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舒芬太尼联合罗哌卡因硬膜外自控镇痛对剖宫产术后应激激素和胃肠动力状态的影响*

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摘要 目的:探讨舒芬太尼联合罗哌卡因硬膜外自控镇痛(PCEA)对剖宫产术后应激激素和胃肠动力状态的影响。**方法:**选择2017年10月~2018年10月于我院择期行剖宫产术的114例孕产妇为研究对象,所有孕产妇按随机数字表法分为对照组(n=51)和研究组(n=63)。对照组术后予以舒芬太尼联合左旋布比卡因PCEA,研究组术后予以舒芬太尼联合罗哌卡因PCEA。比较两组术后24 h PCA按压次数、镇痛液用量、视觉模拟评分(VAS)、手术前后应激激素、胃肠激素、胃电参数、泌乳素(PRL)水平的变化和不良反应的发生情况。**结果:**研究组术后24 h PCA按压次数、镇痛液用量、VAS均显著低于对照组(P<0.05)。术后24 h,两组血管紧张素Ⅱ(AngⅡ)、去甲肾上腺素(NE)、皮质醇(Cor)、胆囊收缩素(CCK)、血管活性肽(VIP)均较术前显著上升,两组胃动素(MTL)、胃电主功率、胃电频率、正常慢波节律比均较术前明显下降,且研究组以上指标变化幅度均明显小于对照组(P<0.05)。研究组术后PRL水平显著高于对照组(P<0.05)。两组总不良反应发生率比较差异无统计学意义(P>0.05)。**结论:**舒芬太尼联合罗哌卡因硬膜外自控镇痛可有效减轻剖宫产术后疼痛,抑制应激激素的分泌,改善胃肠动力状态。

关键词:剖宫产;硬膜外自控镇痛;舒芬太尼;罗哌卡因;应激激素;胃肠动力状态

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Effects of Sufentanil Combined with Ropivacaine for Epidural Controlled Analgesia on the Stress Hormones and Gastrointestinal Motility after Cesarean Section*

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ABSTRACT Objective: To investigate the effects of sufentanil combined with ropivacaine for epidural controlled analgesia on the stress hormones and gastrointestinal motility after cesarean section. **Methods:** 114 cases of pregnant women who underwent cesarean section in our hospital from October 2017 to October 2018 were selected as research objects, all pregnant women were divided into control group (n=51) and research group (n=63) according to the random number table, the control group was treated with sufentanil combined with levobupivacaine PCEA, research group was postoperatively treated with sufentanil combined with ropivacaine PCEA, the changes of postoperative stress hormones, gastrointestinal hormones, electrogastric parameters, prolactin (PRL) levels and adverse reactions were compared between the two groups. **Results:** The number of postoperative pressure of 24 h PCA, dosage of analgesic solution and VAS in the research group were significantly lower than that in the control group, and the difference was statistically significant (P<0.05). Preoperatively, there were no statistically significant differences in stress hormones, gastrointestinal hormones, electrogastric parameters and PRL in both group(P>0.05). 24 h after surgery, angiotensinⅡ (AngⅡ), norepinephrine (NE), cortisol (Cor), the gallbladder contraction (CCK), vascular active peptide (VIP) in both group were significantly higher than those before operation, motilin (MTL), gastric power, gastric electrical frequency, and normal slow wave rhythm ratio in both groups were obviously decreased compared with preoperative, the changes of the above indexes in the study group were significantly smaller than those in the control group (P<0.05). PRL level in the research grou was significant higher than that in the control group (P<0.05). There was no statistically significant difference in the total adverse reaction rate in both group (P>0.05). **Conclusion:** Sufentanil combined with ropivacaine for epidural analgesia can effectively reduce the postoperative pain after cesarean section, inhibit the secretion of stress hormones, and improve the gastrointestinal dynamics.

