30 cases of each group. The same anesthetic induction method was used in the two groups. Bispectral index (BIS) was used as the index of depth of anesthesia, by which the target plasma concentration of propofol was adjusted to maintain the anesthesia. HR, MAP were recorded, recovery time, extubation time, the incidence of postoperative adverse reactions and VRS after extubation for five min were recorded. **Results:** ① Compared with group NS, MAP at T3 to T6, HR at T3 to T5 in group P were lower, and there were statistically significant difference between two groups(P<0.05); ② The recovery time and extubation time showed no differences between group P and group NS. ③ The incidence of agitation and the VRS score were decreased in group P, and there were statistically significant difference between two groups(P<0.05). **Conclusion:** Preemptive analgesia with parecoxib sodium can decrease the changes in hemodynamics, incidence of agitation and the VRS score from intravenous anesthesia with propofol-fentanyl in patients who were undergoing gynecological laparoscopic surgery.

Key words: Parecoxib sodium; Preemptive analgesia; Laparoscopic surgery; Intravenous anesthesia; Haemodynamics

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超前镇痛是指在伤害性刺激前应用镇痛药,可阻止伤害性刺激的传入,抑制中枢敏化效应,从而减轻患者术后疼痛感[1,2]。帕瑞昔布钠是新型注射用高选择性环氧化酶 -2(COX-2)抑制剂[3,4],镇痛效果好、安全性高。目前对其超前镇痛领域的研究多为术后镇痛影响的报道很少涉及到麻醉过程本身。本研究旨在探讨帕瑞昔布钠超前镇痛对妇科腹腔镜手术异丙酚 - 芬太尼全凭静脉麻醉效果的影响。现将相关结果汇报如下:

1 资料与方法

1.1 临床资料

本研究已征得医院伦理委员会批准,患者本人及家属同意并签署知情同意书。选择期行妇科腹腔镜手术患者 60 例,ASA Ⅰ~Ⅱ级,年龄 21~53 岁,体重 41~72kg。将其随机分为帕瑞昔布钠组(P 组)和生理盐水组(NS 组),每组 30 例。选取标准:

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既往无特殊病史,无药物过敏史,近期未服用镇痛及镇静药物。征得医院伦理委员会批准、患者本人及家属同意并签署知情同意书。两组患者的一般资料无显著差异,有可比性。

1.2 方法

所有患者均于术前禁食 12 h,禁饮 6 h,术前 30 min 肌注阿托品 0.5 mg,苯巴比妥钠 0.1 g。入手术室后常规监测 ECG、SpO_2、BP,采用 BIS 监护仪监测 BIS 值。开放静脉通道,输注乳酸林格注射液 10 ml·kg^{-1}·h^{-1}。P 组于麻醉诱导前 15 min 静脉注射帕瑞昔布钠 40 mg(批号:A27TJ,美国辉瑞制药公司),NS 组则静脉注射等容积生理盐水。麻醉诱导以靶控输注异丙酚(批号:JL597/384,阿斯利康公司,意大利),血浆靶浓度为 4 μg/ml,静脉注射咪达唑仑 0.05mg/kg、芬太尼 4 μg/kg、顺阿曲库胺 0.15 mg/kg,当 BIS 值降至 55 以下进行气管插管,连接麻醉机(Fabius,德国 Drager)行机械通气,参数设置为:潮气量 7～10 ml/kg、频率 12～16 次 / 分、吸呼比 1:2,控制 $PETCO_2$ 30～35 mmHg 之间,Paw<30 cm H_2O。手术均采用头低脚高 20° 体位(Trendelenburg 头低位),手术结束后转平卧位,气腹压力 13～15 mmHg。麻醉维持以静脉输注顺阿曲库胺 0.1 μg·kg^{-1}·h^{-1},靶控输注异丙酚血浆浓度为 4 μg/ml,切皮前 5min 静脉注射芬太尼 2 μg/kg。创面止血完毕腹腔冲洗时停止输注顺阿曲库胺,气腹结束时停止输注异丙酚。当术中 SBP 升高幅度 >30%,静脉注射硝酸甘油 0.5 mg;SBP 降低幅度 >30%,静脉注射麻黄碱 10 mg;HR＜50 次 /min 且持续时间 >1min 时,静脉注射阿托品 0.3 mg,HR＞120 次 /min 时,静脉注射艾司洛尔 15 mg。所有手术均由同一术者完成,术中改开腹手术、手术出血＞400 mL 及对麻醉药物出现过敏者排除研究。

于入室后(T1)、插管后(T2)、气腹完成(T3)、气腹后 10 min(T4)、气腹后 30 min(T5)、气腹结束(T6)记录 HR、MAP。记录两组硝酸甘油、麻黄碱、阿托品和艾司洛尔的使用情况。记录两组手术时间、术中出血量、苏醒时间(术毕到睁眼时间)、拔管时间(术毕到拔出气管导管时间),记录苏醒期间呛咳、躁动、恶心呕吐、寒战、术中知晓的发生情况、拔管后 5 min 疼痛 VRS 评分[5,6](词语等级量表评分法,0 分:无疼痛;1 分:隐痛,但不明显;2 分:疼痛轻微;3 分:疼痛,但可以忍受;4 分:疼痛剧烈,有镇痛要求;5 分:疼痛剧烈,无法忍受)。

1.3 统计学处理

采用 SPSS13.0 软件进行统计分析。计量资料以均数± 标准差($\bar{x}$± s)表示,组间比较采用成组 t 检验,计数资料采用卡方检验。以 P＜0.05 为差异有统计学意义。

