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实验研究

Emx2和Emx2OS在小鼠胚胎生殖嵴中的表达……………周吉 沈聪 霍然 (437)

GRIM-19在胚胎停育患者绒毛组织中表达及其作用机制的研究……………
……………陈红蕾 邓晓惠 晁岚,等 (444)

子痫前期患者胎盘组织中降钙素受体刺激肽-3(CRSP-3)的表达及意义……………
……………周佳任 王春晖 张丹丹,等 (451)

白介素β1及凝血酶降低孕早期蜕膜细胞同源框A10基因的表达……………
……………刘雪梅 丛建香 郝翠芳 (456)

临床研究

黄体期促排卵方案在卵巢低反应患者中的初步研究……………
……………唐奕 张红 罗克莉,等 (462)

卵巢子宫内膜异位癌恶变预测方法研究……………肖喜荣 李斌 孙莉 (467)

复发性流产患者子宫动脉血流的超声多普勒变化……………
……………王磊 洪向丽 鲍时华,等 (471)

宫腔填塞联合米索前列醇预防高危因素剖宫产后出血的临床疗效观察……………
……………赵建珍 虞婉亚 (477)

综 述

子宫内膜干细胞在内膜再生方面的研究进展……………胡春敬 刘建华 (483)

辅助生殖技术与DNA甲基化……………池丰丽 童国庆 段涛 (489)

抗苗勒管激素影响因素的研究进展……………张颖 刘丽丽 (493)

表皮生长因子样因子在LH峰效应中的作用及临床研究进展……………
……………王光演 牛志宏 冯云 (497)

临床报道

硫氧还蛋白和硫氧还蛋白结合蛋白-2在子宫内膜异位症的表达及意义……………
……………周晓梅 张海 方锦川,等 (501)

米非司酮药物流产后绒毛蜕膜细胞凋亡的相关研究……………
……………施晓华 钱小泉 张品南,等 (506)

基质细胞衍生因子-1(SDF-1)表达与复发性流产的关系……………
……………徐健荧 杨桂艳 刘彦,等 (511)

卵巢子宫内膜异位囊肿合并不孕患者术后治疗探讨……………
……………付改玲 黄鹏翀 周晓亮 (515)

输卵管阻塞性不孕症宫、腹腔镜术后治疗方法的探讨……………
……………杨宝华 周贤梅 徐军 (519)

专家风采

……………(封二)

特邀编委名单

……………(封三)



Contents

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LABORATORY STUDY

- Profiling the expression of Emx2 and LncRNA-Emx2OS in mouse gonads.....
.....*Ji ZHOU, Cong SHEN, Ran HUO* (437)
- Expression and mechanism of action of GRIM-19 in the villus of missed abortion.....
.....*Hong-lei CHEN, Xiao-hui DENG, Lan CHAO, et al.* (444)
- Expression and clinical roles of calcitonin receptor stimulating peptide-3 in placenta
with preeclampsia*Jia-ren ZHOU, Chun-hui WANG, Dan-dan ZHANG, et al.* (451)
- Interleukin-β1 and thrombin decrease HOXA10 gene expression in human first
trimester decidual cells.....*Xue-mei LIU, Jian-xiang CONG, Cui-fang HAO* (456)

CLINICAL STUDY

- A preliminary study of control ovary hyperstimulation on luteal phase in patients with
poor ovarian response.....*Yi TANG, Hong ZHANG, Ke-li LUO, et al.* (462)
- Study on the prediction of neoplasias arising in endometriosis.....
.....*Xi-rong XIAO, Bin LI, Li SUN* (467)
- Doppler assessment of uterine blood flow in recurrent spontaneous abortions.....
.....*Lei WANG, Xiang-li HONG, Shi-hua BAO, et al.* (471)
- Clinical curative observation on the effect of gauze packing combined with misoprostol
preventing postpartum hemorrhage of high-risk in cesarean section.....
.....*Jian-zhen ZHAO, Wan-ya YU* (477)

REVIEW

- Current outlook of roles of endometrial stem cells in endometrial regeneration.....
.....*Chun-jing HU, Jian-hua LIU* (483)
- Assisted reproductive technology and DNA methylation.....
.....*Feng-li CHI, Guo-qing TONG, Tao DUAN* (489)
- Progress of anti-Müllerian hormone influencing factors*Ying ZHANG, Li-li LIU* (493)
- Role of EGF-like factors in LH surge effect and its clinical research progress.....
.....*Guang-yan WANG, Zhi-hong NIU, Yun FENG* (497)

