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罗哌卡因联合氢吗啡酮硬膜外自控镇痛 在妊娠期糖尿病患者剖宫产术中的应用效果*

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摘要 目的: 研究罗哌卡因联合氢吗啡酮硬膜外自控镇痛在妊娠期糖尿病患者剖宫产术中的应用效果。**方法:** 选择 2018 年 1 月~2019 年 6 月我院行剖宫产术的 81 例妊娠期糖尿病患者, 将其随机分为两组。对照组采用常规肌内注射镇痛的方式进行干预, 当产妇无法忍受疼痛时肌内注射哌替啶 100 mg。观察组在剖宫产术结束后连接自控镇痛泵, 使用氢吗啡酮 0.3 mg+0.75% 罗哌卡因 20 mL。比较两组干预前后的醛固酮(aldosterone, ALD)、皮质醇(cortisol, Cor)、血管紧张素 II (Angiotensin- II, Ang- II)、去甲肾上腺素(noradrenaline, NE)、血管活性肠肽(vasoactive intestinal peptide, VIP)、胃动素(motilin, MTL)、胆囊收缩素(cholecystokinin, CCK)和胃泌素(gastrin, GAS)、血清单核细胞趋化因子蛋白(monocyte chemokine protein-1, MCP-1)、白介素-6(interleukin-6, IL-6)、高迁移率族蛋白(high mobility group protein, HMGB-1)水平的变化。**结果:** 干预后, 两组的 VLD、Cor、Ang- II 和 NE 均较治疗前明显升高($P<0.05$), 且观察组干预后 1 d、2 d 的 VLD、Cor、Ang- II 和 NE 明显低于对照组($P<0.05$); 干预后, 两组的 VIP 和 CCK 均较治疗前明显升高($P<0.05$), MTL 和 GAS 均较治疗前明显降低($P<0.05$), 且观察组干预后 1 d、2 d 的 VIP 和 CCK 明显低于对照组($P<0.05$), MTL 和 GAS 明显高于对照组($P<0.05$); 干预 2 d 后, 两组的血清 MCP-1、IL-6 和 HMGB-1 水平均较治疗前明显降低($P<0.05$), 且观察组的血清 MCP-1、IL-6 和 HMGB-1 水平明显低于对照组($P<0.05$)。**结论:** 罗哌卡因联合氢吗啡酮硬膜外自控镇痛能改善妊娠期糖尿病患者剖宫产术后的胃肠功能, 抑制全身炎症反应。

关键词: 罗哌卡因; 氢吗啡酮; 硬膜外自控镇痛; 妊娠期糖尿病; 剖宫产术

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Effect of Ropivacaine Combined with Hydromorphone on the PCEA in Cesarean Section of Gestational Diabetes Mellitus*

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ABSTRACT Objective: To investigate the effect of ropivacaine combined with hydromorphone on the PCEA in cesarean section of gestational diabetes mellitus. **Methods:** Eighty-one patients with gestational diabetes who underwent cesarean section in our hospital from January 2018 to June 2019 were selected and divided into two groups randomly. The control group used conventional intramuscular injection for analgesia to intervene. When the maternal could not bear the pain, intramuscular injection of pethidine 100 mg. The observation group was connected to a self-controlled analgesic pump after the end of cesarean section and used hydromorphone 0.3 mg+0.75% ropivacaine 20 mL. The levels of ALD, Cor, Ang- II, NE, VIP, MTL, CCK and GAS, serum levels of MCP-1, IL-6, HMGB-1 were compared before and after the intervention between the two groups. **Results:** After intervention, the VLD, Cor, Ang- II and NE of the two groups were significantly higher than before treatment ($P<0.05$), and the VLD, Cor, Ang- II and NE of the observation group were significantly lower than those of the control group ($P<0.05$). After intervention, the VIP and CCK of the two groups were significantly higher than before treatment ($P<0.05$), the MTL and GAS of the two groups were significantly lower than before treatment ($P<0.05$), the VIP and CCK of the observation group were significantly lower than those of the control group ($P<0.05$), the MTL and GAS were significantly higher than those of the control group ($P<0.05$). After 2 days of intervention, the levels of serum MCP-1, IL-6 and HMGB-1 in the two groups were significantly lower than before treatment ($P<0.05$), and the levels of serum MCP-1, IL-6 and HMGB-1 in the observation group were significantly lower than those in the control group ($P<0.05$). **Conclusion:** Ropivacaine combined with hydromorphone could improve gastrointestinal function and inhibit systemic inflammatory response in patients with gestational diabetes mellitus after cesarean section.

