doi: 10.13241/j.cnki.pmb.2019.02.035

卡前列素氨丁三醇注射液联合缩宫素对剖宫产出血患者 FIB 与 D- 二聚体的影响 *

张丽武[1] 黄春燕[1] 李 凯[2] 石伟红[1] 李明丽[1]

（1 广西南溪山医院产科 广西 桂林 541002；2 桂林医学院附属医院 广西 桂林 541001）

摘要 目的：探讨卡前列素氨丁三醇注射液联合缩宫素用于剖宫产产后出血的预防效果及对纤维蛋白原(FBI)、D- 二聚体(D-D)水平的影响。**方法：**选择 2014 年 1 月至 2016 年 10 月我院接诊的 92 例剖宫产产妇，通过随机数表法分为观察组(n=46)和对照组(n=46)。对照组在胎儿娩出后给予缩宫素的宫内注射及静脉滴注，观察组在胎儿娩出后，先给予缩宫素的宫内注射，再在子宫肌壁注射卡前列素氨丁三醇注射液。比较两组产后出血情况、宫缩持续时间、子宫底下降速度、恶露持续时间、FIB、D-D 水平及不良反应的发生情况。**结果：**观察组产后 2 h、24 h 出血量及产后出血率明显低于对照组(P＜0.05)，宫缩持续时间长于对照组(P＜0.05)，子宫底下降速度快于对照组(P＜0.05)，恶露持续时间明显短于对照组组(P＜0.05)。两组治疗前 FIB、D-D 水平比较差异无统计学意义(P＞0.05)。治疗后，两组 FIB、D-D 水平均较治疗前显著降低(P＜0.05)，且观察组 FIB、D-D 水平均明显低于对照组(P＜0.05)；两组恶心呕吐、面部潮红、胸闷、头痛发生率比较差异无统计学意义(P＞0.05)。**结论：**在剖宫产产妇中应用卡前列素氨丁三醇注射液联合缩宫素可降低产后出血发生率，且安全性高，可能与有效减少 FIB、D-D 表达有关。

关键词：剖宫产；卡前列素氨丁三醇注射液；缩宫素；纤维蛋白原；D- 二聚体

中图分类号：R719 **文献标识码：**A **文章编号：**1673-6273(2019)02-358-04

Effect of Carboprost Tromethamine Injection Combined with Oxytocin on FIB and D-dimer of Patients with Postpartum Hemorrhage after Cesarean Section*

ZHANG Li-wu[1], HUANG Chun-yan[1], LI Kai[2], SHI Wei-hong[1], LI Ming-li[1]

(1 Department of Obstetrics, Nanxi Mountain Hospital, Guilin, Guangxi, 541002, China;

2 Department of Obstetrics and Gynecology, the First Affiliated Hospital of Guangxi Medical University, Guilin, Guangxi, 541001, China)

ABSTRACT Objective: To study the preventive effect of Carboprost Tromethamine Injection combined with oxytocin on the postpartum hemorrhage of cesarean section and its effects on the fibrinogen(FIB) and D-dimer(D-D). **Methods:** 92 cases of patients with cesarean section who were treated from January 2014 to October 2016 in our hospital were selected. According to random number table, those patients were divided into the observation group (n=46) and the control group (n=46). The control group was given oxytocin after delivery of fetus intrauterine injection and intravenous drip, the observation group was firstly given oxytocin intrauterine injection, and then the injection of Carboprost Tromethamine into the uterine wall after delivery of fetus. The postpartum hemorrhage, contraction duration, descending rate of uterine fundus, the duration of lochia, FIB, D-D levels and incidence of adverse reactions were compared between two groups. **Results:** Compared with the control group, the bleeding volume at 2 h and 24 h after delivery and the postpartum hemorrhage rate in the observation group were significantly lower(P＜0.05), the contraction duration was longer(P＜0.05), the descending rate of uterine fundus was faster(P＜0.05), the duration of lochia was significantly shorter(P＜0.05). There was no significant difference in the FIB and D-D before treatment between the two groups (P＞0.05). After treatment, the levels of FIB and D-D in both groups were significantly lower than those before treatment (P＜0.05), and the levels of FIB and D-D in the observation group were significantly lower than those of the control group (P＜0.05); there was no significant difference in the incidence of nausea and vomiting, facial flushing, chest tightness and headache (P＞0.05). **Conclusion:** Carboprost Tromethamine Injection combined with oxytocin could effectively reduce the incidence of postpartum hemorrhage with high safety, which might be related to the decrease of FIB, D-D levels.

