左炔诺孕酮宫内节育系统与米非司酮治疗围绝经期功能失调性子宫出血的疗效和安全性比较

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中图分类号　R711　　**文献标志码**　A　　**文章编号**　1001-0408（2016）21-2901-03
DOI　10.6039/j.issn.1001-0408.2016.21.07

摘　要　目的：比较左炔诺孕酮宫内节育系统与米非司酮治疗围绝经期功能失调性子宫出血的疗效和安全性。方法：200例围绝经期功能失调性子宫出血患者随机分为观察组（100例）和对照组（100例）。观察组患者放置左炔诺孕酮宫内节育系统（含左炔诺孕酮52 mg），对照组患者口服米非司酮胶囊10 mg/d。两组疗程均为3个月。观察两组患者的临床疗效和治疗前后子宫内膜厚度、月经量[根据图示应用出血评分法（PBAC）评估]、血红蛋白水平及不良反应发生情况。结果：治疗后，观察组患者总有效率显著高于对照组，不良反应发生率显著低于对照组，差异均有统计学意义（$P<0.01$）。治疗前，两组患者子宫内膜厚度、PBAC评分、血红蛋白水平比较差异无统计学意义（$P>0.05$）；治疗后，两组患者子宫内膜厚度、PBAC评分显著低于同组治疗前，且观察组低于对照组，而血红蛋白水平显著高于同组治疗前，且观察组高于对照组，差异均有统计学意义（$P<0.01$或$P<0.05$）。结论：左炔诺孕酮宫内节育系统治疗围绝经期功能失调性子宫出血的疗效和安全性显著优于米非司酮。

关键词　左炔诺孕酮宫内节育系统；米非司酮；围绝经期；功能失调性子宫出血

Comparison of the Efficacy and Safety of Levonorgestrel Intrauterine System and Mifepristone in the Treatment of Perimenopausal Dysfunctional Uterine Bleeding

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ABSTRACT　OBJECTIVE：To compare the efficacy and safety of levonorgestrel intrauterine system and mifepristone in the treatment of perimenopausal dysfunctional uterine bleeding. METHODS：200 patients with perimenopausal dysfunctional uterine bleeding were randomly divided into observation group（100 cases）and control group（100 cases）. Patients in the observation group placed levonorgestrel intrauterine system（containing levonorgestrel 52 mg），patients in control group received Mifepristone capsule 10 mg/d，oral，the treatment course for 2 groups were 3 months. Clinical efficacy，endometrial thickness，menstruation（PBAC score），hemoglobin level before and after treatment and incidence of adverse reaction in 2 groups were observed. RESULTS：After treatment，the total effective rate in observation group was significantly higher than control group，incidence of adverse reactions was significantly lower than control group，the differences were statistically significant（$P<0.01$）. Before treatment，there were no significant differences in the endometrial thickness，PBAC score and hemoglobin level between 2 groups；after treatment，endometrial thickness and PBAC score were significantly lower than before，and observation group was lower than control group；hemoglobin level was significantly higher than before，and observation group was higher than control group，the differences were statistically significant（$P<0.01$ or $P<0.05$）. CONCLUSIONS：The efficacy and safety of levonorgestrel intrauterine system are significantly superior to mifepristone in the treatment of perimenopausal dysfunctional uterine bleeding.

KEYWORDS　Levonorgestrel intrauterine system；Mifepristone；Perimenopausal；Dysfunctional uterine bleeding

围绝经期功能失调性子宫出血在临床上简称“功血”，是发生在绝经前后一段时间的功能失调性子宫出血，是围绝经期妇女常见的一种生理变化[1]，主要表现为卵巢功能减退，发病机制是下丘脑-垂体-卵巢轴功能失调引起的无排卵。而无排卵可导致雌激素水平偏低，使子宫内膜腺体及血管处于持续增生状态而出现不规则的子宫内膜脱落。左炔诺孕酮宫内节育系统可通过药物局部作用于子宫内膜，从而有效地抑制排卵，达到局部避孕的目的，同时亦能够有效地抑制子宫内膜增生[2]。米非司酮在临床上主要用于药物流产，通过拮抗孕激素受体达到抗早孕的目的，目前其被广泛应用于治疗功能失调性子宫出血，效果较好。本研究对比分析了左炔诺孕酮宫内节育系统与米非司酮治疗围绝经期功能失调性子宫出血的疗效和安全性，旨在为临床提供参考。

