氟比洛芬酯术前预处理对患者术中应激反应的影响

吴明毅[1] 邢翠燕[2] 孙玉明[1] 刘 冰[1] 李江伟[1] 褚文彦[1]

(1 武警山东总队医院麻醉科 山东 济南 250014;2 山东大学附属省立医院麻醉科 山东 济南 250021)

摘要 目的:探讨氟比洛芬酯术前预处理对患者术中应激反应的影响。方法:选择我院行全麻下腹式子宫全切术患者 60 例,随机分为观察组和对照组,每组 30 例。两组均采用相同的麻醉诱导和维持方案,观察组于手术开始前 10min 缓慢静注氟比洛芬酯脂微球注射液 1mg·Kg。记录诱导前、切皮时、探查时和术毕的平均动脉压和心率;放射免疫分析法测定患者血浆中血浆肾素、血管紧张素 II、醛固酮、皮质醇的浓度变化。结果:观察组心率、平均动脉压在切皮时、探查时、术毕时均较对照组低,但无显著性差异(P>0.05);观察组切皮时、探查时、术毕时血浆肾素、血管紧张素 II、醛固酮、皮质醇浓度均较对照组低,且差异具有统计学意义(P<0.05);两组术中的四种麻药用量均有不同,但差异无统计学意义(P>0.05)。结论:氟比洛芬酯术前预处理能降低腹式子宫全切术中机体的应激反应,值得推广应用。

关键词:氟比洛芬酯;应激反应;术前预处理

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Effects of Preoperative Pretreatment of Flurbiprofen on Stress Response of Patients in the Surgery

WU Ming-yi[1], XING Cui-yan[2], SUN Yu-ming[1], LIU Bing[1], LI Jiang-wei[1], CHU Wen-yan[1]

(1 Department of Anesthesiology, Shandong Provincial Corps Hospital, Chinese People's Armed Police Forces, Jinan,250014,China;

2 Department of Anesthesiology,Affiliated Provincial Hospital of Shandong University, Jinan,250021,China)

ABSTRACT Objective: To study the effect of preoperative pretreatment of flurbiprofen to the patients with stress response in the surgery. Methods: 60 patients undergoing abdominal hysterectomy were randomly divided into observation group and control group and 30 cases were in each group. Both of groups were given the same anesthetic induction and maintenance programs, and observation group was slowly injected 1mg/Kg of flurbiprofen by intravenous. Recorded the average arterial pressure and heart rate before induction, at skin incision, exploration and the completion of surgery and determined the changes of concentration of plasma renin, angiotensin II, aldosterone and cortisol. Results: The average arterial pressure and the heart rate in the observation group were higher than that in the control group at the time of incision, probe and surgery, however, there was no significant difference between the two groups (P>0.05); the concentration of plasma renin, angiotensin II, aldosterone and cortisol in the observation group were lower than that in the control group and the difference was statistically significant (P<0.05); the consumption of four anesthetic drugs in the two groups were different, however, the difference was not statistically significant (P>0.05). Conclusion: Preoperative pretreatment of flurbiprofen can reduce the body's stress response of abdominal hysterectomy, which should be widely applied.

Key words: Flurbiprofen; Stress response; Preoperative pretreatment

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手术创伤和疼痛可引起机体出现明显的应激反应,过度的应激反应使机体出现各种并发症[1],术后疼痛不仅引起患者应激,也延长手术后恢复期[2]。因此,抑制手术引起的应激反应是临床麻醉中的一个重要课题。氟比洛芬酯是新型的非甾体类消炎镇痛药,具有起效迅速,持续时间长,靶向分布的优点[3]。本研究选择我院行全麻下腹式子宫全切术患者 60 例,随机分为观察组和对照组,观察组于术前静注氟比洛芬酯脂微球注射液 1mg/Kg,观察其对术中机体应激反应的影响,报告如下。

1 资料与方法

1.1 病例选择

我院拟行全麻下腹式子宫全切术患者 60 例,年龄 23～70 岁,平均 46.8± 16.6 岁,随机分为观察组和对照组,每组 30 例。ASA 分级 1～2 级,心、肺、肝、肾功能正常,无免疫、内分泌系统合并症,未接受过免疫及内分泌治疗,无近期使用类固醇类药物,均无使用氟比洛芬酯脂微球注射液的禁忌症。两组患者一般资料比较差异无统计学意义(P>0.05),具有可比性。