Key words: Cesarean section; Carboprost tromethamine injection; Oxytocin; Fibrinogen; D-dimer

Chinese Library Classification (CLC): R719 Document code: A

Article ID: 1673-6273(2019)02-358-04

前言

产后出血在产科中十分常见，主要指胎儿在分娩出 24 h

* 基金项目：广西壮族自治区卫生厅科研项目(Z2013308)

作者简介：张丽武，女，硕士，副主任医师，研究方向：产后出血，E-mail: zhanggh2010@sina.com

(收稿日期：2018-03-03 接受日期：2018-03-26)

PDF 文件使用 "pdfFactory Pro" 试用版本创建 www.fineprint.cn

内出血量＞500 mL，剖宫产时超过 1000 mL。若得不到及时的治疗，极有可能引发呼吸窘迫综合征、循环衰竭等，对生命造成威胁，而和正常的阴道分娩产妇相比，剖宫产产妇更容易出现产后出血[1,2]。产后出血的发生和子宫收缩乏力密切相关，有报道指出血液的高凝状态和产后出血之间存在着紧密联系[3,4]。因此，增加子宫收缩、改善血液高凝状态，在预防剖宫产后出血显得极关重要。目前，对于产后出血临床上最常用的方式是采用缩宫素，但单独使用缩宫素治疗效果不尽人意[5]。前列素氨丁三醇注射液是种钙离子载体，可促进钙离子浓度提高，从而改善子宫平滑肌的收缩。近年来，该药物也逐渐应用于剖宫产后出血的治疗[6,7]。本研究主要探讨了在剖宫产术后应用卡前列素氨丁三醇注射液联合缩宫素的治疗优势及对纤维蛋白原(FBI)、D- 二聚体(D-D)的影响，现报道如下。

1 资料与方法

1.1 一般资料

选择我院 2014 年 1 月至 2016 年 10 月接诊的 92 例剖宫产产妇。纳入标准[8]：① 符合剖宫产指征；② 存在子宫收缩乏力现象；③ 近期无出血史；④ 对本次研究知情同意。排除标准[9]：① 伴有血液性疾病、自身免疫系统疾病；② 心、肝、肾功能存在严重障碍；③ 对本次药物过敏；④ 伴有恶性肿瘤。通过随机数表法分为 2 组。观察组 46 例，年龄 22~42 岁，平均(31.76± 2.91)岁；孕周 38~42 周，平均(40.24± 0.39)周；初产妇 33 例，经产妇 13 例；术中出血量 430~840 mL，平均(636.94± 44.53)mL。对照组 46 例，年龄 23~41 岁，平均(31.82± 2.86)岁；孕周 39~42 周，平均(40.28± 0.34)周；初产妇 36 例，经产妇 10 例，术中出血量 435~850 mL，平均(637.12± 44.26)mL。两组一般资料比较差异均无统计学意义(P＞0.05)，具有可比性。

1.2 方法

在胎儿娩出后，对照组给予缩宫素(规格 1 mL：10 U，厂家：上海第一生化药业有限公司，国药准字 H31020862)20U 的宫内注射，再给予缩宫素 20U 的静脉滴注。观察组先给予缩宫素 20U 的宫内注射，再在子宫肌壁进行 250 μg 的卡前列素氨丁三醇注射液(规格 1 mL：250 μg，厂家：PharmaciaUpjohn Company，国药准字 H20070251)的注射，必要时可间隔 15~20 min 重复用药，药物使用剂量不多于 2 mg。