CLINICAL REPORT

- Expression and significance of thioredoxin and Trx-binding protein-2 in patients with
endometriosis (EMs).....*Xiao-mei ZHOU, Hai ZHANG, Jin-chuan FANG, et al.* (501)
- Apoptosis and expression of related genes in early pregnant chorionic villi and decidua
.....*Xiao-hua SHI, Xiao-quan QIAN, Pin-nan ZHANG, et al.* (506)
- Relationship between the expression of stromal cell-derived factor 1 (SDF-1) and
recurrent spontaneous abortions..... *Jian-ying XU, Gui-yan YANG, Yan LIU, et al.* (511)
- Treatment of endometriosis associated with infertility patients
.....*Gai-ling FU, Peng-chong HUANG, Xiao-liang ZHOU* (515)
- Discussion about the follow-up treatment on salpinx obstructive infertility postoperation
of hysteroscopy combined laparoscopy.....
.....*Bao-hua YANG, Xian-mei ZHOU, Jun XU* (519)

• 实验研究 •

Emx2和Emx2OS在小鼠胚胎生殖嵴中的表达

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【摘要】目的: 探讨转录因子Emx2和Emx2反义非编码长链RNA(EMX2 opposite strand/antisense RNA, Emx2OS)在小鼠生殖嵴发育过程中的表达模式以及对原始生殖细胞发育的作用。方法: 分别收集孕11.5~14.5 d小鼠的生殖嵴, 通过原位杂交、qRT-PCR和免疫荧光方法, 观察分析Emx2和Emx2OS在生殖嵴中的表达定位及其表达水平的变化。结果: 在孕11.5~14.5 d雌性和雄性小鼠胚胎生殖嵴中均检测到Emx2OS的表达, 而且其表达模式与Emx2高度一致; 在小鼠胚胎原始生殖细胞减数分裂的启动以及性别决定的时间点(孕12.5 d), 雌性胎小鼠生殖嵴中Emx2和Emx2OS的表达量都显著上调($P < 0.001$)。结论: Emx2和Emx2OS在胎小鼠生殖嵴中呈同步表达模式, 并可能参与调控原始生殖细胞减数分裂的启动。

关键词: Emx2; Emx2OS; 生殖嵴; 减数分裂

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Profiling the Expression of Emx2 and LncRNA-Emx2OS in Mouse Gonads

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【ABSTRACT】Objective: To study the expression patterns of Emx2 and Emx2OS in female or male mouse gonads. **Methods:** Mouse gonads from 11.5 d to 14.5 d were collected. *In situ* hybridization and qRT-PCR were used to detected the localization and expression trend of Emx2OS. **Results:** Emx2OS was expressed in the female or male mouse gonads. In addition, Emx2 and Emx2OS transcripts showed remarkable concordance at each stage (from 11.5 d to 14.5 d) in both female and male gonads. At the stage of meiosis entry and the sex determination (12.5 d), the expression of Emx2 and Emx2OS was increased obviously in female gonads ($P<0.001$). **Conclusions:** Emx2 and Emx2OS show a synchronous expression pattern in mouse gonads and may play an important role in meiosis starting regulation.