1.2 方法

两组患者均采用经口明视气管插管全身麻醉。咪唑安定 0.lmg·kg^{-1} 静脉注射,待患者入睡后静脉缓慢注射芬太尼 2μg/kg,维库溴铵 0.1mg/kg,行辅助呼吸,异丙酚 2mg/kg,3min 后经口明视插管。异丙酚和瑞芬太尼维持麻醉,间断注射维库溴胺维持患者肌松。观察组在手术开始前 10min 静脉注射氟比洛芬酯脂微球注射液 1mg/Kg,注射时间大于 1min。

1.3 标本采集及检测方法

作者简介:吴明毅(1974)男,硕士,主治医师,临床麻醉与疼痛治疗,13181722907

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两组患者均在麻醉诱导前、切皮时、探察时和术毕时分别抽取肘静脉血 2mL，以低温离心机 3000 转 /min 离心 15min，取血浆 1mL，置 -20℃冰箱密封保存，成批送检。应用放射免疫分析法检测患者血浆中血浆肾素、血管紧张素 II、醛固酮、皮质醇的浓度变化，并记录各时点平均动脉压、心率及术中麻醉药物用量。

1.4 统计学方法

使用 SPSS13.0 统计学软件，计量资料用均数± 标准差（$\bar{x}\pm s$）表示，进行 t 检验；计数资料用 X^2 检验，P<0.05 表示差异有统计学意义。

2 结果

表 1 可见，对照组与观察组术前心率、血压无著差异。观察组心率、平均动脉压在开皮时、探查时、术毕时均较对照组低，但差异无统计学意义(P>0.05)。

表 1 两组患者麻醉前后平均动脉血压、心率变化（$\bar{x}\pm s$）

Table 1 The changes of mean arterial blood pressure and heart rate in the two groups before and after the anesthesia ($\bar{x}\pm s$)

检测指标	组别 groups	诱导前 Before induction	切皮时 Incision	探查时 Exploration	术毕 After surgery
平均动脉压 Mean arterial pressure (mmHg)	对照组 Control group	95.2± 10.6	100.8± 7.8	99.2± 7.2	101.4± 8.7
	观察组 Observation group	98.6± 15.1	99.7± 15.1	100.5± 12.1	98.9± 10.6
心率 Heart rate (次 /min)	对照组 Control group	81.4± 11.8	85.7± 12.8	84.5± 10.5	89.0± 10.4
	观察组 Observation group	80.9± 13.7	83.6± 9.2	84.6± 11.3	85.7± 10.7

表 2 可见，诱导前对照组与观察组，血浆肾素、血管紧张素 II、醛固酮、皮质醇浓度比较，无显著差异(P>0.05)。观察组切皮时、探查时、术毕时血浆肾素、血管紧张素 II、醛固酮、皮质醇浓度均较对照组低，且差异具有统计学意义(P<0.05)。

表 2 两组患者血浆肾素、血管紧张素 II、醛固酮、皮质醇浓度变化（$\bar{x}\pm s$）

Table2 The concentration changes of the plasma renin, angiotensin II, aldosterone and cortisol in the two groups ($\bar{x}\pm s$)

检测指标 Detection index	组别 Groups	诱导前 Before induction	切皮时 Incision	探查时 Exploration	术毕 After surgery
肾素 Renin (ng/ml·h)	对照组 Control group	0.53± 0.17	0.70± 0.30	0.89± 0.15	0.72± 0.30
	观察组 Observation group	0.51± 0.21	0.52± 0.16▲	0.63± 0.15▲	0.64± 0.16▲
血管紧张素 Angiotensin II(ng/ml)	对照组 Control group	37.1± 14.0	57.8± 31.3	46.3± 23.7	55.3± 28.5
	观察组 Observation group	38.3± l3.7	39.2± 15.2▲	43.6± 18.6▲	40.1± 14.7▲
醛固酮 Aldosterone (ng/ml)	对照组 Control group	171.1± 40.4	223.6± 88.6	274.3± 105.4	256.9± 87.4
	观察组 Observation group	173.1± 59.4	193.7± 50.8▲	216.8± 65.8▲	224.4± 45.4▲
皮质醇 Cortisol μg/ml)	对照组 Control group	218.8± 76	298.6± 156.8	256.6± 88.9	296.8± 157.3
	观察组 Observation group	224.1± 68.2	255.7± 80.9▲	227.8± 79.2▲	268.4± 82.5▲

注：对照组与观察组比较，差异具有统计学意义，▲P<0.05。

Note: the control group and observation group had statistically significant difference, with ▲ P <0.05.