2 结果

2.1 一般资料的比较

两组病人年龄、体重、ASA 分级、手术时间、气腹时间、术中出血量比较,差异无统计学意义,见表 1。

2.2 血流动力学变化比较

与 NS 组相比,P 组 MAP 在气腹期间 T3 至 T6 各时点均明显低于 NS 组(P<0.05);HR 在 T3 至 T5 各时点均明显低于 NS 组(P<0.05),余无明显差异,见表 2;两组术中血管活性药物使用情况无明显差异,见表 3。

2.3 苏醒期各指标的比较

两组无一例病人发生术中知晓,苏醒时间和拔管时间无明显差别。P 组苏醒期躁动发生率为 27%,明显低于 NS 组的 10%(P<0.05)。拔管后 5min 疼痛 VRS 评分为(3.6± 1.1),明显低于 NS 组的(2.0± 0.7)(P<0.05),见表 4。

表 1 比较两组患者的一般资料(n=30)

Table 1 Comparison of preoperative and surgical characteristic of patients between two groups (n=30)

Group	Age (year,$\bar{x}$± s)	weight (kg,$\bar{x}$± s)	ASA (n,Ⅰ/Ⅱ)	Duration of Pneumoperitoneum (min,$\bar{x}$± s)	Duration of surgery (min,$\bar{x}$± s)	Blood loss volume (min,$\bar{x}$± s)
Group NS	39± 5	57± 11	12/18	72± 13	83± 29	107 ± 31
Group P	41± 6	55± 8	13/17	69± 17	80± 27	112± 35

表 2 比较两组患者术中各时点 HR,MAP(n=30,$\bar{x}$± s)

Table 2 Comparison of hemodynamic variables of patients between two groups (n=30, $\bar{x}$± s)

Group	HR(bpm)					
	T1	T2	T3	T4	T5	T6
Group NS	87± 12	94± 15	97± 17	91± 10	90± 10	81± 7
Group P	89± 11	92± 12	91± 11[a]	83± 10[a]	80± 9[a]	79± 8

Group	MAP(mmHg)					
	T1	T2	T3	T4	T5	T6
Group NS	92± 6	101± 10	106± 12	110± 17	100± 12	95± 8
Group P	94± 8	98± 12	98± 11[a]	102± 13[a]	93± 9[a]	89± 5[a]

注:与 NS 组比较,a P<0.05

Note: compared to the group NS, a P<0.05

表 3 比较两组患者术中血管活性药物的使用情况(次,n=30)

Table 3 The use of vasoactive agents of the two groups (n,n=30)

Group	Atropine	Ephedrin	Nitroglycerine	Esmolol
Group NS	0	0	6	5
Group P	0	1	4	4

表 4 比较两组患者苏醒期各指标(n=30)

Table 4 Recovery characteristic of the two groups (n=30)

Group	Emergence time (min,$\bar{x}\pm s$)	extubation time (min,$\bar{x}\pm s$)	cough (%)	agitation (%)	nausea ang vomiting (%)	chill (%)	VRS Score (score, $\bar{x}\pm s$)
Group NS	9± 7	13± 10	10	27	13	3	3.6± 1.1
Group P	10± 9	15± 10	7	10[a]	10	3	2.0± 0.7[a]

3 讨论

全凭静脉麻醉可以抑制大脑皮层边缘或下丘脑对大脑皮层的投射系统,却无法有效地阻断手术区域产生的伤害性刺激向中枢神经的传导,因而很难有效的抑制应激反应[7,8]。在伤害性刺激前使用镇痛药,可阻止其传入,从而抑制中枢敏化效应,产生超前镇痛的效果,减轻患者术后的疼痛感[1]。

帕瑞昔布钠是伐地昔布的前体药物,伐地昔布在临床剂量范围是选择性环氧化酶 -2(COX-2)抑制剂,对 COX-2 的抑制作用是 COX-1 的 28000 倍[3],可显著减少患者服用阿片类药物的剂量及相关的不良反应[9,10]。帕瑞昔布钠在不影响血小板聚集和凝血时间[12,13]的同时显著降低胃肠道不良反应的发生率[11]。

血流动力学的变化被认为是应激反应的间接指标[14],本研究在芬太尼总量及用法一致下,印证了帕瑞昔布钠超前镇痛组在气腹多个时点的血流动力学波动比对照组小。究其原因,可能为帕瑞昔布钠通过抑制外周 COX-2 表达,减少外周前列腺素合成,减轻手术创伤所致的炎症反应和组织水肿,从而发挥镇痛抗炎作用;同时可抑制中枢 COX-2 表达,抑制中枢前列腺素合成而抑制疼痛超敏,发挥外周、中枢双重镇痛优势[15-17]。在切皮、气腹这类伤害性刺激前使用较之受刺激后使用能更好地提高痛阈、降低切口处神经末梢痛觉传导、减轻中枢敏化,从而达到一定的镇痛效果。

腹腔镜手术由于使用二氧化碳气腹造成对腹腔脏器和腹壁的牵拉,术后患者往往出现肩部酸痛和膈下、腹部胀痛[18],这类非切口术后疼痛甚至超过了切口疼痛[19,20]。另外,腹腔镜术手术时间短,静脉麻醉往往倾向于减少阿片类药物用量,以加快苏醒,减少术后呼吸抑制等并发症,但这在一定程度上使得患者出现术后躁动,而超前镇痛恰恰能够填补此类镇痛不足。本研究印证了帕瑞昔布钠超前镇痛组的苏醒期躁动发生率及 VAS 评分都比对照组低。

综上所述,本研究显示超前应用帕瑞昔布钠能减轻异丙酚 - 芬太尼静脉麻醉下妇科腹腔镜手术过程中血流动力学波动,减少苏醒期躁动的发生和疼痛 VAS 评分。

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