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麦角新碱联合米索前列醇治疗前置胎盘的临床疗效 及对血清 ROS、SOD、GSH-px 水平的影响 *

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摘要 目的: 分析麦角新碱联合米索前列醇治疗前置胎盘的临床疗效及对血清活性氧(ROS)、超氧化物歧化酶(SOD)、谷胱甘肽过氧化物酶(GSH-px)水平的影响。**方法:** 选择 2016 年 5 月-2017 年 5 月我院收治的前置胎盘患者 100 例纳入本次研究,根据随机分组法分为观察组(n=52)和对照组(n=48)。对照组使用米索前列醇治疗,观察组采用麦角新碱联合米索前列醇进行治疗。比较两组患者的临床疗效、治疗前后血清 ROS、SOD、GSH-px 水平的变化、术中、术后出血量、止血时间及不良反应的发生情况。**结果:** 治疗后,两组患者的总有效率分别为 96.15%、81.25%,观察组显著高于对照组($P<0.05$);两组患者血清 ROS、SOD、GSH-px 水平均较治疗前显著改善,且观察组患者血清 ROS 低于对照组,血清 SOD、GSH-px 水平显著高于对照组($P<0.05$);观察组患者术中、术后出血量及止血时间均显著低于对照组($P<0.05$);两组患者不良反应总发生率分别为 7.69%、22.92%,观察组显著低于对照组($P>0.05$)。**结论:** 麦角新碱联合米索前列醇治疗前置胎盘的疗效和安全性均显著优于单用米索前列醇治疗,可能与其有效改善血清 ROS、SOD、GSH-px 水平有关。

关键词: 麦角新碱;米索前列醇;前置胎盘;活性氧;超氧化物歧化酶;谷胱甘肽过氧化物酶

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Curative Efficacy of Ergosine Plus Misoprostol in the Treatment of Placenta Previa and Its Effects on the Serum ROS, SOD and GSH-px Levels*

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ABSTRACT Objective: To study the curative efficacy of Ergosine plus misoprostol in the treatment of Placenta previa and its effects on the serum Reactive oxygen species (ROS), superoxide dismutase (SOD), glutathione peroxidase (gsh-px) levels. **Methods:** 100 cases of placenta previa patients admitted to our hospital from May 2016 to May 2017 were selected and divided into the observation group (n=52) and the control group (n=48) according to the random grouping method. The control group was treated with misoprostol, while the observation group was treated with ergoxin combined with misoprostol. The clinical efficacy, changes of serum ROS, SOD and GSH-px levels before and after treatment, intraoperative and postoperative blood loss, hemostasis time and incidence of adverse reactions were compared between the two groups. **Results:** After treatment, the total effective rates of observation group and control group were 96.15% and 81.25%, respectively, which was significantly higher in the observation group than that of the control group ($P<0.05$). The levels of serum ROS, SOD and GSH-px in the two groups were significantly improved compared with those before treatment, and the levels of serum ROS in the observation group were lower than those in the control group, the levels of serum SOD and gsh-px were significantly higher than those in the control group ($P<0.05$). The intraoperative and postoperative blood loss and hemostasis time in the observation group were significantly lower than those in the control group ($P<0.05$). The total incidence of adverse reactions in the two groups was 7.69% and 22.92%, respectively, which was significantly lower in the observation group than that of the control group ($P>0.05$). **Conclusion:** The efficacy and safety of ergoxin combined with misoprostol in the treatment of placenta previa are significantly better than those of misoprostol alone, which may be related to the effective improvement of serum ROS, SOD and GSH-px levels.

Key words: Ergosine; Misoprostol; Placenta previa; Reactive oxygen species; Superoxide dismutase; Glutathione peroxidase

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前言

前置胎盘是妊娠期的严重并发症,多见于经产妇,是导致分娩期出血的主要原因之一,有较大的风险性^[1,2]。前置胎盘是

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指正常妊娠胎盘附着于子宫体部的前后,妊娠 28 周后胎盘则附于子宫下段或覆盖宫颈内口,位置低于胎先露部,若处理不当,将会严重威胁母婴的生命安全^[34]。近年来,随着产妇产育年龄的增高、剖宫产率逐渐上升,前置胎盘的发生率也逐年上升,研究显示国内前置胎盘的发生率为 0.23~1.56%^[56]。

米索前列醇为前列腺素 E1 衍生物,可软化宫颈,同时增强子宫张力和宫内压的作用,但是其对患者产后出血的效果并不明显^[78]。麦角新碱又称 D- 麦角酸β- 氨基丙醇,是从黑麦麦角菌制成,对子宫平滑肌有高度选择性,能够直接作用于子宫平滑肌,且作用强而持久^[9,10]。本研究主要探讨了麦角新碱联合米索前列醇治疗前置胎盘的临床疗效,并观察其对血清 ROS、SOD、GSH-px 的影响,现报告如下。

