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舒芬太尼术后镇痛对剖宫产后产妇血清儿茶酚胺、泌乳素水平及血流动力学的影响*

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摘要 目的:探讨舒芬太尼术后镇痛对剖宫产术后产妇血清儿茶酚胺(CA)、泌乳素(PRL)水平及血流动力学的影响。**方法:**选择我院2015年1月~2016年12月收治的98例剖宫产产妇,术后按不同镇痛方式分为对照组与研究组,每组49例。对照组予以芬太尼镇痛,研究组予以舒芬太尼镇痛。观察并比较两组治疗前后血清多巴胺、去甲肾上腺素、肾上腺素、PRL、心率及平均动脉压水平的变化,镇痛效果及不良反应的发生情况。**结果:**手术后,两组血清多巴胺、去甲肾上腺素、肾上腺素、PRL、心率、平均动脉压、VAS水平均较术前显著上升,且研究组以上指标均显著低于对照组($P<0.05$)。研究组不良反应发生率显著低于对照组($P<0.05$)。**结论:**舒芬太尼用于剖宫产术后的镇痛效果肯定,能够抑制产妇术后CA的分泌,且对泌乳及血流动力学的影响较小。

关键词:剖宫产;舒芬太尼;镇痛;儿茶酚胺;泌乳

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Effects of Postoperative Analgesia by Sufentanil on the Level of Catecholamine and Prolactin and Hemodynamics of Maternal after Cesarean Section*

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ABSTRACT Objective: To discuss the effects of the postoperative analgesia on the serum levels of catecholamine, prolactin and hemodynamics and lactation of patients after the cesarean section maternal. **Methods:** 98 cases of cesarean section maternal from January 2015 to December 2016 were selected and according to different analgesia methods, the patients were divided into the control group and the research group. Then the dopamine, norepinephrine, epinephrine, plasma PRL, visual analogue scale (VAS), heart rate and mean arterial pressure, and incidence of adverse reactions were observed and compared between the two groups before and after the treatment. **Results:** After surgery, the dopamine, norepinephrine, epinephrine, plasma PRL, heart rate, mean arterial pressure and VAS in the two groups were significantly lower than before, and the research group was significantly lower than that of the control group, and the differences were statistically significant ($P<0.05$). There was no statistically significant difference about the incidence of adverse reactions between the two groups ($P>0.05$). **Conclusion:** The effect of sufentanil postoperative analgesia is certain, which can inhibit the secretion of maternal CA level, and less impact on lactation and hemodynamics.

Key words: Caesarean section; Sufentanil; Analgesia; Catecholamine; Lactation

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前言

剖宫术现已成为治疗前置胎盘、胎盘早剥离、子痫等产科并发症及头盆不称、胎位异常、胎儿窘迫等难产以挽救围产儿及产妇生命的重要手段,其属有创手术,可能出现副损伤及大出血,有一定的危险性,且术后疼痛较为明显^[1,2]。Li X等^[3]研究显示剖宫产术后创伤及子宫收缩产生的剧烈疼痛容易导致产妇发生复杂的生理和心理反应的变化,且严重影响产妇产后的

生活质量,延迟产妇术后机体的康复,其次疼痛时可引起交感神经兴奋,儿茶酚胺分泌(CA)增多,下丘脑分泌的生乳激素抑制因子分泌增多,从而抑制泌乳素(PRL)的分泌,进一步影响新生儿初乳及母乳喂养质量^[3-5]。Weigl W等研究^[6]指出选用有效的镇痛模式、配伍不同的镇痛药物对急性疼痛的控制,减少麻醉镇痛药的应用,预防疼痛的发生至关重要,并术后良好的镇痛模式能够一定程度的减轻应激反应。静脉自控镇痛(PCIA)为新型的镇痛方式,产妇可经微量泵自行镇痛,不仅能够使医护

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人员的工作量减少,又可缓解产妇的心理负担。芬太尼是既往术后自控镇痛的主要药物,但剂量过大容易出现多种并发症,有一定局限性^[7,8]。舒芬太尼是芬太尼的一种衍生物,且为术后镇痛的常用药物^[9,10]。本研究旨在观察剖宫术后产妇应用舒芬太尼术后镇痛对其 CA 水平及泌乳的影响。

