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静脉与硬膜外注射地塞米松对吗啡硬膜外术后镇痛的影响 *

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摘要 目的:比较两种不同途径注射地塞米松磷酸钠对吗啡硬膜外术后镇痛的影响。**方法:**选择 200 例(ASAⅠ-Ⅱ)在腰硬联合麻醉下行腹式子宫切除术的患者,随机分为 A、B、C、D 四组(n = 50),各组均给以硬膜外注射 2.5 mg 吗啡作为术后镇痛治疗的同时,A 组静脉注射安慰剂(生理盐水),B 组静脉注射地塞米松磷酸钠 10 mg,C 组静脉注射地塞米松磷酸钠 5 mg,D 组硬膜外注射地塞米松磷酸钠 5 mg 及静脉注射安慰剂(生理盐水),以上均以 5 mL 作为注射容积。观察和比较术后 24 h 内各组恶心和呕吐(PONV)、皮肤瘙痒、补救镇痛、呼吸抑制的发生率、排气时间和补救镇痛时间。**结果:**B、C、D 三组的 PONV 总发生率显著低于 A 组(P<0.0083),而 B、C、D 三组之间比较无显著差异(P>0.0083);A、B、C、D 四组间恶心的发生率无显著差异(P>0.05),而 D 组呕吐的发生率明显低于 A 组(P<0.0083);B 组皮肤瘙痒的发生率明显低于 A 组(P<0.0083);四组患者的 VAS 评分比较无显著差异,均达到满意的镇痛效果(P>0.05)。四组患者补救镇痛的发生率、补救镇痛药量和排气时间比较无明显差异(P>0.05),而 C、D 组的补救镇痛时间明显比 A 组延长(P<0.0083),四组患者均未出现呼吸抑制。**结论:**地塞米松磷酸钠可降低吗啡硬膜外术后恶心和呕吐的发生率,延长补救镇痛时间;硬膜外注射地塞米松磷酸钠对降低呕吐的发生率更有效;静脉注射地塞米松磷酸钠 10 mg 可降低瘙痒的发生率,且无明显的不良反应。

关键词:地塞米松磷酸钠;静脉与硬膜外注射;吗啡;硬膜外镇痛;腹式子宫全切手术

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The Effect of Dexamethasone on Postoperative Epidural Analgesia of Morphine: a Comparasion Study of Intravenous and Epidural Injection Routes*

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ABSTRACT Objective: A prospective, randomized, double-blinded and placebo-controlled study was designed to compare the effects of dexamethasone sodium phosphate administration Intravenously or epidurally on the postoperative epidural analgesia of morphine. **Methods:** A total of 200 patients(ASAⅠ-Ⅱ) who had scheduled for elective simple abdominal hysterectomy under combined spinal-epidural anesthesia were randomly divided into four groups, A, B, C and D (n = 50). After peritoneal suture, each patient received epidural morphine 2.5 mg as postoperative analgesia. At the same time, each patient in group A received I.V. saline as placebo; each patient in group B received I.V. dexamethasone sodium phosphate 10 mg; each patient in group C received I.V. dexamethasone sodium phosphate 5 mg; each patient in group D received epidural dexamethasone sodium phosphate 5 mg and I.V. saline. the incidence of pruritus, nausea and vomiting (PONV), remedy analgesia and respiratory depression, the exhaust time and the remedy analgesia time were recorded and compared among different groups. **Results:** The incidence rates of PONV in group B, C and D were significantly lower (P<0.0083) than group A, but no significant difference was found among group B, C and D; no significant difference of the incidence rates of nausea was found among four groups, the incidence rate of vomiting in group D was significantly lower than that of group A (P<0.0083). The incidence rate of pruritus in group B was significantly lower than that of group A (P<0.0083); the time course before without remedial analgesic in group C and D were significant longer than that in group A (P<0.0083) and no respiration inhibition was observed in the four groups. **Conclusion:** Combined with morphine as postoperative epidural analgesia, Dexamethasone could reduce the incidence rate of PONV and vomiting; prolong the time course without remedial analgesic regardless of intravenous or epidural injection. Epidural dexamethasone sodium phosphate significantly reduced the incidence of vomiting more effectively than I.V. dexamethasone.I.V; Dexamethasone sodium phosphate 10 mg significantly reduced the incidence of pruritus without significant side effect.