Key words: Emx2; Emx2OS; gonads; meiosis

GRIM-19在胚胎停育患者绒毛组织中表达及其作用机制的研究

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【摘要】目的: 探讨干扰素/维甲酸联合应用诱导细胞凋亡相关基因(gene associated with retinoid-interferon-induced mortality-19, GRIM-19)与胚胎停育的关系及作用机制。方法: 选择50例胚胎停育患者为实验组, 50例非意愿妊娠要求行人工流产的正常早孕患者为对照组。用免疫组织化学法对绒毛组织中GRIM-19进行定位检测; 采用Western blotting和Real-time PCR检测绒毛组织中GRIM-19蛋白和mRNA水平。应用荧光探针JC-1测定绒毛细胞线粒体跨膜电位, AnnexinV/PI双染色法检测细胞凋亡率。采用GRIM-19-siRNA转染技术使HTR-8/SVneo细胞低表达GRIM-19, 并测定转染后细胞线粒体跨膜电位与细胞凋亡率。结果: GRIM-19在所有患者绒毛中均有不同程度的表达, 与对照组相比, 实验组绒毛中GRIM-19蛋白和mRNA的表达量降低, 差异有统计学意义($P < 0.01$)。实验组绒毛细胞线粒体膜电位较对照组降低, 细胞凋亡率显著升高, 差异有统计学意义($P < 0.05$)。转染后HTR-8/SVneo细胞线粒体膜电位明显降低、细胞凋亡率升高, 较转染前均有统计学差异($P < 0.05$), 且线粒体膜电位与细胞凋亡率之间存在着明显的负相关性($r = -0.754, P < 0.01$)。结论: GRIM-19在早期妊娠中起重要作用, 而GRIM-19的低表达可能通过影响线粒体功能, 增加细胞凋亡参与了胚胎停育的发生、发展。

关键词: 干扰素/维甲酸联合应用诱导细胞凋亡相关基因(GRIM-19); 胚胎停育; 线粒体膜电位; 细胞凋亡

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Expression and Mechanism of Action of GRIM-19 in the Villus of Missed Abortion

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【ABSTRACT】 Objective: To explore gene associated with retinoid-interferon-induced mortality-19 (GRIM-19) role on missed abortion. **Methods:** Fifty pregnant women diagnosed with first-trimester missed abortion (experimental group), and 50 women in unplanned healthy pregnancy (control group) were involved this study. Immunohistochemistry was used to assess the GRIM-19 location in the trophoblast, Western blotting and real-time PCR were used to analyse levels of GRIM-19 protein and mRNA in villous samples. JC-1 and AnnexinV/PI were used to measure the mitochondrial membrane potential ($\Delta\Psi$) and apoptotic changes of the chorionic villus cells and HTR-8/SVneo cell line response to GRIM-19 knockdown by siRNA *in vitro* study. **Results:** GRIM-19 was expressed in cytoplasm of the two groups' villi, and the protein and mRNA level in missed abortion were both significantly lower than those in normal pregnancies ($P<0.01$). The chorionic villus cells of missed abortion had depressed mitochondrial membrane potential ($\Delta\Psi$) and increased apoptosis; after transfection, the $\Delta\Psi$ of HTR-8/SVneo cells significantly reduced, the apoptosis rate significantly increased, they were significantly different from those before transfection ($P<0.05$), and the increased percentage of low $\Delta\Psi$ with JC-1 showed a significant negative correlation with a simultaneous increase apoptotic cells ($r=-0.754$, $P<0.01$). **Conclusion:** GRIM-19 is essential for early pregnancy development, and GRIM-19 deficiency in the villi may be associated with missed abortion via influencing mitochondria and increasing apoptosis.

Key words: gene associated with retinoid-interferon-induced mortality-19 (GRIM-19); missed abortion; mitochondrial membrane potential; apoptosis

子痫前期患者胎盘组织中降钙素受体刺激肽-3 (CRSP-3)的表达及意义

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【摘要】 目的: 研究子痫前期患者胎盘组织中降钙素受体刺激肽-3(CRSP-3)的表达与正常妊娠者之间的差异及其临床意义。方法: 采用免疫组织化学方法检测住院分娩的50例子痫前期患者(子痫前期组: 轻度子痫前期25例, 重度子痫前期25例)和30例正常晚期妊娠孕妇(对照组)胎盘组织中CRSP-3的表达定位, Real-time PCR及Western blotting方法检测胎盘组织中CRSP-3mRNA和蛋白的表达。结果: 子痫前期和正常妊娠者胎盘组织细胞滋养细胞和合体滋养细胞中均表达CRSP-3。子痫前期患者胎盘组织中CRSP-3mRNA及其蛋白表达水平均高于正常妊娠组(P 均 <0.05)。其中重度子痫前期患者胎盘组织中CRSP-3mRNA和蛋白表达水平显著高于正常对照组(P 均 <0.01), 虽重度子痫前期胎盘组织中CRSP-3表达略高于轻度子痫前期, 但组间无统计学差异(P 均 >0.05)。结论: CRSP-3上调可能参与子痫前期的发病, 但是与疾病的进展及严重程度无关。