1 资料与方法

1.1 一般资料

选择我院 2015 年 1 月~2016 年 12 月收治的 98 例剖宫产产妇,入选标准^[11]:① 单胎、足月、头正位,初产妇;② 剖宫产手术指征明确;③ 乳房未见发育缺陷;④ 未见产科合并症;⑤ ASA 分级 I~II 级;⑥ 神经系统未见异常。排除标准:① 凝血功能明显异常;② 心肝肾等主要脏器异常;③ 胎盘前置、先天畸形等;④ 过敏性体质。对照组术后予以芬太尼镇痛,年龄 23~34 岁,平均(27.09±2.11)岁;身高 150~170 cm,平均(164.92±1.98)cm;体重 65~87 kg,平均(78.21±2.85)kg;妊娠周期 37~41 周,平均(39.11±0.63)周。研究组术后予以舒芬太尼镇痛,年龄 23~32 岁,平均(27.81±2.52)岁;身高 151~171 cm,平均(165.36±1.92)cm;体重 66~85 kg,平均(77.94±2.81)kg;妊娠周期 37~41 周,平均(39.35±0.61)周。两组一般资料比较差异均无统计学意义,存在可比性(P>0.05)。

1.2 方法

1.2.1 麻醉方法 常规建立上肢静脉,输注乳酸钠林格溶液(四川美大康佳乐药业有限公司,500 mL,140311)500 mL,并于 10 min 后进行麻醉,鼻导管以 2~3 L/min 持续给氧,并指导产妇为左侧卧位。选择 L3~4 间隙正中作为穿刺入路,消毒铺巾后取 16G Tuohy 针实施硬膜外穿刺,于硬膜外针管内置入 25G 腰麻穿刺针,直至蛛网膜下腔,回抽后可见脑脊液即穿刺成功。将 2 mL 生理盐水(安徽安科恒益药业有限公司,10 mL:90 mg,

140204)和 15 mg/2 mL 的盐酸布比卡因(上海朝晖药业有限公司,5 mL:25 mg,140312)加脑脊液稀释至 3 mL,并推注 2 mL 于蛛网膜下腔,调节麻醉组织平面为 T6 水平,术毕前 5 min 接通静脉镇痛泵。

1.2.2 镇痛方法 对照组术后予以芬太尼镇痛,将 5 mg 托烷司琼(西南药业股份有限公司,2 mg,140206)+20 μg/kg 芬太尼(宜昌人福药业,2 mL:0.1 mg,140220)+100 mL 生理盐水配制成 PCIA 泵。研究组术后予以舒芬太尼镇痛,5 mg 托烷司琼+2 μg/kg 舒芬太尼(宜昌人福药业,1 mL:50 μg,114021)+100 mL 生理盐水配制成 PCIA 泵。两组 PCIA 泵剂量均控制在 2 mL/h,单次追加剂量控制在 2 mL,锁定时间在 15 min。观察并记录两组入室时及术毕 24 h 时平均动脉压、心率及不良反应的发生情况。

1.3 观察指标

指标测定:于入室时及术毕 24 h 收集产妇晨起静脉血 2 mL,将其进行常规分离后并保存。CA 水平选用化学比浊法进行。血清 PRL 按酶联免疫法进行。视觉模拟评分(VAS)观察:分值为 0 至 10 分,0 分表示无痛,分数越高提示疼痛程度越为严重^[12]。

1.4 统计学分析

选用 SPSS18.0 进行数据处理,计量资料以($\bar{x} \pm s$)表示,组间比较选用 t 检验,用[例(%)]表示计数资料,组间比较用 χ^2 检验,以 P<0.05 为差异具有统计学意义。

2 结果

2.1 两组手术前后血清 CA 水平的比较

手术前,两组血清多巴胺、去甲肾上腺素和肾上腺素水平比较差异无统计学意义(P>0.05);手术后,两组血清多巴胺、去甲肾上腺素和肾上腺素水平均较术前显著上升,且研究组上升血清多巴胺、去甲肾上腺素和肾上腺素水平明显低于对照组(P<0.05),见表 1。

表 1 两组手术前后血清 CA 水平的比较($\bar{x} \pm s$)

Table 1 Comparison of the serum CA level between two groups before and after the surgery ($\bar{x} \pm s$)

Groups	n	Time	Dopamine(ng/L)	Norepinephrine(ng/L)	Adrenalin(ng/L)
Control group	49	Before surgery	107.85±13.38	520.75±65.09	60.53±7.53
		After surgery	122.65±15.60	725.11±90.61	89.27±11.75
Research group	49	Before surgery	106.43±13.90	522.49±64.11 ^b	60.91±7.90 ^b
		After surgery	142.52±17.89	659.36±82.97 ^{ab}	73.42±9.13 ^{ab}

Note: Compared with the control group, ^aP<0.05; Compared with before surgery, ^bP<0.05.

