

doi: 10.13241/j.cnki.pmb.2022.02.019

卡贝缩宫素联合 Bakri 球囊压迫对宫缩乏力性产后出血患者卵巢功能和凝血功能的影响*

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摘要 目的: 探讨卡贝缩宫素、Bakri 球囊压迫联合治疗对宫缩乏力性产后出血患者卵巢功能以及凝血功能的影响。**方法:** 选取 2017 年 2 月 -2021 年 3 月我院接诊治疗的 86 例宫缩乏力性产后出血患者,以随机数字表法分为对照组、研究组,分别给予 Bakri 球囊压迫单一治疗及卡贝缩宫素、Bakri 球囊压迫联合治疗。检测对比患者的卵巢功能指标包括 LH、FSH、E₂ 水平,记录两组患者舒张压(DBP)、收缩压(SBP)、心率、出血量变化和止血起效时间,测定纤维蛋白原(FIB)、凝血酶原时间(PT)和活化部分凝血活酶时间(APTT),对比两组不良反应发生情况。**结果:** 两组患者 DBP、SBP 及心率变化波动较小,治疗后数据显示差异无统计学意义($P>0.05$);两组患者治疗后 2 h、24 h 出血量减少,且研究组治疗后 2 h、24 h 出血量及止血起效时间短于对照组($P<0.05$);治疗后 3 d,两组患者 FIB 水平降低,PT、APTT 水平升高,且研究组 FIB 水平低于对照组,PT、APTT 水平高于对照组($P<0.05$);治疗后 3 d,两组患者血清 E₂ 水平升高,FSH、LH 水平降低,且研究组血清 E₂、FSH、LH 水平优于对照组($P<0.05$);研究组不良反应发生率(8.89%)高于对照组(4.88%),但是未见显著性差异($P>0.05$)。**结论:** 卡贝缩宫素联合 Bakri 球囊压迫可改善宫缩乏力性产后出血的卵巢功能及凝血功能,提升产后止血效果,增强患者子宫收缩能力。

关键词: 卡贝缩宫素;Bakri 球囊;宫缩乏力性产后出血;卵巢功能;凝血功能

中图分类号: R714.461 **文献标识码:** A **文章编号:** 1673-6273(2022)02-299-05

Effects of Carbetocin Combined with Bakri Balloon Compression on Ovarian Function and Coagulation Function in Patients with Uterine Asthenia Postpartum Hemorrhage*

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ABSTRACT Objective: To investigate the effects of carbetocin and Bakri balloon compression on ovarian function and coagulation function in patients with uterine asthenia postpartum hemorrhage. **Methods:** 86 patients with uterine asthenia postpartum hemorrhage who were treated in our hospital from February 2017 to March 2021 were selected, and they were randomly divided into control group and study group by random number table method. They were treated with Bakri balloon compression alone and carbetocin and Bakri balloon compression combined. Ovarian function indexes including luteinizing hormone (LH), follicle stimulating hormone (FSH) and estradiol (E₂) were detected and compared. The changes of diastolic blood pressure (DBP), systolic blood pressure (SBP), heart rate, bleeding volume and hemostasis onset time in two groups were recorded. Fibrinogen (FIB), prothrombin time (PT) and activated partial thromboplastin time (APTT) were measured, the adverse reactions of the two groups were compared. **Results:** The changes of DBP, SBP and heart rate in the two groups fluctuated little, and there was no significant difference after treatment ($P>0.05$). The bleeding volume at 2 h and 24 h after treatment in two groups decreased, and the bleeding volume and hemostasis onset time in the study group at 2 h and 24 h after treatment were shorter than those in the control group($P<0.05$). 3 d after treatment, the level of FIB in the two groups decreased, and the levels of PT and APTT increased, and the level of FIB in the study group was lower than that in the control group, and the levels of PT and APPT were higher than those in the control group($P<0.05$). 3 d after treatment, the levels of serum E₂ in the two groups increased, and the levels of FSH and LH decreased, and the levels of serum E₂, FSH and LH in the study group were better than those in the control group($P<0.05$). The incidence of adverse reactions in the study group(8.89%) was higher than that in the control group (4.88%), but there was no significant difference ($P>0.05$). **Conclusion:** The combined treatment of carbetocin and Bakri balloon compression can effectively improve the ovarian function and coagulation function of patients with uterine asthenia postpartum hemorrhage, improve the postpartum hemostasis effect, and enhance the uterine contractility of patients.