Key words: Dexamethasone sodium phosphate; Intravenous and epidural injection; Morphine; Epidural analgesia; Abdominal

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前言

硬膜外镇痛模式的安全性及有效性已经得到了人们的广泛认可,与芬太尼和哌替啶等阿片类药物相比,吗啡因其水溶性和长效性,可产生良好和持久的镇痛效果。虽然人们不断探索硬膜外注射吗啡的最佳用量,但在使用最小有效剂量时,有些不良反应的发生率仍然很高,如恶心和呕吐的发生率为 30%-65%,皮肤瘙痒发生率为 10%-50%[1]。1981 年,地塞米松首次被证实对于肿瘤化疗病人的呕吐是有效的[6];还有研究证实静脉注入地塞米松对于减少硬膜外吗啡引起的恶心和呕吐同样有效。地塞米松强化吗啡镇痛效果和减轻其不良反应的作用已经得到广泛的研究和证实。但大多数研究采用静脉注射地塞米松,只有少数研究关注硬膜外注入地塞米松对吗啡硬膜外术后镇痛的影响[3]。究竟哪一种方式具有更高的镇痛疗效和安全性目前尚无定论。本研究通过观察不同途径注入地塞米松对吗啡硬膜外术后镇痛的影响,以期为临床术后急性疼痛的治疗方案的优化提供参考依据。

1 资料与方法

1.1 研究对象

经过哈尔滨医科大学附属第四医院的伦理委员会批准,选择 200 例行腹式子宫切除术的病人,ASAⅠ~Ⅱ级,年龄 30~60 岁,体重 50~70 mg。排除标准:有严重心血管系统、肝肾系统、呼吸系统等疾病;术前 48 小时应用镇痛和镇吐药物;有晕动史、便秘史、腰痛史和糖尿病病史;阿片类药物及地塞米松磷酸钠禁忌症;椎管内麻醉禁忌症。

1.2 麻醉方法

病人入手术室常规开放静脉,监测心电图、脉搏血氧饱和度、无创血压。于 L3~4 行腰硬联合麻醉,腰麻液为 0.5% 布比卡因(重比重)2.5 ± 0.5 mL,向头侧置管 3~4 cm,麻醉平面向上控制到 T4~T6 水平。手术开始前给予患者咪达唑仑 0.05 mg/kg 镇静。术中给予患者持续低流量吸氧,维持患者气道通畅及循环稳定,必要时追加 1.33%的利多卡因。病人随机分为 A、B、C、D 四组(n=50),在各组均给以硬膜外注射 2.5 mg 吗啡作为术后镇痛治疗的同时,A 组静脉注射安慰剂(生理盐水),B 组静脉注射地塞米松 10 mg,C 组静脉注射地塞米松 5 mg,D 组硬膜外注射地塞米松 5 mg 及静脉注射安慰剂,以上均以 5 mL 作为注射容积。应用 VAS 进行镇痛评分(0 分表示无痛,10 分表示剧痛,中间部分表示不同程度的疼痛),当 VAS>4 分时,静脉注射氟比洛芬酯注射液 100mg 作为补救镇痛。

1.3 观察指标

术后 24 h 内观察恶心和呕吐(PONV)、皮肤瘙痒、补救镇痛、呼吸抑制的发生情况,同时观察排气时间和补救镇痛时间。VAS 评分大于 4 分,采取补救镇痛;呼吸抑制定义为 SpO_2<90%。

1.4 统计学分析

应用 spss17.0 软件进行统计学分析,计量资料用均数± 标准差($\bar{x}$± s)表示,组间比较采用单因素方差分析;连续型变量用中位数(四分位数间距)表示,采用秩和检验比较有无差别;分类变量用例数(百分比)表示,用 X^2 检验比较有无差别,以 P<0.05 为差异有统计学意义。连续型变量和分类变量两两比较时,调整为 0.0083,P<0.0083 有统计学意义。