1.3 观察指标

1) 产后出血情况：包括产后 2 h、24 h 出血量，出血量 =[胎儿娩出后接血敷料湿重(g)- 接血前敷料干重(g)/1.05(血液比重，g/mL)]，以产后出血量＞1000 mL 剖宫产应为 1000 mL 判定为产后出血；2) 记录宫缩持续时间、子宫底下降速度、恶露持续时间；3) 治疗前及治疗后 2 d，抽取 3 mL 静脉血，测定 FBI、D-D 水平，FIB 的测定使用免疫比浊法，D-D 使用酶联免疫吸附法，试剂盒均由上海研谨生物科技有限公司提供；4) 记录药品不良反应的发生情况。

1.4 统计学分析

采用 spss18.0 软件包处理实验数据，计量资料用均数± 标准差($\bar{x}$± s)表示，组间比较采用 t 检验，计数资料采用 x^2 检验，以 P<0.05 表示差异具有统计学意义。

2 结果

2.1 两组产后出血情况的比较

观察组产后 2 h、24 h 出血量明显低于对照组(P＜0.05)，观察组产后出血率为 6.52%，明显低于对照组(23.91%，P＜0.05)，见表 1。

表 1 两组产后出血情况比较[$\bar{x}$± s，n(%)]

Table 1 Comparison of the postpartum hemorrhage between the two groups [$\bar{x}$± s, n(%)]

Groups	Postpartum 2 h	Postpartum 24 h	Postpartum hemorrhage rate
Observation group(n=46)	638.45± 78.83*	734.12± 98.34*	3(6.52)*
Control group(n=46)	749.12± 93.82	817.39± 101.83	11(23.91)

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

2.2 两组宫缩持续时间、子宫底下降速度、恶露持续时间比较

观察组宫缩持续时间长于对照组，子宫底下降速度快于对照组，恶露持续时间明显短于对照组(P＜0.05)，见表 2。

表 2 两组宫缩持续时间、子宫底下降速度、恶露持续时间比较($\bar{x}$± s)

Table 2 Comparison of the contraction duration, descending rate of uterine fundus and the duration of lochia between the two groups ($\bar{x}$± s)

Groups	Contraction duration(h)	Descending rate of uterine fundus(cm/d)	The duration of lochia(d)
Observation group(n=46)	3.57± 0.63*	1.18± 0.27*	13.84± 3.12*
Control group(n=46)	1.58± 0.29	0.57± 0.12	21.47± 4.10

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

2.3 两组治疗前后 FIB、D-D 水平的比较

治疗前，两组 FIB、D-D 水平比较差异无统计学意义 (P＞0.05)，治疗后，两组 FIB、D-D 水平较治疗前均显著降低(P＜0.05)，且观察组 FIB、D-D 水平均明显低于对照组(P＜0.05)，见表 3。

2.4 两组不良反应发生情况的比较

观察组恶心呕吐、面部潮红、胸闷、头痛发生率分别为 4.35%、4.35%、2.17%、4.35%，和对照组的 (8.69%、6.52%、4.35%、4.35%)比较差异均无统计学意义(P＞0.05)，两组不良反应总发生率比较差异无统计学意义(P＞0.05)，见表 4。

PDF 文件使用 "pdfFactory Pro" 试用版本创建 www.fineprint.cn

表 3 两组治疗前后 FIB、D-D 水平的比较($\bar{x}\pm$ s)

Table 3 Comparison of the FIB and D-D levels between two groups ($\bar{x}\pm$ s)

Groups		FIB(g/L)	D-D(mg/L)
Observation group(n=46)	Before treatment	4.76± 0.45	3.64± 0.43
	After treatment	3.28± 0.27*#	1.27± 0.21*#
Control group(n=46)	Before treatment	4.79± 0.42	3.62± 0.45
	After treatment	4.17± 0.34*	2.75± 0.33*

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

表 4 两组不良反应发生情况的比较[n(%)]

Table 4 Comparison of the incidence of adverse reactions between the two groups[n(%)]