Key words: Ropivacaine; Hydromorphone; Epidural Analgesia; Gestational Diabetes Mellitus; Cesarean Section

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前言

妊娠期糖尿病是指在妊娠前存在潜在的糖耐量减退或者糖代谢正常,但是在妊娠期间发生或被发现的一种特殊类型的糖尿病^[1,2]。妊娠期糖尿病患者的分娩方式大多为剖宫产术,但是剖宫产术在很大程度上会受麻醉效果的影响,麻醉药物以及麻醉方式的选择常常会决定剖宫产术的最终结果^[3]。硬膜外自控镇痛是现在临床上广泛使用的一种剖宫产术后镇痛方式。氢吗啡酮在疼痛治疗领域前景广阔,具有镇痛作用强、起效快、代谢产物无活性和不良反应少等特点,其镇痛作用为吗啡的8~10倍^[4,5]。

罗哌卡因常常被用于硬膜外阻滞麻醉和外科麻醉中,也可用于分娩后或者术后的急性止痛,且同时具备镇痛效果以及麻醉效果,对心脏的毒性较小,药物作用的时间较长^[6,8]。临床上虽已有将罗哌卡因联合氢吗啡酮硬膜外自控镇痛应用于剖宫产术中的研究报道,但其主要分析了对产妇氧化应激、血流动力学、内质网应激的影响^[9]。且尚未见其应用于妊娠期糖尿病患者剖宫产术中的报道。由于手术和高血糖的存在均会对胃肠功能产生不良影响,对此类剖宫产产妇进行产后镇痛干预的过程中需要特别重视对机体胃肠动力情况的改善效果。因此,本研究主要分析了罗哌卡因联合氢吗啡酮硬膜外自控镇痛对妊娠期糖尿病患者剖宫产术后胃肠动力的影响。

1 资料与方法

1.1 一般资料

选择2018年1月~2019年6月我院行剖宫产术的81例妊娠期糖尿病患者,纳入标准:(1)确诊为妊娠期糖尿病,胎儿发育基本正常,无前置胎盘或者畸形胎盘;(2)行择期剖宫产手术;(3)为单胎和足月,均知情同意;(4)凝血功能和精神状态均正常。排除标准:(1)阿片类药物或酒精依赖者;(2)合并高血压综

合征、心功能不全者;(3)意识障碍者和不愿参加此次研究者。

用抽签法将患者随机分为两组。观察组40例,年龄20~43岁,平均(27.59±1.44)岁;孕周35~42w,平均(38.79±1.26)w;体重59~87kg,平均(65.14±7.29)kg。对照组41例,年龄20~43岁,平均(27.44±1.38)岁;孕周35~42w,平均(38.54±1.17)w;体重59~87kg,平均(65.27±6.39)kg。两组的基线资料比较差异均无统计学意义,具有可比性($P>0.05$)。

1.2 麻醉方法

对照组采用常规肌内注射镇痛的方式进行干预,当产妇无法忍受疼痛时肌内注射哌替啶100mg。观察组在剖宫产术结束后连接自控镇痛泵,使用氢吗啡酮0.3mg+0.75%罗哌卡因20mL,用0.9%氯化钠溶液稀释为100mL。剂量为每小时2mL,设置为每次0.5mL,Lock 25min。

1.3 观察指标

两组分别在产前(干预前)和干预后1d、2d采集3mL外周静脉血,用ELISA法检测两组的应激激素指标:ALD、Cor、Ang-II、NE;胃肠激素指标:VIP、MTL、CCK和GAS。

两组分别在干预前和干预后2d采集3mL外周静脉血,用ELISA法检测血清MCP-1、IL-6、HMGB-1水平,试剂盒均购自上海岚派生物。

1.4 统计学分析

采用SPSS 21.0进行数据分析,两组间计量资料用($\bar{x}\pm s$)表示,对比用t检验,计数资料用百分比或率表示,组间比较采用 χ^2 检验,以 $P<0.05$ 为差异有统计学意义。