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1　资料与方法

1.1　研究对象

选择2013年1月－2015年1月在我院治疗的200例围绝经期功能失调性子宫出血患者，月经周期在21 d以内，年龄为45～55岁。所有患者均符合围绝经期功能失调性子宫出血的诊断标准[1]。将所有患者按照随机数字表法分为观察组（100例）和对照组（100例）。两组患者年龄、发病时间、血红蛋白水平及子宫内膜厚度等基本资料比较，差异均无统计学意义（$P>0.05$），具有可比性，详见表1。本研究方案经医院医学伦理委员会审核通过，所有患者均签署了知情同意书。

1.2　纳入与排除标准

纳入标准：（1）月经量过多，月经周期规则，经期超过7 d或者经量超过80 ml；（2）不规则子宫出血，表现为周期不规则，月经量过多，或者月经期延长而月经量正常。排除标准：（1）对米非司酮和左炔诺孕酮过敏的患者；（2）避孕环脱落者；（3）

心、肝、肾功能不全者；(4)哮喘患者；(5)合并宫颈炎、子宫内膜炎或恶性肿瘤的患者；(6)因药物导致出血者。

表1　两组患者基本资料比较($\bar{x}\pm s$)

Tab 1　Comparison of basic data between 2 groups($\bar{x}\pm s$)

组别	n	年龄,岁	发病时间,年	血红蛋白水平,g/L	子宫内膜厚度,mm
观察组	100	47.7±3.6	5.1±3.1	81.57±15.85	13.24±4.05
对照组	100	48.2±3.4	5.0±3.6	83.22±14.36	13.53±3.98
t		−0.826	0.339	−0.635	−0.426
P		0.383	0.738	0.524	0.675

1.3　用药方法

观察组患者在进行诊断性刮宫术后放置左炔诺孕酮宫内节育系统(含左炔诺孕酮52 mg,拜耳医药保健有限公司广州分公司,批准文号:国药准字J20090144);对照组患者首先进行刮宫术,术后给予米非司酮胶囊(北京紫竹药业有限公司,规格:每粒5 mg,批准文号:国药准字H20050395)10 mg/d,口服。两组疗程均为3个月。

1.4　观察指标

观察两组患者治疗前后的子宫内膜厚度、血红蛋白水平,根据图示应用出血评分(PBAC)法评估患者月经量,同时记录治疗期间患者恶心、呕吐等不良反应发生情况。

1.5　疗效判定标准[3]

治愈:围绝经期功能失调性子宫出血患者在进行治疗后进入绝经期状态,或月经稀发,量明显减少;有效:月经期明显缩短,月经量明显减少;无效:治疗前后月经量及月经周期无变化。总有效率=(治愈例数+有效例数)/总例数×100%。

1.6　统计学方法

采用SPSS 13.0统计软件进行数据分析。计量资料以$\bar{x}\pm s$表示,采用t检验;计数资料以%表示,采用χ^2检验。$P<0.05$为差异有统计学意义。

2　结果

2.1　两组患者临床疗效比较

治疗后,观察组患者总有效率显著高于对照组,差异有统计学意义($P<0.01$),详见表2。

表2　两组患者临床疗效比较[例(%)]

Tab 2　Comparison of clinical efficacy between 2 groups[case(%)]

组别	n	治愈	有效	无效	总有效
观察组	100	85(85)	9(9)	6(6)	94(94)
对照组	100	56(56)	12(12)	32(32)	68(68)
χ^2		14.167	0.318	15.407	15.407
P		<0.01	0.573	<0.01	<0.01

2.2　两组患者治疗前后子宫内膜厚度、血红蛋白水平及PBAC评分比较

治疗前,两组患者子宫内膜厚度、血红蛋白水平及PBAC评分比较,差异无统计学意义($P>0.05$);治疗后,两组患者子宫内膜厚度、PBAC评分显著低于同组治疗前,且观察组低于对照组,而血红蛋白水平显著高于同组治疗前,且观察组高于对照组,差异均有统计学意义($P<0.01$或$P<0.05$),详见表3。