关键词: 降钙素受体刺激肽-3(CRSP-3); 胎盘; 子痫前期

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Expression and Clinical Roles of Calcitonin Receptor Stimulating Peptide-3 in Placenta with Preeclampsia

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【ABSTRACT】 Objective: To explore calcitonin receptor stimulating peptide-3 (CRSP-3) in the placenta relationship with the pathology of preeclampsia. **Methods:** Fifty cases of preeclampsia (25 cases of mild and severe preeclampsia each) were enrolled in the study and 30 cases of normal pregnant women were selected as the control. The expression location of CRSP-3 was detected by immunohistochemistry, and the expression level of CRSP-3 in placental tissues was detected by RT-qPCR and Western blotting. **Results:** CRSP-3 protein was distributed in the cytotrophoblast cells and syncytiotrophoblast cells. The expressions of CRSP-3mRNA and protein in the preeclampsia group were significantly higher than those in the control ($P<0.05$). Especially, CRSP-3mRNA and protein levels in severe preeclamptic women were higher than those in the control ($P<0.01$). CRSP-3mRNA and protein levels in severe preeclamptic women were higher than those in mild preeclamptic women, but without any significance ($P>0.05$). **Conclusion:** The up-regulation of CRSP-3 in placenta of preeclamptic patients may be associated with the etiology of preeclampsia, but may have no relation with progress and degree of preeclampsia.

Key words: calcitonin receptor stimulating peptide-3 (CRSP-3); placenta; preeclampsia

白介素 β 1及凝血酶降低孕早期蜕膜细胞同源框A10基因的表达

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【摘要】 目的: 探讨炎症及出血导致流产的作用机制。方法: 选择复发性流产(RSA)及正常妊娠孕6~10周的蜕膜组织各10例, 并在体外分离培养正常妊娠的蜕膜细胞, 加入雌、孕激素、白介素 β 1(IL- β 1)及凝血酶处理后, 用实时荧光定量RT-PCR及Western blotting检测RSA患者、正常妊娠者蜕膜组织及培养处理的各组蜕膜细胞内的同源框A10(HOXA10)的表达情况。结果: ①HOXA10基因在孕早期蜕膜细胞中有表达; 与正常妊娠者相比, RSA患者蜕膜组织HOXA10的表达明显下降($P < 0.05$)。②雌、孕激素处理组的蜕膜细胞HOXA10 mRNA的表达显著增加($P < 0.05$), 是未处理组的9.5倍。③进一步加入IL- β 1或凝血酶后, HOXA10 mRNA表达显著下降($P < 0.05$); 与雌、孕激素组相比, 分别下降89.5%和74.9%。结论: ①HOXA10基因在孕早期蜕膜细胞中有显著表达, 在RSA患者中的表达显著下降。②雌、孕激素促进HOXA10的表达, 而IL- β 1及凝血酶抑制HOXA10的表达。

关键词: 同源框A10(HOXA10); 白介素 β 1(IL- β 1); 凝血酶; 复发性自然流产(RSA)

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Interleukin- β 1 and Thrombin Decrease *HOXA10* Gene Expression in Human First Trimester Decidual Cells

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【ABSTRACT】 Objective: To explore the effect of interleukin β 1(IL- β 1) and thrombin on the expression of *HOXA10* gene and the mechanism by which inflammation or bleeding affect pregnancy loss. **Methods:** Twenty decidual samples from recurrent spontaneous abortion (RSA group, $n=10$) and unexpected normal pregnancy (control group, $n=10$)(6–10 weeks) were studied. The decidual cells were isolated from decidual tissue of unexpected normal pregnancy and cultured *in vitro*, adding 17β estradiol (E_2 , 10^{-8} mol/L) and medroxyprogesterone acetate (MPA, 10^{-7} mol/L), IL- β 1 (1 ng/ml) or thrombin (2.5 U/ml). The expression of *HOXA10* was demonstrated by real-time fluorescence quantitative RT-PCR and Western blotting. **Results:** 1) *HOXA10* gene was expressed in early pregnancy decidual cells. The expression of *HOXA10* in RSA decidual tissue was decreased significantly compared with normal pregnancy ($P<0.05$). 2) The mRNA expression of *HOXA10* was significantly increased in E_2 and MPA group (9.5 times higher) compared with the control ($P<0.05$). 3) The expression of *HOXA10* decreased significantly in IL- β 1 or thrombin group ($P<0.05$), compared with E_2 and MPA group (decreased 89.5% and 74.9%, respectively). **Conclusion:** 1) *HOXA10* gene is expressed in decidual cells, and the expression is decreased in the decidua of RSA compared with that of normal pregnancies. 2) IL- β 1 and thrombin inhibit the expression of *HOXA10*, but estrogen and progestin improve it.