表 3 可见，对照组与观察组术中的四种麻药用量具有不同程度差异，但差异无统计学意义，P>0.05。

表 3 术中麻醉药用量的比较（$\bar{x}\pm s$）

Table 3 The comparison of anesthesia consumption between the two groups ($\bar{x}\pm s$)

组别 Groups	芬太尼 Fentanyl (μg)	瑞芬太尼 Remifentanil (μg)	异丙酚 Propofol (mg)	维库溴铵 Vecuronium (mg)
对照组 Control group	382.1± 30.9	1018.5± 193.8	661.0± 99.4	14.2± 2.1
观察组 Observation group	422.1± 36.8*	968.5± 170.6*	685.7± 89.8*	12.9± 2.4*

注：两组比较，*P>0.05。

Note: there was no statistically significant difference between the two groups, with *P>0.05.

3 讨论

氟比洛芬酯是新型的非甾体类靶向静脉镇痛药，是强效 Cox 非特异性前列腺素合成抑制剂[4-5]，目前在国内外已用于术后镇痛。氟比洛芬酯具有一定的亲脂性，可溶于大豆油制成脂微球载体制剂[6]。具有抑制外周和中枢神经系统敏感化，它具有靶向镇痛并可增强阿片类药物镇痛作用，它具有靶向镇痛并可增强阿片类药物镇痛作用，而不影响脑血流及氧合，不影响麻醉深度，不抑制呼吸[7]。当机体受到疼痛等刺激时，下丘脑一腺垂体一肾上腺皮质轴的活动增强，引起各种应激激素大量释放；同时交感一肾上腺髓质系统的活动也加强，血液中儿茶酚胺的含量增加[8]。研究显示[9]，氟比洛芬酯具有良好的镇痛效果，

总有效率达 98%，对照药安慰剂为 43.9%。注射氟比洛芬酯后 15min 出现镇痛作用，30min 镇痛效果明显，在 1-5h 达到最佳镇痛效果，作用持续时间可达 6h 以上。静脉注射后经体内酯酶作用迅速水解成活性代谢物氟比洛芬的前体，迅速提高氟比洛芬的局部血药浓度，主要通过外周和中枢作用，抑制环氧化酶减少前列腺素的生物合成[10-12]。用药后 48h 尿中药物累积排泄量约为给药剂量的 85%。未发现药物在体内的蓄积[13]。Nkaayama 等人的实验证明麻醉期间静脉给予 1mg/kg 氟比洛芬酯注射液降低了腹式子宫切除术患者术后止痛药的需求，并且术前 30min 给药优于术后给药[14]。

机体在受到创伤、手术和感染等打击后，可刺激免疫细胞和累及细胞产生多种细胞因子，引起炎症反应。产生免疫调节作用[15]。柴小青等[16]研究发现，术前静脉输注氟比洛芬酯注射液对开胸手术患者通过抑制前列腺素 2、TNF-α 及 IL-6 的产生。有学者认为[17]，组织损伤前使用非甾体类消炎镇痛药会抑制受损感受器官的过敏化，从而有可能减少对中枢神经系统的刺激。本研究结果显示，观察组与对照组比较证明，氟比洛芬酯能够有效抑制术中的应激反应，这可能是由于氟比洛芬酯与阿片类药物通过平衡镇痛作用减轻了患者的应激反应[18]。本研究中，两组术中的四种麻药用量具有不同程度差异，但差异无统计学意义 (P>0.05)，与此前报道，氟比洛芬酯脂微球注射液 1mg/Kg 术前应用对术中麻醉药物用量影响不大[19]，相符合。

综上所述，氟比洛芬酯能有效减少末梢的伤害性感受及痛觉，抑制外周神经敏化，发挥超前镇痛的作用[20]。氟比洛芬酯脂微球注射液能降低腹式子宫全切术中机体的应激反应，提高手术治疗效果，降低术中可能出现的并发症，大大改善预后，值得临床推广应用。

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明。

临床医生必须区分长期或短期应用质子泵抑制剂患者中CgA的假阳性的升高，在对CgA数值进行临床应用之前应慎重，必须在去除质子泵抑制剂的应用后重新评估CgA水平。而且，通过本研究表明：是否使用PPI对CgA的数值影响较大，特别是对于冠心病患者，联合使用氯吡格雷时，应慎重评估联合使用PPI患者CgA升高的临床意义。由于研究时间的限制，尚不能明确PPI应用后导致CgA水平升高，是否会产生一些心血管事件，尚有待进一步研究。

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