Key words: Cesarean section; Epidural controlled analgesia; Sufentanil; Ropivacaine; Stress hormones; Gastrointestinal motility

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前言

剖宫产为产科领域的重要手术，现已成为解决产科并发症、难产的有效手段，但剖宫产术后组织创伤能够发生持续性的伤害传入冲动，引起多种应激激素异常分泌，导致内环境紊乱，促使脊髓敏化，从而导致急性疼痛[1,2]。研究表明[3,4]疼痛所致的交感神经系统兴奋能够一定程度的抑制胃肠道功能，引起括约肌张力及平滑肌张力改变，影响术后胃肠功能恢复。Huang J等[5]研究报道剖宫产术后疼痛干预不当能够增加产后出血、产后感染等严重并发症的发生可能性，影响围手术期的恢复质量。

硬膜外自控镇痛(PCEA)为术后镇痛的主要方式之一，通过于硬膜外间隙注入镇痛药，抑制相应传入神经及疼痛刺激的传递，消除或抑制疼痛刺激所致的应激反应，具有持续、稳定镇痛的优势，对患者循环、呼吸等生理功能的影响较小[6,7]。相关研究显示[8]阿片类药物联合局麻药可减少药物使用剂量，增加药物安全性，起到更为有效的镇痛效应。罗哌卡因作为一种酰胺类局麻药，现已广泛开展于产科镇痛中，有研究证实其可明显缓解产妇的主观疼痛反应，但有研究认为[9,10]部分产妇单用罗哌卡因的镇痛效果不甚理想，术后痛感明显。吗啡为既往剖宫产术后的常用阿片类药物，可持续镇痛，但起效缓慢，不良反应发生率较高。舒芬太尼为脂溶性阿片类药物，结合 μ 阿片受体后可起到强效的镇痛效果，但镇痛时间相对较短[11]。尽管目前临床有关二者联合应用的报道较多，但其对术后应激激素和胃肠动力的影响尚未明确。因此，本研究主要分析舒芬太尼联合罗哌卡因硬膜外自控镇痛对剖宫产术后应激激素和胃肠动力状态的影响，以期为临床应用提供更多的参考。

1 资料与方法

1.1 一般资料

选择 2017 年 10 月 ~2018 年 10 月于我院择期行剖宫产术的 114 例孕产妇为研究对象，纳入标准[12]：单胎、足月、头正位，初产妇；剖宫产手术指征明确；无妊娠期糖尿病、先兆子痫等产科合并症；ASA 分级Ⅰ~Ⅱ级；神经系统无异常。排除标准：硬膜外穿刺麻醉禁忌证；药物或酒精滥用史；凝血功能明显异常；心肝肾等主要功能不全；胎盘前置、先天畸形等；阿片类药物过敏史。所有孕产妇按随机数字表法分为对照组(n=51)和研究组(n=63)，对照组年龄 22~34 岁，平均(26.71± 5.43)岁；孕周 38~41 周，平均(39.31± 0.75)周；经产妇 21 例，初产妇 30 例。研究组年龄 23~35 岁，平均 (27.28± 5.01) 岁；孕周 38~41 周，平均(39.46± 0.71)周；经产妇 26 例，初产妇 37 例。两组的基线资料比较均无统计学差异(P>0.05)，具有可比性。

1.2 方法

1.2.1 麻醉方法 常规创建外周静脉通路，静脉滴注 500 mL 林格液(厂家：潍坊市仁康药业有限公司，规格：500 mL，批号：20170513)。给予面罩吸氧，流量控制在 3 L/min。产妇采用左侧体位，在 L2~3 间隙进行穿刺，头向置管 3.5 cm 并加以固定。于蛛网膜下腔注射 10~15 mL 2.0%利多卡因(厂家：常州凯乔生物科技有限公司，规格：5 mL: 100 mg，批号：20170121)。常规监测孕产妇的血压、心电图、血氧饱和度，子宫缝合后接通静脉镇痛泵。