* 基金项目:江苏省卫生计生委科研项目(H2017065)

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(收稿日期:2021-06-25 接受日期:2021-07-21)

Key words: Carbetocin; Bakri balloon; Uterine asthenia postpartum hemorrhage; Ovarian function; Coagulation function

Chinese Library Classification(CLC): R714.461 **Document code:** A

Article ID: 1673-6273(2021)02-299-05

前言

产后出血是指产后阴道分娩 24 h 出血量超过 500 毫升,剖宫产术后 24 h 出血量超过 1000 毫升^[1]。产后出血一般发生在产后 2 h 以内,短时间内大量失血,严重的可迅速出现失血性休克,若救治不及时,可危及患者的生命安全^[2,3]。产后出血的救治原则是针对出血的原因,立即止血,补充血容量,以防失血性休克和感染^[4]。临床治疗宫缩乏力性产后出血的常用方法有应用宫缩剂、填塞宫腔等^[5,6]。Bakri 球囊压迫是临床常见止血方法,但治疗方法较单一、起效较慢,达不到预期效果^[8,9]。卡贝缩宫素是主要预防子宫收缩乏力和产后出血的药物,李慧敏^[10]等人的研究也证实了卡贝缩宫素对于宫缩乏力性产后出血的良好应用效果。基于此,本研究通过应用卡贝缩宫素、Bakri 球囊压迫联合治疗,分析其对宫缩乏力性产后出血患者卵巢功能和凝血功能的影响。

1 对象与方法

1.1 研究对象

以 2017 年 2 月 -2021 年 3 月我院接诊治疗的 86 例宫缩乏力性产后出血患者,根据随机数字表法分组:对照组 41 例,年龄 24-38 岁,平均年龄(31.0±5.6)岁,孕周 38-42 周,平均(40.0±0.6)周;研究组 45 例,年龄 27-39 岁,平均年龄(33.0±4.8)岁,孕周 38-41 周,平均(40.2±0.4)周。两组患者基本资料比较未见统计学差异($P>0.05$),具有可比性。纳入标准:符合宫缩乏力性产后出血相关诊断标准^[11];分娩 24 h 内,阴道分娩出血量>500 mL;剖宫产出血量>1000 mL。排除标准:有生殖系统性疾病者;患血液、内分泌、免疫系统性疾病者;对本研究使用药物过敏者;产前凝血功能障碍者。

1.2 方法

对照组患者待胎儿娩出后,常规给予缩宫素 10u 肌注,阴道分娩出血量超过 500 mL,剖宫产出血量超过 1000 mL 时,联合给予欣母沛(卡前列素氨丁三醇注射液,厂家:Pharmacia & Upjohn Company,批准文号:H20120388)及 Bakri 球囊压迫进行治疗;Bakri 子宫填塞球囊导管(厂家:青岛东方卫尔医疗科技有限公司,国械注进 20153774201),外阴阴道行常规消毒后,超声下清除宫腔积血、残留物等,将球囊送置入宫腔底部,固定导管,注入无菌生理盐水,待宫腔充盈球囊压住出血口且出血明显减少时,固定球囊,停止注射。根据子宫大小向球囊内注入无菌 0.9%NaCl 230-400 mL(<500 mL)。宫颈松弛的患者于阴道顶端填塞大纱布支撑球囊防止滑脱。剖宫产产术中植入球囊后关闭子宫切口,监测产妇的出血情况、生命体征并记录出血引流量,同时使用抗菌药物预防感染。球囊放置 16-24 h 抽出液体,该过程未出现出血,可将球囊置于 8-24 h 后取出。研究组在对照组的基础上给予卡贝缩宫素注射液(厂家:Draxis Specialty Pharmaceuticals Inc,国药准字:H20093500,规格:1 mL:100 μg)治疗,单次给予静脉推注剂量为 1 mL 卡贝缩宫素注射

液,注射过程要缓慢,持续时间在 1 min 左右。

1.3 观察指标

1.3.1 血压、心率相关指标、出血量和止血起效时间 观察两组患者治疗前后舒张压(DBP)、收缩压(SBP)和心率变化。观察并记录治疗前、治疗后 2 h、24 h 出血量和止血起效时间,分娩时将积血垫置于患者臀部,称重法计算出血量。

1.3.2 凝血功能相关指标检测 所有入院患者均采集次日清晨 6 点空腹静脉血 5 mL,高速离心机(常州市亿能实验仪器厂;型号:TG16G)离心 10 min(转速:3500 r/min,离心半径 8 cm),-30℃冰箱保存待测。采用日立全自动生化分析仪 7180 检测两组治疗前、治疗后 3 d 血清纤维蛋白原(FIB)、凝血酶原时间(PT)、活化部分凝血活酶时间(APTT)。相关检测试剂盒由长沙三行生物技术公司提供。