2.2 两组手术前后血清 PRL 水平的比较

手术前,两组血清 PRL 水平比较差异无统计学意义(P>0.05);

手术后,两组血清 PRL 水平均较术前显著上升,且研究组血清 PRL 水平明显高于对照组(P<0.05),见表 2。

表 2 两组手术前后血清 PRL 水平的比较($\bar{x} \pm s$)

Table 2 Comparison of the plasma PRL level between two groups before and after the surgery ($\bar{x} \pm s$)

Groups	n	Time	plasma PRL(μg/L)
Control group	49	Before surgery	191.08±23.85
		After surgery	311.52±38.45 ^b
Research group	49	Before surgery	190.52±22.97
		After surgery	375.89±46.76 ^{ab}

Note: Compared with the control group, ^aP<0.05; Compared with before surgery, ^bP<0.05.

2.3 两组手术前后 VAS 评分的比较

手术前, 两组 VAS 评分比较差异无统计学意义($P>0.05$);

手术后, 两组 VAS 评分均较手术前显著上升, 且研究组 VAS 评分明显低于对照组($P<0.05$), 见表 3。

表 3 两组手术前后 VAS 评分的比较($\bar{x} \pm s$)

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

Groups	n	Time	VAS(points)
Control group	49	Before surgery	3.65 $\pm$ 0.45
		After surgery	5.21 $\pm$ 0.67 ^b
Research group	49	Before surgery	3.52 $\pm$ 0.43
		After surgery	4.89 $\pm$ 0.62 ^{ab}

Note: Compared with the control group, ^a $P<0.05$; Compared with before surgery, ^b $P<0.05$.

2.4 两组手术前后血流动力学指标的比较

手术前, 两组血流动力学指标比较差异均无统计学意义($P>0.05$); 手术后, 两组心率及平均动脉压均较治疗前显著上

升, 研究组心率及平均动脉压显著低于对照组($P<0.05$), 见表 4。

表 4 两组手术前后血流动力学指标的比较($\bar{x} \pm s$)

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

Groups	n	Time	Heart rate(time /min)	Mean arterial pressure(mmHg)
Control group	49	Before surgery	72.11 $\pm$ 9.05	84.90 $\pm$ 10.52
		After surgery	87.09 $\pm$ 10.83 ^b	93.53 $\pm$ 11.69 ^b
Research group	49	Before surgery	72.50 $\pm$ 9.54	84.67 $\pm$ 10.97
		After surgery	76.23 $\pm$ 9.85 ^{ab}	89.21 $\pm$ 11.32 ^{ab}

Note: Compared with the control group, ^a $P<0.05$; Compared with before surgery, ^b $P<0.05$.

2.5 两组产妇不良反应发生情况的比较

研究组不良反应发生率为 32.65%, 显著低于对照组

(55.10%, $P<0.05$), 见表 5。

表 5 两组产妇不良反应发生情况的比较[例(%)]

Table 5 Comparison the incidence of maternal adverse reactions between two groups[n(%)]

Groups	n	Skin itching	Nausea and vomiting	Pull reflection	Bradycardia	Low blood pressure	Adverse reaction rate
Control group	49	4(8.16)	7(14.29)	6(12.24)	6(12.24)	4(8.16)	27(55.10)
Research group	49	2(4.08)	5(10.20)	4(8.16)	3(6.12)	2(4.08)	16(32.65) ^a

Note: Compared with the control group, ^a $P<0.05$.