Key words: *HOXA10*; IL- β 1; thrombin; recurrent spontaneous abortion (RSA)

• 临床研究 •

黄体期促排卵方案在卵巢低反应患者中的初步研究

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【摘要】目的: 探索黄体期促排卵方案在卵巢低反应患者中应用的可行性及其初步效果。方法: 分析77例接受黄体期促排卵的不孕症患者的卵泡期和黄体期促排卵时血清激素水平及获卵数、胚胎情况和助孕结局。结果: 经过卵泡期和黄体期2次取卵, 77例均有取卵机会, 且获得卵子的患者数和有胚胎冻存的患者数均比仅接受卵泡期取卵的患者数显著增加($P<0.001$ 和 $P<0.05$); 卵泡期与黄体期扳机日内分泌水平亦有统计学差异($P<0.001$), 黄体期促排卵周期的回收卵子数、冷冻胚胎数均显著多于卵泡期($P<0.001$); 已接受了冻融胚胎移植(FET)的34例患者中20例获得了临床妊娠。结论: 在卵巢低反应患者中实施黄体期促排卵取卵是可行的, 可以增加获卵数及获得胚胎的机会, 从而为提高妊娠率提供可能。

关键词: 黄体期促排卵; 卵巢低反应; 拮抗剂方案; 冻融胚胎移植(FET)

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A Preliminary Study of Control Ovary Hyperstimulation on Luteal Phase in Patients with Poor Ovarian Response

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【ABSTRACT】 Objective: To explore the application feasibility and preliminary results of the protocol of control ovary hyperstimulation (COH) on the luteal phase for poor ovarian response patients. **Methods:** Totally 77 infertile patients with poor ovarian response receiving IVF/ICSI-ET were analyzed retrospectively, they all accepted COH protocol on the luteal phase. The average number of retrieved oocytes, embryos obtained and pregnancy outcomes were analyzed. **Results:** After oocytes retrieved on the follicular phase and luteal phase separately, all of 77 patients accepted opportunities of oocytes retrieve, the number of patients who obtained oocytes was statistically increased compared with only retrieved oocytes on the follicular phase ($P<0.001$), the number of patients who obtained embryos that could be freezed was statistically increased compared with only retrieved ovum on the follicular phase ($P<0.05$). The hormone levels on trigger day were significantly different between follicular phase and luteal phase ($P<0.001$). The average number of retrieved oocytes and frozen embryos obtained on luteal phase were significantly increased compared with that on follicular phase ($P<0.001$); 34 patients had undergone frozen-thawed embryo transfer (FET), and 20 patients had been pregnant. **Conclusion:** Control ovary hyperstimulation on luteal phase in poor ovarian response is feasible, the opportunity of obtained oocytes and embryo increased, and then the clinical pregnancy outcome may be improved.

Key words: control ovary hyperstimulation on luteal phase; poor ovarian response; antagonist protocol; frozen-thawed embryo transfer (FET)

卵巢子宫内膜异位癌恶变预测方法研究

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【摘要】 目的: 寻求预测子宫内膜异位症(EMs)相关卵巢癌恶变的方法。方法: 采用病例-对照研究的方法, 以21例卵巢子宫内膜异位症恶变患者为病例组, 以45例卵巢内膜样囊肿患者为对照组, 分析卵巢子宫内膜异位症恶变患者的病史特点、血清CA125水平、超声学改变。结果: 病例组中囊壁见乳头或血流丰富者显示多于对照组, 组间差异有统计学意义($P<0.05$); 囊肿直径 >8 cm的恶变风险 $OR=8.7(95\%CI=2.6\sim 29.3, P<0.001)$; $CA125>200$ IU/ml的恶变风险 $OR=2.3$, 但差异无统计学意义($95\%CI=0.4\sim 12.7, P=0.33$); 病程 >5 年的恶变风险 $OR=1.3(95\%CI=0.4\sim 4.3, P=0.72)$, 囊肿超声见分隔或囊肿周围粘连在病例组和对照组中差异无统计学意义($P>0.05$)。结论: 囊壁有乳头或囊壁见血流、囊肿直径 >8 cm为恶变的高危因素; $CA125>200$ IU/ml、病程 >5 年可能是恶变的高危因素, 但不能有效预测恶变的发生。