1.3.3 卵巢能相关指标测定 以 ELISA 法检测患者治疗前、后 3 d 促黄体生成素(LH)、卵泡刺激素(FSH)、雌二醇(E₂)水平变化。将血清标本从冰箱拿出室温放置 30 s,备置标准血清及溶液,配置 300 μL 洗板液洗板半分钟后倒出,并将微孔拍干。微孔里导入 50 μL 检测缓冲液,将 50 μL 标准液及样本和检测抗体放置微孔里,封板,1000 r/min 震荡,室温(37℃)孵育 2 h,洗板,将 100 μL 的酶标记物导入检测孔,封板,1000 r/min 震荡,恒温放置 45 min,洗板,将 100 μL 底物液加入微孔,温室遮光孵育 30 min,加入 100 μL 终止液,震荡均匀,酶标仪在 450 nm 处测其吸光值。

1.3.4 不良反应 记录患者治疗期间不良反应发生率。

1.4 统计学分析

以 SPSS26.0 分析数据,计量资料用($\bar{x} \pm s$)描述再行 t 检验。计数资料以%表示再行 χ^2 检验,检验水准 $\alpha=0.05$ 。

2 结果

2.1 血压及心率变化情况

如表 1 所示,两组患者血压及心率变化波动较小,治疗前、后差异无统计学意义($P>0.05$)。

2.2 两组不同时间出血量和止血起效时间比较

如表 2 所示,治疗前,两组出血量比较差异无统计学意义($P>0.05$);治疗后 2 h、24 h 出血量较治疗前减少,且研究组治疗后 2 h、24 h 出血量、止血起效时间短于对照组($P<0.05$)。

2.3 两组凝血功能指标变化

如表 3 所示,治疗后 3 d,两组患者 FIB 水平降低,PT、APPT 水平升高,且研究组 FIB 水平低于对照组,PT、APPT 水平高于对照组($P<0.05$)。

2.4 两组卵巢功能指标变化

如表 4 所示,治疗后 3 d,两组患者血清 E₂ 水平升高,FSH、LH 水平降低,且研究组血清 E₂、FSH、LH 水平优于对照组($P<0.05$)。

2.5 两组不良反应比较

如表 5 所示,治疗期间,研究组不良反应总发生率(8.89%)高于对照组(4.88%),但无明显差异($P>0.05$)。

表 1 两组血压及心率变化情况($\bar{x} \pm s$)

Table 1 Changes of blood pressure and heart rate in the two groups($\bar{x} \pm s$)

Groups	n	SBP(mmHg)		DBP(mmHg)		Heart rate(beats/min)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Control group	41	116.13± 11.63	116.89± 10.72	79.23± 8.36	78.73± 8.14	76.53± 5.16	75.34± 4.64
Study group	45	115.19± 11.68	117.86± 10.74	79.76± 8.17	77.84± 8.31	76.25± 5.03	75.18± 4.35
t		0.374	0.419	0.297	0.501	0.255	0.165
P		0.710	0.676	0.767	0.617	0.800	0.869

表 2 两组不同时间出血量及止血起效时间比较($\bar{x} \pm s$)

Table 2 Comparison of bleeding volume and hemostasis onset time between the two groups at different times($\bar{x} \pm s$)

Groups	n	Bleeding volume before	Bleeding volume 2 hours	Bleeding volume 24 hours	Hemostasis onset time
		treatment(mL)	after treatment(mL)	after treatment(mL)	(min)
Control group	41	629.63± 36.85	158.43± 15.88*	297.53± 33.46*	25.24± 6.76
Study group	45	630.29± 39.08	128.82± 13.56*	232.76± 26.87*	11.56± 3.14
t		0.080	9.323	9.938	12.210
P		0.936	<0.001	<0.001	<0.001

Note: compared with before treatment, *P<0.05.

表 3 治疗前后两组凝血功能指标变化($\bar{x} \pm s$)

Table 3 Changes of coagulation function indexes in the two groups before and after treatment($\bar{x} \pm s$)

Groups	n	FIB(g/L)		PT(s)		APPT(s)	
		Before treatment	3 d after treatment	Before treatment	3 d after treatment	Before treatment	3 d after treatment
Control group	41	3.73± 0.23	2.93± 0.28*	8.53± 0.86	10.86± 1.14*	19.52± 2.34	23.46± 3.91*
Study group	45	3.79± 0.28	1.52± 0.14*	8.56± 0.87	16.24± 1.71*	19.55± 2.38	28.95± 4.54*
t		1.080	29.930	0.161	16.990	0.059	5.981
P		0.283	<0.001	0.873	<0.001	0.953	<0.001

Note: compared with before treatment, *P<0.05.