Groups	Nausea and vomiting	Facial flushing	Chest tightness	Headache	Total incidence rate
Observation group(n=46)	2(4.35)	2(4.35)	1(2.17)	2(4.35)	7(15.22)
Control group(n=46)	4(8.69)	3(6.52)	2(4.35)	2(4.35)	11(23.91)

3 讨论

产后出血的发生主要和宫缩乏力、软产道损伤、胎盘组织功能障碍、凝血功能障碍等存在着密切的关系,其中宫缩乏力最为关键[10,11]。而在剖宫产产妇中,普遍有多胎妊娠、巨大儿、前置胎盘等现象,均是引发宫缩乏力的高危因素,再加上手术过程中麻醉的影响,会明显增加产后出血率,对产妇、婴儿的生命造成威胁[12,13]。

缩宫素主要由动物垂体所提取或人工合成,其可促进子宫的强直性宫缩,从而预防产后出血[14]。但该药物在进入体内后,在很短的过程中会被胎盘生存的缩宫素酶和肝、肾灭活并清除,半衰期较短,大约在 3~4 min,且仅可刺激子宫上段收缩,在受体位点达到饱和状态后,即便是追加药物剂量也得不到令人满意的效果[15,16]。卡前列素氨丁三醇注射液作为前列腺素 2α 的衍生物,和传统的前列腺素类药物(例如米索前列醇片)相比,卡前列素氨丁三醇注射液的 15- 羟基被甲基所替代后,可抵抗 15- 羟基脱氧酶对其的灭活作用,达到使半衰期延长并增加生物活性的作用[17,18]。Quan ZF 等[19]数据显示卡前列素氨丁三醇注射液使用 250 μg 注射后,在 3 min 则可起效,30min 可达到高峰,时间维持 2 h,在 15~90 min 内可重复使用,总剂量不超过 2 mg,是一种强力且安全性较高的收缩剂。X Bai J 等[20]研究证实与常规缩宫素比较,在剖宫产产后出血中应用卡前列素氨丁三醇注射液可更有效的预防产后出血。

本研究中,联合用药的患者在产后 2 h、24 h 的出血量明显比单独应用缩宫素的患者显著降低,产后出血率仅为 6.52%,优于单独用药的 23.91%,且胎儿分娩后的宫缩持续时间更长,子宫底下降速度更快,恶露持续时间更短,显示出联合用药可发挥协同效应,进一步促进子宫收缩和产后子宫恢复,有利于预防产后出血。卡前列素氨丁三醇注射液所产生的不良反应包括胃肠道反应、发热、胸闷等,和其对平滑肌的收缩存在着关系[21]。本研究中,联合用药的患者恶心呕吐、面部潮红、胸闷、头痛的发生率均较低,且无需特殊处理,在 24 h 均得到自行消退,显示出联合用药安全性高。

FIB 和 D-D 是反映机体血液流变学的两种常用指标。FIB 主要合成于肝脏,当其水平增加时,极易引发血栓;D-D 是交联纤维蛋白的降解产物,若其表达过高,可提示机体处于高凝状态和纤溶亢进,在预测产后出血中具有较高的临床价值[22]。研究证实在产后出血的孕妇中,FIB、D-D 的表达明显较高[23]。因此,及时改善产妇的 FIB、D-D 水平有利于减少产后出血。本研究显示两种治疗方式的患者治疗后 FIB、D-D 水平均明显下降,但联合用药的患者下降程度更令人满意,分析可能是由于卡前列素氨丁三醇注射液具有促进血小板聚集和血管收缩的作用,从而改善血液的高凝状态,降低 FIB、D-D 的表达。这也可能是联合用药患者产后出血发生率更低的内在机制之一。

综上所述,在剖宫产产妇中应用卡前列素氨丁三醇注射液联合缩宫素可降低产后出血发生率,且安全性高,可能与有效减少 FIB、D-D 表达有关。

参 考 文 献(References)

[1] Chen CY, Su YN, Lin TH, et al. Carbetocin in prevention of postpartum hemorrhage: Experience in a tertiary medical center of Taiwan [J]. Taiwan J Obstet Gynecol, 2016, 55(6): 804-809