1.2.2 镇痛方法 研究组术后予以舒芬太尼联合罗哌卡因 PCEA，镇痛液成分：0.5 μg/mL 舒芬太尼(厂家：宜昌人福药业有限公司，规格：2 mL: 0.1 mg，批号：20161021)+0.2%罗哌卡因(厂家：济南宏方德医药科技有限公司，规格：10 mL: 100 mg，批号：20160712)；对照组术后予以舒芬太尼联合左旋布比卡因(厂家：珠海物美科技有限公司，规格：5 mL: 37.5 mg，批号：20160520) PCEA，镇痛液成分：0.5 μg/mL 舒芬太尼 +0.125%左旋布比卡因。自控剂量为 3 mL，持续背景输注剂量 2 mL/h，锁定时间为 30 分钟，镇痛时间为 48 h。

1.3 观察指标

记录两组术后 24hPCA 按压次数、镇痛液用量、VAS(分值为 0~10 分，分数越高说明疼痛越明显)，和不良反应发生情况。于术前及术后 24h 采集产妇外周静脉血 2 mL，分离血清后予以放射免疫法测定血管紧张素Ⅱ(AngⅡ)、去甲肾上腺素(NE)、皮质醇(Cor)、泌乳素(PRL)浓度。予以放射免疫计数仪测定胆囊收缩素(CCK)、胃动素(MTL)浓度，予以酶联免疫法测定血管活性肽(VIP)浓度。予以胃肠电图仪测定胃电主功率、胃电频率、正常慢波节律比。

1.4 统计学分析

数据处理选用 SPSS18.0 软件包，计量资料用($\bar{x}$± s)表示，组间比较选用 t 检验，计数资料用[(例)%]表示，组间比较用 x^2 检验比较，P<0.05 表示差异有统计学意义。

2 结果

2.1 两组术后 24hPCA 按压次数、镇痛液用量、VAS 的比较

研究组术后 24hPCA 按压次数、镇痛液用量、VAS 均明显低于对照组，差异有统计学意义(P<0.05)，见表 1。

表 1 两组术后 24hPCA 按压次数、镇痛液用量、VAS 比较($\bar{x}$± s)

Table 1 Comparison of the number of PCA compressions, analgesic solution, and VAS at 24 h after surgery between two groups($\bar{x}$± s)

Groups	n	Number of PCA presses (times)	Dosage of analgesic solution (mL)	VAS(points)
Control group	51	9.85± 1.43	21.08± 3.72	3.06± 0.45
Research group	63	6.76± 0.86#	13.29± 1.65#	2.62± 0.33#

Note: Compared with the control group, #P<0.05.

2.2 两组手术前后应激激素水平的变化比较

术前，两组血管紧张素Ⅱ(AngⅡ)、去甲肾上腺素(NE)、皮质醇(Cor)水平比较差异均无统计学意义(P>0.05)；术后 24h，两组血管紧张素Ⅱ(AngⅡ)、去甲肾上腺素(NE)、皮质醇(Cor)水平均较术前明显上升，但研究组以上指标均显著低于对照组，差异有统计学意义(P<0.05)，见表 2。

表 2 两组手术前后应激激素水平的比较($\bar{x}\pm s$)

Table 2 Comparison of levels of stress hormone before and after surgery between two groups($\bar{x}\pm s$)

Groups	n	Time	Ang-Ⅱ(ng/mL)	NE(pg/mL)	Cor(ng/L)
Control group	51	Before surgery	44.21± 4.40	251.90± 33.29	187.62± 23.19
		At 24 h after surgery	70.88± 9.85$^{\triangle}$	455.10± 68.06$^{\triangle}$	279.05± 39.04$^{\triangle}$
Research group	63	Before surgery	43.75± 5.81	254.01± 30.85	184.91± 25.09
		At 24 h after surgery	59.07± 7.32$^{\triangle\#}$	390.28± 50.42$^{\triangle\#}$	236.04± 30.87$^{\triangle\#}$

Note: Compared with the control group, $^{\#}P$<0.05; Compared with the same group before treatment, $^{\triangle}P$<0.05.