2 结果

2.1 各组患者一般基线资料的比较

四组患者的一般资料和手术特征比较无统计学差异(P>0.05),见表 1。

表 1 各组患者一般基线资料的比较(n=50, $\bar{x}$± s)

Table 1 Comparison of the base-line information among four groups (n=50, $\bar{x}$± s)

	Groupe A	Groupe B	Groupe C	Groupe D
Age(yr)	45.2 6.3	45.3 7.4	46.4 6.2	45.4 5.8
Height(cm)	162.0 3.0	161.8 3.2	162.6 3.2	162.2 3.3
weight(kg)	60.9 5.1	60.1 4.9	59.8 5.2	59.2 4.5
Bleeding amount (ml)	180 25	178 23	173 23	176 26
Fluid volume (ml)	1604 284	1600 242	1592 240	1628 219
Duration of anesthesia(min)	110.4 11.8	109.6 10.4	108.8 11.8	108.6 10.6
Duration of operation(min)	101.0 11.5	99.6 10.4	100.2 11.9	98.6 10.6
Lidocaine(ml)	9.8 2.6	9.6 2.8	10.0 2.4	10.0 2.6

2.2 各组患者 PONV、瘙痒、排气时间和疼痛情况的比较

B、C、D 三组的 PONV 总发生率显著低于 A 组(P<0.0083),而 B、C、D 三组之间比较无显著差异 (P>0.0083);A、B、C、D 四组间恶心的发生率无显著差异(P>0.05),而 D 组呕吐的发生率明显低于 A 组 (P<0.0083);B 组皮肤瘙痒的发生率明显低于 A 组(P<0.0083);四组患者的 VAS 评分比较无显著差异,均达到

表 2 各组 PONV、瘙痒、排气时间和疼痛情况的比较(n=50)

Table 2 Comparison of the PONV, pruritus, exhaust time and pain among four groups (n = 50)

	Groupe A	Groupe B	Groupe C	Groupe D
Scores of VAS	3(3-4)	3(3-4)	3(3-4)	3(3-4)
Remedy analgesia	14(28)	8(16)	6(12)	6(12)
The time of remedy analgesia(h)	24(18-24)	24(24-24)	24(24-24)%	24(24-24)%
Pruritus	25(50)	11(22)$	15(30)	13(26)
Exhaust time(min)	32(26-38)	32(26-38)	32(25-38)	31(20-36)
PONV	32(64)	17(34)*	17(34)*	15(30)*
Nausea	10(20)	6(12)	5(10)	9(18)
Vomiting	22(44)	11(22)	12(24)	6(12)#

注:与 A 组比较,*p<0.0083,#p<0.0083,$p<0.0083,%p<0.0083.

Note: Compared with group A, *p<0.0083, #p<0.0083, $p<0.0083, %p<0.0083.

满意的镇痛效果(P>0.05),见图 1、表 2。

2.3 各组患者补救镇痛的发生率、补救镇痛药量和排气时间的比较

四组患者补救镇痛的发生率、补救镇痛药量和排气时间比较无明显差异(p>0.05),而 C、D 组的补救镇痛时间明显比 A 组延长(P<0.0083),四组患者均未出现呼吸抑制,见表 2。

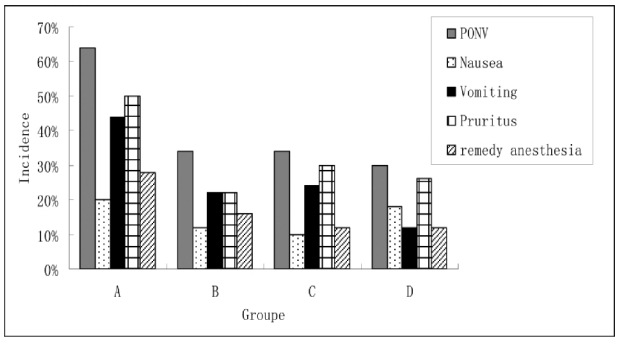

图 1 各组吗啡相关不良反应和补救镇痛的发生率比较

Fig.1 Comparison of the incidence rates of morphine-related adverse reactions and the remedy analgesia among four groups