关键词: 子宫内膜异位症(EMs); 卵巢癌; CA125; 超声

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Study on the Prediction of Neoplasias Arising in Endometriosis

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【ABSTRACT】 Objective: To seek a method for predicting reoplasias arised from endometriosis (EMs). **Methods:** The study compared the cases with 21 samples of malignant neoplasmas arising in EMs and the controls with 45 samples of EMs, for their levels of serum CA125, ultrasonic imaging and clinical characteristics. **Results:** The sonographic features, papilla or doppler blood flow seen in the mass was high than that of the control, with statistical differences between the two groups. The diameter of the mass was predictive, especially ≥ 8 cm, for canceration ($OR=8.7$, $95\%CI=2.6-29.3$, $P<0.001$). The clinical features, the serum CA125 ≥ 200 IU/ml or the course > 5 years after its diagnosis of EMs, also had some predictive value ($OR=2.3$, $95\%CI=0.4-12.7$ vs $OR=1.3$, $95\%CI=0.4-4.3$), but the P value was 0.33 and 0.72, respectively. There were no statistical differences between the two groups for the seperation in the mass or adhesion around. **Conclusion:** The features, papilla or doppler blood flow seen in the mass and diameter ≥ 8 cm, are high risk factors for predicting the canceration. The clinical features, the serum CA125 ≥ 200 IU/ml or the course > 5 years after its diagnosis of EMs, may be the high risk factors of canceration, but they can not predict the canceration effectively.

Key words: endometriosis (EMs); cancer; serum CA125; ultrasound

复发性流产患者子宫动脉血流的超声多普勒变化

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【摘要】 目的: 探讨复发性流产(RSA)患者子宫动脉血流超声的血流参数及频谱波形的特征。方法: 共纳入87例早孕妇女, 其中有RSA史妇女41例, 无流产史早孕妇女(对照组)46例, 所有对象均行阴道超声多普勒测量子宫动脉血流参数, 测量指标有: 收缩期峰值流速/舒张末期流速(S/D)、搏动指数(PI)、阻力指数(RI)。随访妊娠结局, 排除无流产史妇女中发生难免流产者。根据受试者工作曲线(ROC)比较各参数诊断价值, 另将子宫动脉波形进行分类, 同时比较RSA组和对照组波形的分布差异。结果: 正常对照组排除难免流产7例后为39例。RSA组患者平均年龄 29.7 ± 3.4 岁, 正常对照组 28.2 ± 4.2 岁。RSA组的子宫动脉S/D、PI、RI分别为 6.98 ± 1.67 、 1.46 ± 0.12 、 0.84 ± 0.04 ; 正常对照组分别为 5.30 ± 1.05 、 1.31 ± 0.15 、 0.81 ± 0.12 。RSA组的子宫动脉S/D与PI均高于对照组, 差异有统计学意义, RI值组间差异无统计学意义($P > 0.05$)。ROC曲线下面积三者均 > 0.8 , 其中以PI最大; 血流频谱波形A、0型的发生率较对照组高。结论: RSA患者的S/D、PI明显高于正常早孕妇女, 高阻力血流波形发生率明显高于正常早孕妇女。

关键词: 彩色多普勒; 子宫动脉血流; 复发性流产(RSA)

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Doppler Assessment of Uterine Blood Flow in Recurrent Spontaneous Abortions

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【ABSTRACT】 Objective: To explore uterine artery Doppler index and flow velocity waveforms (FVWs) in women with recurrent spontaneous abortions (RSA). **Methods:** A study was conducted with 87 women in early pregnancy, 41 women with recurrent pregnancy loss and 46 women with no history of abortion. Pregnancy outcome was followed, excluding inevitable abortion happens in women without a history of abortion (7 women). Transvaginal ultrasonography associated with Doppler flow was performed to calculate the S/D, RI, and PI and analyze the uterine artery FVWs. **Results:** The women with RSA had a significantly higher uterine artery S/D and PI than those in the control respectively, as well as a higher incidence of FVWs of type A and type 0. **Conclusion:** Compared with the control, a higher S/D, RI, and PI and a higher incidence of FVW of the type A and type 0 and thus a higher uterine artery impedance were found among women with RSA.