2 结果

2.1 两组患者干预前后不同时间点的应激激素水平对比

干预后,两组的VLD、Cor、Ang-II和NE均较干预前明显升高($P<0.05$),且观察组干预后1d、2d的VLD、Cor、Ang-II和NE明显低于对照组($P<0.05$),见表1。

表1 两组患者干预前后不同时间点的应激激素对比($\bar{x}\pm s$)

Table 1 Comparison of stress hormones between two groups at different time points before and after intervention ($\bar{x}\pm s$)

| Group | n | | VLD (ng/ mL) | Cor (ng/ L) | Ang-II (ng/ mL) | NE(pg/ mL) |
|-------------------|----|-----------------------------|-----------------|-----------------|-----------------|-----------------|
| Control group | 41 | Before intervention | 83.46±11.27 | 193.42±22.57 | 45.27±10.13 | 263.84±17.19 |
| | | At 1 day after interventio | 162.48±15.79 # | 265.41±17.45 # | 67.38±11.24 # | 467.25±24.38 # |
| | | At 2 days after interventio | 154.37±12.25 # | 253.42±13.28 # | 63.24±11.65 # | 439.24±22.34 # |
| Observation group | 40 | Before intervention | 82.45±10.19 | 192.57±20.44 | 36.15±10.26 | 264.53±18.53 |
| | | At 1 day after interventio | 138.69±12.24 ** | 241.36±18.27 ** | 60.42±10.38 ** | 387.54±20.13 ** |
| | | At 2 days after interventio | 132.27±11.44 ** | 139.14±12.25 ** | 57.34±9.14 ** | 382.51±17.36 ** |

Note: Compared with the control group, * $P<0.05$; compared with before intervention, # $P<0.05$.

2.2 两组患者干预前后不同时间点的胃肠激素对比

干预后,两组的VIP和CCK均明显升高($P<0.05$),MTL和GAS均明显降低($P<0.05$),且观察组干预后1d、2d的VIP和CCK明显低于对照组($P<0.05$),MTL和GAS明显高于对照组($P<0.05$),见表2。

2.3 两组患者干预前后不同时间点的血清炎症介质水平对比

干预2d后,两组的血清MCP-1、IL-6和HMGB-1水平均明显降低($P<0.05$),且观察组的血清MCP-1、IL-6和HMGB-1水平明显低于对照组($P<0.05$),见表3。

表 2 两组患者干预前后不同时间点的应激激素对比($\bar{x}\pm s$)Table 2 Comparison of gastrointestinal hormones in two groups at different time points before and after intervention ($\bar{x}\pm s$)

| Groups | n | | VIP(pg/ mL) | MTL(ng/L) | CCK(pg/mL) | GAS(pg/mL) |
|-------------------|----|------------------------------|--------------------------|----------------------------|--------------------------|---------------------------|
| Control group | 41 | Before intervention | 22.27±3.46 | 163.48±15.27 | 12.39±1.14 | 59.38±12.29 |
| | | At 1 day after intervention | 37.24±4.53 [#] | 129.27±14.38 [#] | 17.36±2.25 [#] | 36.27±7.45 [#] |
| | | At 2 days after intervention | 31.54±2.25 [#] | 131.57±12.15 [#] | 15.41±1.47 [#] | 47.31±10.25 [#] |
| Observation group | 40 | Before intervention | 23.15±3.47 | 164.69±16.38 | 12.25±1.63 | 60.14±13.37 |
| | | At 1 day after intervention | 32.28±1.76 | 134.57±16.29 | 15.24±1.38 | 42.23±8.41 |
| | | At 2 days after intervention | 25.37±2.64 ^{#*} | 142.57±13.64 ^{#*} | 12.79±1.14 ^{#*} | 53.67±12.25 ^{#*} |

Note: Compared with the control group, * $P<0.05$; compared with before intervention, [#] $P<0.05$.

表 3 两组患者干预前后不同时间点的血清炎症介质水平对比($\bar{x}\pm s$)Table 3 Comparison of serum inflammatory mediators between the two groups at different time points before and after intervention ($\bar{x}\pm s$)

| Groups | n | | MCP-1(ng/mL) | IL-6(pg/ mL) | HMGB-1(ng/mL) |
|-------------------|----|------------------------------|--------------------------|--------------------------|-------------------------|
| Control group | 41 | Before intervention | 25.39±2.74 | 103.48±11.25 | 18.27±3.64 |
| | | At 2 days after intervention | 17.43±1.52 [#] | 78.34±10.17 [#] | 10.31±1.72 [#] |
| Observation group | 40 | Before intervention | 25.14±3.62 | 101.75±12.24 | 17.92±3.25 |
| | | At 2 days after intervention | 10.27±1.26 ^{#*} | 42.25±6.34 ^{#*} | 5.24±1.36 ^{#*} |

Note: Compared with the control group, * $P<0.05$; compared with before intervention, [#] $P<0.05$.