2.3　不良反应

观察组患者有3例乳房胀痛、3例下腹痛、3例恶心/呕吐,不良反应发生率为9%;对照组患者有9例头痛、12例下腹痛、9例恶心/呕吐、8例乳房胀痛,不良反应发生率为38%。观察组患者不良反应发生率显著低于对照组,差异有统计学意义($P<0.01$)。

3　讨论

表3　两组患者治疗前后子宫内膜厚度、血红蛋白水平及PBAC评分比较($\bar{x}\pm s$)

Tab 3　Comparison of endometrial thickness, hemoglobin level, PBAC score between 2 groups before and after treatment($\bar{x}\pm s$)

组别	n	时期	子宫内膜厚度,mm	血红蛋白水平,g/L	PBAC评分,分
观察组	100	治疗前	13.24±4.05	81.57±15.85	36.35±3.21
		治疗后	6.03±1.45$^{\#}$	123.56±3.53$^{\#}$	21.28±1.86$^{\triangle}$
对照组	100	治疗前	13.53±3.98	83.22±14.36	36.38±2.96
		治疗后	7.58±3.12$^{\#*}$	106.21±6.53$^{\#*}$	29.16±2.11$^{\#*}$

注:与治疗前比较,$^{\#}P<0.05$,$^{\triangle}P<0.01$;与观察组比较,$^{*}P<0.05$

Note: vs. before treatment, $^{\#}P<0.05$, $^{\triangle}P<0.01$; vs. observation group, $^{*}P<0.05$

功能失调性子宫出血临床上主要表现为不规律子宫出血、经期时间不等,由于出血量多、持续时间长,患者多伴有贫血症状,常有精神不佳、食欲不振、心慌等临床表现,部分患者还会出现乳房及下腹部胀痛不适[3]。米非司酮和左炔诺孕酮宫内节育系统是近年来临床应用最多的治疗围绝经期功能失调性子宫出血的方法,疗效均较好[4]。米非司酮是一种孕激素受体拮抗药,具有抗孕激素及糖皮质激素的作用[5],能够通过直接或间接的方式影响下丘脑-垂体-卵巢内分泌轴及子宫内膜,降低雌激素水平,阻滞子宫内膜发育[6]。左炔诺孕酮宫内节育系统主要成分为左炔诺孕酮,是一种具有抗雌激素活性的孕激素,可通过降低子宫内膜对雌激素的敏感性,转化子宫内膜,从而有效减少月经量[7]。

相关研究表明,左炔诺孕酮宫内节育系统治疗围绝经期功能失调性子宫出血,可以显著减少患者月经量及子宫内膜厚度,升高患者血红蛋白水平,疗效显著优于米非司酮,且不良反应发生率显著低于米非司酮。提示米非司酮对子宫内膜血管的抑制作用相对较小,内膜转化不够彻底,治疗效果欠佳而不良反应发生率较高[8]。

本研究结果显示,治疗后观察组患者总有效率显著高于对照组,不良反应发生率显著低于对照组,差异均有统计学意义。治疗前,两组患者子宫内膜厚度、PBAC评分、血红蛋白水平比较差异无统计学意义;治疗后,两组患者子宫内膜厚度、PBAC评分显著低于同组治疗前,且观察组低于对照组,而血红蛋白水平显著高于同组治疗前,且观察组高于对照组,差异均有统计学意义。

综上所述,左炔诺孕酮宫内节育系统治疗围绝经期功能失调性子宫出血的疗效和安全性显著优于米非司酮。由于本研究样本量较小,观察时间较短,此结论有待更多设计严格、长期随访的大样本临床研究加以验证。

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SOX方案与改良mFOLFOX6方案治疗弥散型进展期胃癌的疗效和安全性比较

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中图分类号 R735.2 **文献标志码** A **文章编号** 1001-0408(2016)21-2903-04
DOI 10.6039/j.issn.1001-0408.2016.21.08