[2] Sentilhes L, Brun S, Madar H, et al. Re: Does tranexamic acid prevent postpartum haemorrhage? A systematic review of randomised controlled trials: A very welcome publication [J]. BJOG, 2017, 124(6): 982

[3] Lisonkova S, Mehrabadi A, Allen VM, et al. Atonic Postpartum Hemorrhage: Blood Loss, Risk Factors, and Third Stage Management[J]. J Obstet Gynaecol Can, 2016, 38(12): 1081-1090

[4] Holm C, Thomsen LL, Norgaard A, et al. Single-dose intravenous iron infusion or oral iron for treatment of fatigue after postpartum haemorrhage: a randomized controlled trial [J]. Vox Sang, 2017, 112(3): 219-228

[5] Koen S, Snyman LC, Pattinson RC, et al. A randomised controlled trial comparing oxytocin and oxytocin + ergometrine for prevention of postpartum haemorrhage at caesarean section [J]. Afr Med J, 2016, 106(4): 55-56

[6] Balki M, Erik-Soussi M, Ramachandran N, et al. The Contractile Effects of Oxytocin, Ergonovine, and Carboprost and Their Combinations: an In Vitro Study on Human Myometrial Strips [J]. Anesth Analg, 2015, 120(5): 1074-1084

PDF 文件使用 "pdfFactory Pro" 试用版本创建 www.fineprint.cn

[7] Mallick R, Ajala T, Kelly AJ. Carboprost: A useful adjunct in laparoscopic resection of a cornual ectopic pregnancy[J]. J Obstet Gynaecol, 2015, 35(7): 761-762

[8] Vijayasree M. Efficacy of Prophylactic B-Lynch Suture during Lower Segment Caesarian Section in High Risk Patients for Atonic Postpartum Haemorrhage[J]. Kathmandu Univ Med J (KUMJ), 2016, 14(53): 9-12

[9] Malone C, Acheson JR, Hinds JD, et al. Uterotonics for Non-emergent Caesarean Section: Protocol Change During UK-Licensed Drug Shortage[J]. Ulster Med J, 2016, 85(3): 174-177

[10] Kayem G, Deneux-Tharaux C. Authors' reply Quantifying haemorrhage is a central difficulty when dealing with primary postpartum haemorrhage[J]. BJOG, 2017, 124(3): 526-527

[11] Lumala A, Sekweyama P, Abaasa A, et al. Assessment of quality of care among in-patients with postpartum haemorrhage and severe pre-eclampsia at st. Francis hospital nsambya: a criteria-based audit [J]. BMC Pregnancy Childbirth, 2017, 17(1): 29

[12] Jardine JE, Law P, Hogg M, et al. Haemorrhage at caesarean section: a framework for prevention and research [J]. Curr Opin Obstet Gynecol, 2016, 28(6): 492-498

[13] Bojinova S, Porozhanova K. The use of prostaglandin F2al pha (Prostin 15M) for terminationof second trimester pregnancy[J]. Akush Ginekol (Sofiia), 2013, 52(2): 53-55

[14] Miller JL, Tamura R, Butler MG, et al. Oxytocin treatment in children with Prader-Willi syndrome: A double-blind, placebo-controlled, crossover study[J]. Am J Med Genet A,2017, 173(5): 1243-1250

[15] Sobkowski M, Celewicz Z, Kalinka J, et al. Costs of the use of carbetocin in the prevention of uterine atony following delivery of the infant by Caesarean section - retrospective multicenter study [J]. Ginekol Pol, 2016, 87(9): 621-628

[16] Jagielska I, Kazdepka-Ziemińska A, Kaczorowska A, et al. Evaluation of carbetocin and oxytocin efficacy in prevention of postpartum hemorrhage in women after cesarean section [J]. Ginekol Pol, 2015, 86(9): 689-693