3 讨论

妊娠期糖尿病好发于妊娠的中晚期,且会合并不同程度的代谢障碍,不利于母婴的安全^[10,11]。临床中对于妊娠期糖尿病患者的分娩干预有比较高的重视程度,而剖宫产手术在此类产妇中具有更高的临床应用率^[12]。子宫收缩及手术创伤都能导致剖宫产术后疼痛,不但能加重产妇的不良情绪,还能刺激产妇出现儿茶酚胺分泌增多以及交感神经兴奋等,从而抑制泌乳素的分泌过程,造成泌乳量的减少,不利于术后的母婴康复。硬膜外自控镇痛是剖宫产术后常用的镇痛方式,该种镇痛方法的用药剂量较小,且可以按照产妇的具体情况对用药剂量和用药次数进行调整^[13]。罗哌卡因不仅用药剂量低、作用时间长、安全性高,而且不会影响子宫及胎盘的血流量^[14-18]。氢吗啡酮的作用机制与吗啡比较相似,可以特异性激动阿片受体而产生明确的镇痛效果,但是其在化学结构上与吗啡并不相同,因而具有更快的起效速度和更高的脂溶性^[19-21]。另外,氢吗啡酮可以迅速地在肝脏中代谢成氢吗啡酮-3 葡糖苷酸,且代谢产物没有生物活性,因而能明显减小对呼吸的抑制效果,有更高的安全性^[22-24]。

妊娠期糖尿病患者由于受到高血糖的影响,可导致患者的胃肠功能指标出现明显的异常^[25]。胃肠激素可以有效反映机体的胃肠功能状态,而胃肠激素中的 VIP、MT、CCK 和 GAS 属于胃肠激素中比较重要的几个指标,其对于肠道和胃部功能都具有比较高的监测价值。当机体的胃肠道受到不良的应激刺激后,包括手术创伤造成的应激刺激,上述指标会出现比较明显

的波动。应激激素可以有效反映机体综合应激程度和创伤程度,其在手术患者中具有比较高的检测意义,其不但能反映机体受到的创伤应激程度,而且可以在一定程度上反映胃肠道功能的异常改变情况^[26]。本研究中,观察组应激激素、胃肠激素等胃动力状态指标的波动幅度相对更小,且恢复时间更短,表明罗哌卡因联合氢吗啡酮硬膜外自控镇痛可以更加有效的控制妊娠期糖尿病患者剖宫产术后胃肠功能受到的不良应激程度,而这与硬膜外自控镇痛有效减轻了患者的不良应激,进而控制了由此引发的胃肠道不良影响相关。

剖宫产的手术创伤和术后的疼痛都能直接引起患者出现全身炎症反应,炎症介质的过量释放也能使痛觉神经纤维的敏感性进一步增加,从而形成恶性循环。IL-6 属于一种最为典型的促炎因子,能诱导中性粒细胞聚集在创伤局部,且促使炎症反应的扩大^[27,28]。HMGB-1 和 MCP-1 都属于新型的炎症反应因子,在机体炎症反应后的中晚期,其合成量明显增加且释放入血,其表达水平与炎症反应的严重程度相一致。干预 2 d 后,观察组的血清 MCP-1、IL-6 和 HMGB-1 水平明显低于对照组,表明罗哌卡因联合氢吗啡酮硬膜外自控镇痛能更加有效的减轻妊娠期糖尿病患者剖宫产术后患者的全身炎症反应,这可能是其发挥镇痛作用的一个重要机制。罗良英等将氢吗啡酮联合罗哌卡因硬膜外自控镇痛用于骨科术后中,患者的炎症介质水平明显降低,与本研究结果一致。

综上所述,罗哌卡因联合氢吗啡酮硬膜外自控镇痛能改善妊娠期糖尿病患者剖宫产术后的胃肠功能,抑制全身炎症反应。

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