Key words: color Doppler; uterine artery blood flow; recurrent spontaneous abortions (RSA)

宫腔填塞联合米索前列醇预防高危因素剖宫产 产后出血的临床疗效观察

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【摘要】目的: 探讨宫腔填塞联合米索前列醇预防高危因素剖宫产产后出血的临床疗效。方法: 有剖宫产产后出血高危因素产妇 125 例, 随机分为 A 组($n=63$)和 B 组($n=62$)。A、B 组所有患者均于胎儿娩出后给予子宫壁肌肉内注射缩宫素 20 U、静脉滴注缩宫素 10 U, 手术结束后给予宫腔米索前列醇 400 μg 。但 A 组另于胎盘娩出、宫腔清理后给予纱布填塞宫腔。观察术中、术后 2 h、术后 24 h 出血量及手术时间、产褥感染、不良反应情况。结果: A 组术中、术后 2 h、术后 24 h 出血量分别为: 150.3 ± 42.3 ml, 282.2 ± 55.2 ml, 355.8 ± 92.5 ml; 产后出血率为 1.59%; B 组术中、术后 2 h、术后 24 h 出血量分别为: 206.7 ± 33.9 ml, 456.2 ± 75.3 ml, 568.4 ± 83.2 ml; 产后出血率为 12.90%; A 组出血量及产后出血发生率明显低于 B 组($P<0.05$), 而手术时间、产褥感染、不良反应情况组间无统计学差异($P>0.05$)。结论: 宫腔填塞纱布联合米索前列醇预防高危因素剖宫产产后出血疗效显著, 可明显减少产后出血发生率。

关键词: 纱布宫腔填塞; 米索前列醇; 剖宫产术; 产后出血

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Clinical Curative Observation on the Effect of Gauze Packing Combined with Misoprostol Preventing Postpartum Hemorrhage of High-risk in Cesarean Section

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【ABSTRACT】 Objective: To investigate the clinical curative effect of gauze packing combined with misoprostol plugging preventing postpartum hemorrhage of high-risk in cesarean section. **Methods:** A total of 125 puerperas with the risk factors of postpartum hemorrhage in cesarean section were randomly divided into group A ($n=63$) and group B ($n=62$). Both group A and group B were given 20 U oxytocin injected into the intramural uterine muscle and given 10 U oxytocin by intravenously guttae after delivery of fetus combined with misoprostol 0.4 mg plugging in anus after the surgery. On the basis of this, gauze packing in uterine cavity were applied in group A after placental expulsion and cleaning up the uterine cavity. The average volume of bleeding during an operation or in 2 h, 24 h after operation, postpartum hemorrhage and operative time, puerperal infection, adverse reaction between the two groups were observed and analyzed. **Results:** The average volume of bleeding during these operations or in 2 h and 24 h after operations of group A were 150.3 ± 42.3 ml, 282.2 ± 55.2 ml, 355.8 ± 92.5 ml, postpartum hemorrhage ratio was 1.59%. The average volume of bleeding during these operations or in 2 h and 24 h after operations of group B were 206.7 ± 33.9 ml, 456.2 ± 75.3 ml, 568.4 ± 83.2 ml; postpartum hemorrhage ratio was 12.90%. The volume of bleeding during these operations or in 2 h, 24 h after operations and the rate of postpartum hemorrhage between the two group puerperas were statistically significant ($P<0.05$). However, operative time, puerperal infection, apparent adverse reaction between the two groups were not significantly different ($P>0.05$). **Conclusion:** Combined gauze packing and misoprostol plugging could effectively reduce the volume of bleeding and prevent postpartum hemorrhage in cesarean section.