1 资料与方法

1.1 一般资料

选择 2016 年 5 月 -2017 年 5 月我院收治的前置胎盘患者 100 例进行研究,研究获得伦理委员会批准实施。通过随机数表法将所有患者分为 2 组,观察组 52 例;年龄 21~45 岁,平均(30.76± 5.31)岁,孕周 38~40 周,平均(39.19± 1.31)周。对照组 48 例;年龄 22~46 岁,平均(31.13± 5.45)岁,孕周 38~41 周,平均(39.30± 1.41)。两组患者一般资料比较差异无统计学意义($P>0.05$),具有可比性。

纳入标准^[11]:(1)符合《凶险型前置胎盘的诊断及处理》诊断标准;(2)无妊娠期高血压;(3)无长期服用影响检测结果的药物。排除标准:(1)脏器性疾病;(2)严重肺部及心脏病变者;(3)血

液感染性疾病。

1.2 治疗方法

对照组患者使用米索前列醇(规格 0.2 mg,厂家:湖北葛店人福药业有限责任公司,国药准字:H20130668)腹腔打开时舌下含服 200 μg。观察组在对照组的基础上给予麦角新碱(规格 1 mL:0.2 mg,厂家:成都倍特药业有限公司,国药准字:H20140728)0.2 mg 宫体注射,注射时间≥ 1 min。

1.3 观察指标

采集患者 5 mL 空腹静脉血,抗凝后,以 3000 r·min⁻¹ 的速度进行离心,时间 10 min,提取上层血清后,置于零下 20℃ 的冷冻箱内存储以备检测,血清 ROS、SOD、GSH-px 的测定采用双抗体夹心酶联免疫吸附法(ELISA);观察记录两组患者术中、术后出血量、止血时间及不良反应的发生情况。

疗效评定标准:显效:阴道失血量小于 50 mL;有效:治疗后 60 min,阴道失血量大于 100 mL;无效:阴道失血量大于 300 mL。显效 + 有效 = 总有效率。

1.4 统计学分析

以 SPSS18.0 软件包处理数据,计量资料用均数± 标准差($\bar{x} \pm s$)表示,均为正态分布,组间比较使用独立样本 t 检验,计数资料以率表示, χ^2 检验,以 $P<0.05$ 表示差异具有统计学意义。

2 结果

2.1 两组疗效的比较

治疗后,两组患者的总有效率分别为 96.15%、81.25%,观察组显著高于对照组($P<0.05$),见表 1。

表 1 两组疗效比较[例(%)]

Table 1 Comparison of the efficacy between two groups[n(%)]

Groups	n	Effective	Valid	Invalid	Total effective rate
Observation group	52	39(75.00)	11(21.15)	2(3.85)	50(96.15)
Control group	48	23(47.92)	16(33.33)	9(18.75)	39(81.25)
χ^2 value					5.663
P value					0.014

2.2 两组患者治疗前后血清 ROS、SOD、GSH-px 水平的比较

治疗前,两组患者血清 ROS、SOD、GSH-px 水平比较无显著性差异;治疗后,两组患者血清 ROS、SOD、GSH-px 水平均

较治疗前显著改善,且观察组患者血清 ROS 低于对照组,血清 SOD、GSH-px 水平显著高于对照组($P<0.05$),见表 2。

表 2 两组患者治疗前后血清 ROS、SOD、GSH-px 水平比较($\bar{x} \pm s$)

Table 2 Comparison of the serum ROS, SOD and gsh-px levels between the two groups before and after treatment($\bar{x} \pm s$)

Groups	n	ROS(μmol/L)		SOD(U/L)		GSH-px(nmol/L)	
		Before the treatment	After treatment	Before the treatment	After treatment	Before the treatment	After treatment
Observation group	52	8.92± 0.96	4.25± 0.54	231.29± 27.86	427.56± 52.74	273.62± 27.84	453.61± 50.14
Control group	48	8.94± 0.97	7.04± 0.81	231.35± 27.89	320.62± 23.53	274.01± 27.93	362.37± 40.17
t value		0.104	20.410	0.011	12.909	0.070	9.990
P value		0.918	0.000	0.991	0.000	0.944	0.000

2.3 两组患者术中、术后出血量及止血时间比较

观察组患者术中、术后出血量及止血时间均显著低于对照

组($P<0.05$),见表 3。

表 3 两组患者术中及术后出血量比较($\bar{x} \pm s$)

Table 3 Comparison of the intraoperative and postoperative blood loss between the two groups($\bar{x} \pm s$)