表 4 治疗前后两组卵巢功能指标变化($\bar{x} \pm s$)

Table 4 Changes of ovarian function indexes in the two groups before and after treatment($\bar{x} \pm s$)

Groups	n	E ₂ (pmol/mL)		FSH(IU/L)		LH(IU/L)	
		Before treatment	3 d after treatment	Before treatment	3 d after treatment	Before treatment	3 d after treatment
Control group	41	18.53± 1.17	23.33± 3.1*5	5.07± 0.26	4.18± 0.46*	4.42± 0.84	3.76± 0.56*
Study group	45	18.61± 1.16	31.22± 4.1*7	5.06± 0.30	3.24± 0.21*	4.85± 0.83	2.63± 0.37*
t		0.318	9.826	0.164	12.370	2.386	11.130
P		0.751	<0.001	0.870	<0.001	0.019	<0.001

Note: compared with before treatment, *P<0.05.

表 5 不良反应比较[n(%)]

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

Groups	n	Facial flushing	Diarrhea	Abdominal pain	Nausea	Total incidence rate
Control group	41	1	0	0	1	2(4.88)
Study group	45	2	0	1	1	4(8.89)
χ^2						0.532
P						0.466

3 讨论

产后出血为产科分娩的并发症之一^[12],由于产后产程时间过长,产妇比较疲劳,容易形成子宫收缩乏力,引起产后出血^[13-15]。产后出血具有较严重的并发症,包括失血性贫血、垂体梗死、输血及其并发症^[16]。近年来,Bakri 球囊被证实明可有效控制产后出血,具有降低感染及隐匿性出血的特点^[17]。Bakri 球囊是一种新型宫腔止血技术,球囊结构可根据宫腔形状来调节整体大小,可塑性较强,可与宫腔创面紧密相贴、广泛压迫宫腔创面进而起到止血目的^[18,19]。但是随着应用的增多,单纯的 Bakri 球囊压迫治疗也存在疗效不足的现象,难以在短时间内缓解患者的宫缩乏力。卡贝缩宫素与普通缩宫素类似,具有持久性长、见效较快,不良反应较少等特点,可有效预防子宫收缩力不足和产后出血^[20]。

本研究显示两组患者治疗后 2 h、24 h 出血量减少,FIB 水平降低,PT、APPT 水平升高,且研究组的疗效更显著,止血起效时间缩短。FIB、PT、APPT 是临床诊断患者有无凝血功能异常的关键指标^[21,22]。相关研究中表明,APTT、PT、FIB 检测,可及时发现凝血异常,减少产后大出血的发生^[23]。本研究结果显示,卡贝缩宫素、Bakri 球囊压迫联合治疗凝血功能改善效果优于单一治疗,这是因为卡贝缩宫素注射液是一种新型的长效激素类治疗药物,对于预防和治疗患者剖宫产术后的张力不足以及产后出血有较好的治疗效果^[24]。卡贝缩宫素进入患者体内后能够特异性的作用于患者的子宫平滑肌,与相应的催产素受体紧密结合后,引起患者的子宫节律性收缩,进而可有效增强患者的子宫收缩力、收缩频率及子宫张力,同时收缩力的增强也可改善患者的凝血功能指标^[25]。

FSH 又称卵泡刺激素,是一种由机体的脑垂体合成分泌的具有多种功能的糖蛋白。在女性机体中,FSH 的主要作用是促进卵泡发育和成熟,并能与 LH 发挥协同作用,促使发育成熟的卵泡分泌雌激素和排卵,参与女性的生理周期的形成^[26]。FSH 合成分泌过程受到机体的下丘脑促性腺释放激素的调节控制,同时受卵巢 E₂ 水平的反馈调控。FSH、LH、E₂ 是鉴别诊断下丘脑、垂体或性腺功能障碍时的常用指标^[27]。治疗后患者 E₂ 水平升高,FSH、LH 水平降低,且卡贝缩宫素、Bakri 球囊压迫联合治疗的疗效明显优于单一治疗,提示卡贝缩宫素、Bakri 球囊压迫后止血效果显著提高,患者卵巢功能得到改善。卡贝缩宫素注射液可促进下丘脑中促性腺激素释放激素的表达,增强 E₂ 对子宫内膜的修复作用^[28]。卡贝缩宫素和 Bakri 球囊联合使用可有效改善产后子宫收缩能力,卡贝缩宫素可通过与子宫平滑肌的催产素受体特异性结合,引起子宫节律性的强效收缩;Bakri 球囊可显著减少出血,降低子宫损伤,操作简便、止血迅速^[29,30]。两者结合应用可起到互补互助的作用,不仅能有效止血,还可改善卵巢功能。两组患者血压及心率变化波动较小,治疗前、后差异无统计学意义,且两组患者治疗期间的不良反应发生率比较无差异,体现了该联合治疗方案有良好的安全性。

综上所述,卡贝缩宫素、Bakri 球囊压迫联合治疗方案可有效改善患者卵巢功能和凝血功能,显著控制产后出血,增强患者子宫收缩能力。本文研究亦存在样本纳入量较小、观察时间有限的不足,需进一步加大样本量深入研究。

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