3 讨论

手术后疼痛是临床最常见和最需紧急处理的急性疼痛。硬膜外腔给药适用于胸、腹部及下肢手术后疼痛的控制,腹部手术后硬膜外腔给药可改善肠道血流,利于肠蠕动恢复,下肢深静脉血栓的发生率低且可完全阻断手术创伤引起过高的应急反应;阿片类药物镇痛作用强,无器官毒性,几乎无封顶效应,但也应遵循能达到最大镇痛和不产生严重副作用的原则;吗啡因其水溶性和长效性,硬膜外腔注射可产生良好和持久的镇痛效果,因此成为硬膜外腔注射的首选药物[12]。费宝良、杭燕南等通过探讨硬膜外注射吗啡术后镇痛的最佳剂量证实,吗啡的最小有效剂量,仍然会引起不同程度的不良反应,如恶心和呕吐、皮肤瘙痒和呼吸抑制等[1]。虽然 5-HT3 受体拮抗剂对吗啡引起的恶心和呕吐有效,但价格昂贵;抗组胺药、抗胆碱药和多巴胺受体拮抗剂虽然价格低廉,但可引起明显的副作用,如过度镇静、口干、静坐不能、心动过速和锥体外系征、皮肤瘙痒等[5]。

糖皮质激素地塞米松的价格低廉,可以经静脉与硬膜外注射,且为水溶制剂,对组织刺激小,局部注射和硬膜外给药疗效可维持约 24 小时,硬膜外注射地塞米松的最佳剂量为 5～10 mg[2]。单次注射地塞米松并未发现明显的不良反应,但长期注射可引起刀口延迟愈合、股骨头缺血性坏死、消化性溃疡、肾上腺皮质功能减退和延迟性胃排空等[3-15]。静脉注射地塞米松减少恶心和呕吐的最小有效剂量为 5 mg[5,18],硬膜外注射地塞米松可减少术后疼痛和镇痛的需求[3,4]。

吗啡可直接作用于中枢呕吐化学受体敏感区,PONV 的发生率高达 30%-65%[6]。地塞米松减少硬膜外吗啡引起的恶心和呕吐的发生率的可能机制为通过中枢和外周两种途径抑制 5-HT 的产生和释放,改血脑屏障对血清蛋白的通透性,降低血液中 5-HT 作用于延髓极后区化学感受器触发区的浓度等[21]。但以上机制都缺乏直接的实验证据,相比于这些可能机制,其本质抗炎效应更有说服力,地塞米松能有效减少术后局部的炎症反应,从而减少炎症触发的副交感神经系统传入到呕吐中枢的刺激[15]。而硬膜外腔注入地塞米松,部分吸收入血,产生与静脉注药相似的作用,同时部分逐渐透过硬膜进入脑脊液,作用于脊髓及相应的神经根,也有小部分可经脑脊液扩散至大脑中枢,这可能解释硬膜外地塞米松组呕吐的发生率低于对照组[19]。

硬膜外腔注入吗啡可引起皮肤瘙痒,确切机制尚不清楚。目前多认为与吗啡直接激动脊髓背角受体密切相关。实验中静脉 10 mg 地塞米松组瘙痒的发生率低于单纯吗啡组,可能与地塞米松稳定参与过敏反应细胞的细胞膜,抑制体内缓激肽、5-羟色胺、组胺和前列腺素的释放有关[14]。在获得满意镇痛的前提下,四组间 VAS 评分和补救镇痛的发生均无显著差异,而地塞米松组平均补救镇痛的时间明显长于单纯吗啡组。地塞米松发挥镇痛的可能机制是通过抑制前列腺素的合成,从而降低脊髓后角神经元敏化和继发的中枢“上发条”、(wind-up)现象[2]。由于术后常规留置导尿管,本研究未能观察术后硬膜外吗啡镇痛引起尿潴留的发生情况,所有纳入研究的患者未发现呼吸抑制。

综上所述,地塞米松磷酸钠可降低吗啡硬膜外术后镇痛引起的恶心和呕吐的发生率,延长补救镇痛时间,硬膜外注射可更有效降低呕吐的发生率,静脉注射 10mg可降低瘙痒的发生

率,且无明显的不良反应。

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