2.3 两组手术前后胃肠激素水平的比较

术前，两组 CCK、MTL、VIP 水平比较差异均无统计学意义(P>0.05)；术后 24h，两组 CCK、VIP 水平均较治疗前显著上升，MTL 水平均较治疗前显著下降，研究组以上指标的变化程度明显小于对照组，差异有统计学意义(P<0.05)，见表 3。

表 3 两组手术前后胃肠激素比较($\bar{x}\pm s$)

Table 3 Comparison of the gatrogen hormone before and after surgery between two groups($\bar{x}\pm s$)

Groups	n	Time	CCK(pg/mL)	VIP(pg/mL)	MTL(ng/L)
Control group	51	Before surgery	12.60± 1.52	21.88± 3.07	161.90± 20.11
		At 24 h after surgery	18.63± 3.02$^{\triangle}$	38.19± 6.02$^{\triangle}$	116.33± 11.20$^{\triangle}$
Research group	63	Before surgery	12. 31± 1.86	21.20± 3.85	157.62± 23.76
		At 24 h after surgery	15.80± 2.59$^{\triangle\#}$	31.76± 4.99$^{\triangle\#}$	135.21± 15.74$^{\triangle\#}$

Note: Compared with the control group, $^{\#}P$<0.05; Compared with the same group before treatment, $^{\triangle}P$<0.05.

2.4 两组手术前后胃电参数比较

术前，两组胃电参数比较差异无统计学意义(P>0.05)；术后 24 h，两组胃电参数均较术前明显下降，研究组显著高于对照组，差异有统计学意义(P<0.05)，见表 4。

表 4 两组手术前后胃电参数比较($\bar{x}\pm s$)

Table 4 Comparison of the gastric parameters before and after surgery between two groups($\bar{x}\pm s$)

Groups	n	Time	Primary gastric power (%)	Gastric electrical frequency(times/min)	Normal slow wave rhythm ratio(%)
Control group	51	Before surgery	60.13± 7.72	3.21± 0.37	79.63± 9.66
		At 24 h after surgery	31.20± 4.11$^{\triangle}$	1.62± 0.22$^{\triangle}$	56.33± 7.32$^{\triangle}$
Research group	63	Before surgery	58.75± 8.95	3.17± 0.42	78.41± 11.27
		At 24 h after surgery	37.61± 5.04$^{\triangle\#}$	2.35± 0.31$^{\triangle\#}$	64.80± 8.54$^{\triangle\#}$

Note: Compared with the control group, $^{\#}P$<0.05; Compared with the same group before treatment, $^{\triangle}P$<0.05.

2.5 两组手术前后 PRL 水平比较

术前，两组 PRL 水平比较差异无统计学意义(P>0.05)；术后 24 h，两组 PRL 水平均较术前明显上升，且研究组高于对照组，差异有统计学意义(P<0.05)，见表 5。

表 5 两组手术前后 PRL 水平比较($\bar{x}\pm s$)

Table 5 Comparison of the levels of PRL before and after surgery between two groups($\bar{x}\pm s$)

Groups	n	Time	PRL(ng/mL)
Control group	51	Before surgery	189.75± 26.12
		At 24 h after surgery	313.19± 39.05$^{\triangle}$
Research group	63	Before surgery	192.07± 23.86
		At 24 h after surgery	360.86± 45.71$^{\triangle\#}$

Note: Compared with the control group, $^{\#}P$<0.05; Compared with the same group before treatment, $^{\triangle}P$<0.05.

2.6 两组不良反应发生情况比较

两组均有皮肤瘙痒、恶心呕吐发生，组间总不良反应发生率比较差异无统计学意义(P>0.05)，见表 6。

3 讨论

剖宫产术后疼痛为伤害性疼痛，多源于子宫收缩及腹部切

口，容易引起多种负面情绪，导致机体发生系列的生理病理改变，影响产妇体力恢复及睡眠[13,14]。有效的术后镇痛可提高围手术期安全，减少并发症的发生。患者自控镇痛(PCA)为外科术后常用的镇痛方式，患者可通过自身疼痛感受，自行予以镇痛药物，保持用药个体化，PCEA 在临床应用上已获得了理想的镇痛效果[15,16]。

表 6 两组不良反应发生情况比较[例(%)]

Table 6 Comparison of the incidence of adverse reaction between two groups[n(%)]