Groups	n	The bleeding(mL)		The bleeding time(min)
		Intraoperation	Postoperation	
Observation group	52	135.31± 14.36	69.41± 6.59	13.24± 3.05
Control group	48	251.96± 22.71	186.34± 13.42	26.21± 4.27
t value		30.946	55.961	17.580
P value		0.000	0.000	0.000

2.4 两组患者不良反应发生情况比较

组显著低于对照组,差异具有统计学意义($P>0.05$),见表 4。

两组患者不良反应总发生率分别为 7.69%、22.92%, 观察

表 4 两组患者不良反应发生情况的比较[例(%)]

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

Groups	n	Vomiting	Nausea	Chest tightness	Heart palpitations	Have a headache	The total incidence of
Observation group	52	1	1	0	1	1	4(7.69)
Control group	48	2	3	2	1	3	11(22.92)
χ^2 value							4.538
P value							0.033

3 讨论

前置胎盘通常是指妊娠 28 周后附着于子宫下段的胎盘,胎盘下缘到达或覆盖宫颈内口,低于胎儿暴露部位^[12,13],主要表现为反复的无痛性阴道流血,其发病原因尚不明确。Saleh G S^[14]等研究认为多次分娩、剖宫产、人工流产等因素是前置胎盘的高危因素。多次分娩会损伤子宫内膜,引起子宫内膜炎症或退行性改变,并在第二次妊娠期间导致血液供应不足。为了增加胎儿摄取足够的营养,胎盘区向下延伸至子宫下段形成前置胎盘,严重威胁产妇及胎儿的生命安全^[15,16]。

米索前列醇是临床上治疗前置胎盘的常用药物,是前列腺素 E1 衍生物,具有强大的抑制胃酸分泌的作用,可软化宫颈、增强子宫张力和宫内压,但是其效果并不特别显著,故较多学者提出在此基础上联合治疗以提高其临床疗效^[17,18]。麦角新碱是一种强有力的血管收缩剂,1932 年被发现,是历史上最早使用的子宫收缩药,对子宫平滑肌有高度选择性,对子宫体、子宫颈也有很强的收缩作用,其作用的强弱与子宫的生理状态和用药剂量有关^[19,21]。Mauritz A A^[21]等研究表明麦角新碱治疗前置胎盘有较好的疗效,是治疗产后出血的理想药物。

本研究结果显示联合麦角新碱治疗的患者的临床总有效率高达 96.15%,明显高于单独使用米索前列醇治疗的患者,且不良反应发生率为 7.69%,明显低于单独使用米索前列醇治疗的患者,与 Zhu Y^[22]研究结果相似。以上结果提示联合治疗安全有效,能明显提高患者的临床疗效。Kim J W^[23]研究结果表明麦角新碱治疗前置胎盘能有效降低患者的出血量。本研究结果也显示联合治疗的患者术中、术后出血量及止血时间均显著低于单独使用米索前列醇治疗的患者,与上述观点基本一致。分析原因是因为米索前列醇具有宫颈软化、增强子宫张力及宫内压

作用。麦角新碱则是一种半合成生物碱,在刺激子宫肌纤维的同时对血管产生的兴奋物,且其对子宫肌的收缩作用强于缩宫素几倍,能使胎盘种植处子宫肌内血管受到压迫而起到止血的效果,两组药物联合治疗从而降低其术后出血量。

ROS 是体内一类氧的单电子还原产物,是指机体内或者自然环境中由氧组成,化学反应活性强、寿命短^[24,25]。SOD 是一种从生命中提取的活性物质,能消除代谢过程中产生的有害物质,具有抗衰老的特殊效果^[26,27]。GSH-px 是机体内广泛存在的一种重要的过氧化物分解酶,其活力大小可以反映机体硒水平^[28,29]。本研究结果显示联合麦角新碱治疗的患者的血清 ROS 低于,血清 SOD、GSH-px 水平显著高于单独治疗的患者,与 Nonaka T^[30]研究结果相似。分析是因为米索前列醇药物药性温和,具有前列腺素的作用,可软化宫颈、增强子宫张力和宫内压,能够增加妊娠子宫自发收缩的频率和幅度,影响子宫血液循环;而麦角新碱直接作用于子宫平滑肌,同时对子宫底和子宫颈颈部有较强的收缩作用,增强机体机能,缓解产后出血患者的氧化应激反应,两种药物联合治疗,以增强患者机体免疫力,清除机体自由基,改善患者的 ROS、SOD、GSH-px 水平,最终起到抗氧化的作用。

综上所述,麦角新碱联合米索前列醇治疗前置胎盘的疗效和安全性均显著优于单用米索前列醇治疗,可能与其有效改善血清 ROS、SOD、GSH-px 水平有关。

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