摘 要 目的:比较替吉奥联合奥沙利铂(SOX方案)与5-氟尿嘧啶(5-FU)、左亚叶酸钙联合奥沙利铂(改良mFOLFOX6方案)治疗弥散型进展期胃癌的疗效和安全性。方法:回顾性收集128例弥散型进展期胃癌患者资料,按用药方案不同将所有患者分为SOX组(66例)和mFOLFOX6组(62例)。SOX组患者给予替吉奥胶囊,体表面积<1.25 m^2为40 mg,1.25~1.5 m^2为50 mg,>1.5 m^2为60 mg,早晚餐后口服,d_{1-14}+注射用奥沙利铂130 mg/m^2,静脉滴注,d_1;3周为1个周期,每2个周期评价疗效,最多治疗8个周期,至少治疗2个周期。mFOLFOX6组患者给予注射用奥沙利铂85 mg/m^2,静脉滴注,d_1+注射用左亚叶酸钙200 mg/m^2,静脉滴注,d_1+注射用5-FU 400 mg/m^2,快速静推,d_1,后给予5-FU 2 400 mg/m^2,持续泵入维持46 h;2周为1个周期,每3个周期评价疗效,最多治疗12个周期,至少治疗3个周期。观察两组患者的临床疗效,疾病进展时间、生存时间及毒副反应发生情况。结果:SOX组患者客观有效率、中位疾病进展时间、中位生存时间均显著优于mFOLFOX6组,差异均有统计学意义(P<0.05或P<0.01)。两组患者疾病控制率、毒副反应发生率比较,差异均无统计学意义(P>0.05)。结论:SOX方案治疗弥散型进展期胃癌的疗效优于改良mFOLFOX6方案,可延长患者生存时间,且安全性相似。

关键词 弥散型进展期胃癌;替吉奥;奥沙利铂;5-氟尿嘧啶;左亚叶酸钙;疗效;安全性

Comparison of Efficacy and Safety of Gio Combined with Oxaliplatin versus Fluorouracil Combined with Calcium Folinate and Oxaliplatin in the Treatment of Diffuse Advanced Gastric Cancer

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ABSTRACT OBJECTIVE: To compare the efficacy and safety of gio combined with oxaliplatin (SOX) versus 5-fluorouracil (5-FU) combined with calcium folinate and oxaliplatin (mFOLFOX6) in the treatment of diffuse advanced gastric cancer. METHODS: The data of 128 patients with diffuse advanced gastric cancer was retrospectively analyzed and patients were divided into SOX group (66 cases) and mFOLFOX6 group (62 cases) by different medication. SOX group received Gio capsule after breakfast and dinner, which was <1.25 m^2, 40 mg, 1.25-1.5 m^2, 50 mg, >1.5 m^2, 60 mg, d_{1-14}+130 mg/m^2 Oxaliplatin for injection, intravenously, d_1; 3-week was regarded as a treatment course, the efficacy was evaluated every 2 courses, and it lasted a maximum of 8 courses but a minimum of 2 courses. mFOLFOX6 group received 85 mg/m^2 Oxaliplatin for injection, intravenously, d_1+200 mg/m^2 calcium folinate, intravenously, d_1+400 mg/m^2 5-FU for injection by rapid intravenous injection, d_1, then 2 400 mg/m^2 5-FU, maintaining 46 h by continuous infusion. 2-week was regarded as a treatment course, the efficacy was evaluated every 3 courses, and chemotherapy was conducted in a maximum of 12 courses but a minimum of 3 courses. Clinical efficacy, time to progression, survival time and incidence of toxicities in 2 groups were observed. RESULTS: The objective response rate, time to progression and median survival time in SOX group was significantly higher than mFOLFOX6 group, the difference was statistically significant (P<0.05 or P<0.01). There was no significant difference in the disease control rate and incidence of toxicities in 2 groups (P>0.05). CONCLUSIONS: The efficacy of SOX is superior to mFOLFOX6 in the treatment of diffuse advanced gastric cancer, it can prolong the survival time, with similar safety.

KEYWORDS Diffuse advanced gastric cancer; Gio; Oxaliplatin; 5-fluorouracil; Calcium folinate; Efficacy; Safety

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(收稿日期:2015-12-28 修回日期:2016-05-16)
(编辑:申琳琳)

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