3 讨论

剖宫产术后疼痛是一种伤害性疼痛, 多源于子宫收缩及腹部切口, 容易引起抑郁发生、烦躁等负面情绪的出现, 且可诱导机体发生免疫、泌尿、消化及呼吸等系统的生理病理改变, 明显影响产妇体力恢复及睡眠^[13,14]。有研究显示良好的术后镇痛能提高围手术期的安全性, 减少并发症的发生, 显著改善母儿生活质量, 其主要选择不良反应低的药物或简单的方式, 最大程度地满足产妇对术后镇痛的要求, 其中静脉自控镇痛对产妇的影响较少, 是目前研究的一大热点^[15,16]。

术后镇痛的最常见药物配方是选择性环氧酶抑制药或者对乙酰氨基酚及阿片类药物、曲马多配合, 是术后缓解中重度疼痛的最常用配方。近几年, 有研究显示环氧酶抑制药虽

不影响神志, 有良好的消炎和制止运动痛的作用, 且相关副作用的报道极少, 但缺乏严格对照、多中心、大批量的观察报道, 结果可能有一定差异。芬太尼作为一种阿片受体的激动剂, 能够起到与吗啡相同的麻醉效果, 动物研究实验表明其镇痛效力明显强于吗啡, 且镇痛作用产生快, 但持续时间较短, 且大剂量芬太尼可产生系列并发症, 导致患者躁动, 降低镇痛效果^[17,18]。舒芬太尼为芬太尼的一种衍生物, 属新型强效镇痛药物, 主要作用于 μ 阿片受体, 血清蛋白结合性及亲脂性明显高于芬太尼, 更容易作用于血脑屏障, 且分布容积相对较小, 镇痛效果更为确切^[19,20]。同时, 舒芬太尼能够生成存在一定药理活性的代谢产物, 并经胆汁及尿液排出, 因此药效的作用时间明显优于芬太尼^[21,22]。

Dede H 等^[23]研究显示手术创伤与术后疼痛等伤害性刺激

可导致一定程度的应激反应,属于机体防御反应,适当的应激强度能够减轻不良刺激对机体产生的损伤,过度的应激则可产生系列不良反应。应激反应主要以中枢神经系统改变为主,刺激 CA 水平的释放及分泌,引起多巴胺、去甲肾上腺素及肾上腺素的升高,以抵御应激反应所致内环境损伤^[24,25]。CA 结合受体后能够经多种途径导致免疫抑制,其浓度增加和机体创伤及疼痛程度有着良好的相关性。国外研究显示剖宫产术后 CA 水平平均明显上升,本研究也显示两组剖宫产术后 CA 水平均有增加,但经舒芬太尼镇痛组上升幅度更小,证实剖宫产可导致机体出现明显的应激反应,但舒芬太尼能够对其产生良好的缓解作用,可能与其能够使神经阻滞,引起内分泌反应受到阻断,从而降低 CA 浓度,减轻机体的应激强度^[26]。剖宫术由于尿管刺激、疼痛等因素,能够使产妇产后血流动力学产生变化,主要表现为血压上升、心率增快等。本研究结果显示:舒芬太尼镇痛后产妇产后血流动力学较为稳定,平均动脉压及心率仅有轻微上升,考虑与舒芬太尼能更有效减轻疼痛有关。

剖宫产术后腹部伤口及宫缩疼痛能够引起产妇多种生理病理改变,抑制 PRL 的分泌,从而影响泌乳素的分泌。血清 PRL 是促进乳腺发育,引起并维持泌乳的最主要因素,能够为乳腺生长发育提供有利条件,利于泌乳的进行。妊娠早期时 PRL 开始分泌增多,哺乳期达高峰,分娩后 2 小时 PRL 水平明显增加,成为初乳分泌的生理基础,产后 24 小时产妇产后血清 PRL 浓度与产妇的乳汁分泌呈正相关。乳汁的产生与分泌是受内分泌、生理、环境及遗传等诸多因素影响的神经内分泌调节过程,其中血清 PRL 的浓度对乳汁分泌起决定作用。本研究结果显示两组镇痛后血清 PRL 水平均较术前显著上升,但舒芬太尼镇痛后血清 PRL 水平相对较高,提示其对泌乳的影响较小,考虑与其镇痛效果确切,能够减轻疼痛对 PRL 分泌产生的刺激,从而减轻对术后泌乳量的影响,利于早期的母乳喂养。本研究中,舒芬太尼镇痛后 VAS 评分下降更明显,进一步证实其镇痛的可行性。此外,其不良反应发生率更低,提示舒芬太尼能够使内脏牵拉痛受到抑制,对产妇产后血液与呼吸等循环的影响较小。但本研究由于纳入样本量较小,结果可能存在一定偏差,有待临床进一步考察。

综上所述,舒芬太尼用于剖宫产术后的镇痛效果肯定,能够抑制产妇产后 CA 的分泌,且对泌乳及血流动力学的影响较小。

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