[17] Zhang R, Shi H, Ren F, et al. Assessment of carboprost tromethamine for reducing hemorrhage in laparoscopic intramural myomectomy[J]. Exp Ther Med, 2015, 10(3): 1171-1174

[18] Yamada T, Akaishi R, Oda Y, et al. Antenatal fibrinogen concentrations and postpartum haemorrhage [J]. Int J Obstet Anesth, 2014, 23 (4): 365-370

[19] Quan ZF, Tian M, Chi P. Large doses of uterotonic drugs caused type II second degree sinoatrial block during cesarean section[J]. Int J Clin Pharmacol Ther, 2016, 54(1): 62-64

[20] Bai J, Sun Q, Zhai H. A comparison of oxytocin and carboprost tromethamine in the prevention of postpartum hemorrhage in high-risk patients undergoing cesarean delivery [J]. Exp Ther Med, 2014, 7(1): 46-50

[21] Milchev N, Amaliev G, Amaliev I, et al. The use of carboprost tromethamole for prevention and treatment of postpartal haemorrhage [J]. Akush Ginekol (Sofiia), 2011, 50(2): 6-10

[22] Habek JA, Habek D, Gulin D. Refractory baradycardia-a rare complication of carboprost tromethamine for induction of abortion [J]. Acta Clin Croat, 2016, 55(2): 323-325

[23] Butwick AJ, Walsh EM, Kuzniewicz M, et al. Patterns and predictors of severe postpartum anemia after Cesarean section [J]. Transfusion, 2017, 57(1): 36-44

（上接第 333 页）

[12] Xu Yue. Early functional rehabilitation nursing analysis of elderly patients with femoral neck fracture joint replacement surgery[J]. Dietary care, 2017, 4(8): 157-158

[13] Antoniou J, Epure LM, Huk OL, et al. Hospital Discharge within 2 Days Following Total Hip or Knee Arthroplasty Does Not Increase Major-Complication and Readmission Rates [J]. J Bone Joint Surg Am, 2016, 98(17): 1419-1428

[14] Huang Zhong-Lian, Qiu Kai-Feng, Chen Hong-Jiang, et al. Effect of hemi-shoulder arthroplasty on joint motion and prognosis in patients with proximal humeral fracture [J]. Modern diagnosis and treatment, 2016, 27(12): 2191-2192

[15] Ke Zhi-yong. Treatment of femoral neck fractures in the elderly using total hip arthroplasty and fracture internal fixation [J]. Chinese and foreign medical research, 2014, 12(9): 15-16

[16] Lee JH, Kweon HH, Choi JK, et al. Association between Periodontal disease and Prostate cancer: Results of a 12-year Longitudinal Cohort Study in South Korea[J]. J Cancer, 2017, 8(15): 2959-2965

[17] Chander RJ, Lim L, Handa S, et al. Atrial Fibrillation is Independently Associated with Cognitive Impairment after Ischemic Stroke [J]. J Alzheimers Dis, 2017, 60(3): 867-875

[18] Li Shun. Analysis of Risk Factors and Intervention Effect of Sputum after Total Hip Replacement in Elderly Patients [J]. Frontiers of medicine, 2017, 7(2): 28-29

[19] Zhao Yan-xian, Zhou Cui-ling. Analysis of the causes of cerebral infarction after joint replacement and preventive measures [J]. Chinese Orthopedic Journal, 2013, 21(20): 2118

[20] Su Guan, Liu Wen-qin, Lin Huan-huan, et al. Risk factors and nursing of secondary cerebral infarction after total hip arthroplasty [J]. Nurse Training Magazine, 2014, 29(14): 1289-1291

[21] Li Qing-min, Zhang Chun-yan. Perioperative Nursing Intervention in Elderly Patients with Total Hip Replacement [J]. Guangdong Medicine, 2013, 34(14): 2274-2276

[22] Zhang Juan. Nursing Care of Patients with Femoral Neck Fractures in Hip with Hip Arthroplasty[J]. Nursing practice and research, 2012, 09 (16): 69-70

PDF 文件使用 "pdfFactory Pro" 试用版本创建 www.fineprint.cn