Groups	n	Itchy skin	Nausea and vomiting	Total adverse reaction rate
Control group	51	1(1.96)	1(1.96)	2(3.92)
Research group	63	2(3.17)	3(4.76)	5(7.94)

目前，阿片类药物复合局麻药是术后 PECA 的常用方法之一，可减少二者单一用药的绝对剂量和浓度，从而减少药物的副作用[17]。舒芬太尼作为一种人工合成类阿片药，其镇痛持续时间、及与 μ 受体的亲和力明显高于芬太尼，血液稳定性良好，对呼吸的抑制作用相对较弱，有着更高的安全性[18]。舒芬太尼经硬膜外腔给药可更好的穿透血脑屏障，作用于蛛网膜下腔，从而选择性地结合脊髓阿片受体，起到强烈的镇痛作用[19,20]。罗哌卡因为常用局麻药，其对中枢神经系统和心血管系统的毒性较低，能够作用于外周血管，几乎不影响胎盘、子宫血流。罗哌卡因在镇痛、外周神经阻滞等方面的作用较为突出，可选择性抑制神经兴奋的传导，阻滞感觉神经作用，且几乎不影响产妇的运动神经阻滞[21,22]。研究显示[23]罗哌卡因应用期间患者能够自由活动，且有利于自主排尿。本研究结果显示舒芬太尼联合罗哌卡因组术后 24hPCA 按压次数、镇痛液用量、VAS 评分相对较低，表明二者联合作用更能麻醉镇痛需要，可有效减轻产妇术后疼痛，减少 PCA 的按压需求。

手术创伤和术后疼痛作为一种伤害性刺激，能够引起全身应激反应，导致内分泌激素的异常分泌，破坏机体内分泌功能[24]。Ang-Ⅱ的表达上升可引起细胞液外渗，增加切口红肿、疼痛程度。Ne 为神经递质，可加强心肌收缩力，加快心率，另外又可刺激小静脉及小动脉血管的强烈收缩，增加产后出血量[25]。Cor 的生物学作用较为广泛，可增强机体对应激和创伤能力，且有一定的升糖效应，可促进糖异生和糖原分解，引起应激性高血糖[26]。Bi YH 等[27]研究显示 Ang-Ⅱ、NE 及 Cor 等激素和手术创伤程度有良好相关性，能够客观反映机体应激状态。本研究结果显示术后 24 h，两组 Ang-Ⅱ、NE 及 Cor 水平均有上升，但舒芬太尼联合罗哌卡因组变化幅度较小，说明二者联合能够有效阻断交感神经的传出和伤害性刺激的传入，从而抑制应激激素的分泌，减轻机体应激状态，利于产妇术后的恢复。

剖宫产术后的切口疼痛较为明显，可限制产妇的自主活动，从而不利于胃肠功能的恢复，影响胃肠动态状态[28]。CCK、VIP、MTL 等胃肠激素为胃肠道功能的主要调节激素，能够经多种分泌方式参与消化系统运动，胃肠道受到手术创伤等外界刺激可引起以上指标的波动。胃电参数可有效监测机体胃部动力，从而反映胃肠道功能[29]。本研究结果显示术后 24 h，两组胃肠激素及胃电参数均有波动，但舒芬太尼联合罗哌卡因组变化幅度较小，说明二者联合更能有效控制手术、疼痛对产妇胃肠功能的不良刺激，可能与联合作用的镇痛效果更佳，从而减轻机体不良反应有关。此外，研究表明[30]剖宫产术后疼痛能够导致交感神经兴奋，促进儿茶酚胺分泌，抑制 PRL 的生成，从而延长初乳时间，影响新生儿母乳喂养。本研究结果显示舒芬太尼联合罗哌卡因组术后 PRL 水平相对较高，证实有效的术后镇痛能够抑制交感神经兴奋，促进 PRL 分泌，从而提高血清 PRL 浓度，有利于母乳喂养形成的良性循环。此外，两组皮肤瘙痒、恶心呕吐的发生率相当，安全性均较高。

综上所述，舒芬太尼联合罗哌卡因可有效减轻剖宫产术后疼痛，抑制应激激素的分泌，改善胃肠动态状态。

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