Key words: gauze packing; misoprostol; cesarean section; postpartum hemorrhage

• 综述 •

子宫内膜干细胞在内膜再生方面的研究进展

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【摘要】 人类子宫内膜中存在干细胞, 其对子宫内膜的再生起着关键作用。子宫内膜干细胞位于基底层, 并存在上皮、间充质和内皮细胞3种类型, 它们在子宫内膜上皮修复、再生中都起着重要的作用; 子宫内膜干细胞的分布和功能异常将导致子宫内膜再生相关性疾病(如Asherman综合征、子宫内膜异位症)的发生。

关键词: 子宫内膜; 干细胞; 子宫内膜再生

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Current Outlook of Roles of Endometrial Stem Cells in Endometrial Regeneration

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【ABSTRACT】 Stem cells are present in human endometrium and play a key role in endometrial regeneration. This review briefly describes the discovery, markers and related characteristics of 3 kinds of endometrial stem cells (epithelial stem cell, mesenchymal stem cells and endothelial stem cell), and summarizes recent advances in basic and clinical application of endometrial stem cells in endometrial regeneration both at home and abroad. Also described is the relationship between the abnormalities in the location and function of endometrial stem cells and the pathogenesis of endometrial regeneration-related diseases such as Asherman syndrome and endometriosis.

Key words: endometrium; stem cells; endometrial regeneration

辅助生殖技术与DNA甲基化

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【摘要】辅助生殖技术(assisted reproductive technology, ART)已经成为治疗不孕症的有效方法。但近年来一些研究指出, ART可能增加基因印记紊乱的发病风险, 而DNA甲基化修饰则是其重要机制。ART干预了基因印记发生的主要阶段, 即配子发育和胚胎植入前阶段, 可能造成11p15、15q11-13等区域相关基因DNA甲基化异常, 导致一些相关疾病的发病风险增高。但其相关性仍待进一步探索, 而我們也需要不断改进操作技术来提高ART的遗传安全性。

关键词: 辅助生殖技术; DNA甲基化; 基因印记

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Assisted Reproductive Technology and DNA Methylation

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【ABSTRACT】 Assisted reproductive technology (ART) has become an effective treatment of infertility. But recent studies show that, ART may increase the risk of genomic imprinting disorders, and DNA methylation is the important mechanism. ART intervene the main stage of genomic imprinting, such as gametes development and preimplantation stage. It may cause abnormal DNA methylation of genes in region of 11p15, 15q11-13 and other genes, leading to increased risk of BWS, AS, PWS, SRS and other diseases. But its relevance needs further verification, and we should improve techniques to make ART more safety.

Key words: assisted reproductive technology (ART); DNA methylation; genomic imprinting

抗苗勒管激素影响因素的研究进展

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【摘要】 抗苗勒氏管激素(anti-Müllerian hormone, AMH)又称为苗勒管抑制物(Müllerian-inhibiting substance, MIS), 是转化生长因子 β (transforming growth factor, TGF- β)超家族的成员。AMH具有良好的稳定性, 一般情况下在整个月经周期中无明显波动, 但是仍有一些因素影响AMH的分泌水平, 这些变化在临床中有着重要的意义和价值。本文从多囊卵巢综合征、年龄、肥胖、季节、卵巢储备和性分化异常等6个方面总结了可能引起AMH变化的因素, 从而深入认识AMH变化的临床意义和价值。

关键词: 抗苗勒管激素(AMH); 年龄; 促卵泡生成素(FSH); 多囊卵巢综合征(PCOS); 肥胖

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Progress of Anti-Müllerian Hormone Influencing Factors

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【ABSTRACT】 Anti-Müllerian hormone (AMH), also known as Müllerian-inhibiting substance (MIS), is a member of transforming growth factor- β (TGF- β) superfamily. Because of the stability of AMH, there is almost no significant fluctuation throughout the menstrual cycle. Several factors may influence the secretion of AMH, and these changes may imply significance clinical values, in order to better understand the clinical significances and the value of AMH, this paper summarizes six factors that may affect AMH secretion, including PCOS, age, obesity, season, ovary reserve and abnormal sexual differentiation

Key words: anti-Müllerian hormone (AMH); age; ovarian reserve; PCOS; obesity

表皮生长因子样因子在LH峰效应中的作用 及临床研究进展

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【摘要】表皮生长因子样因子(epidermal growth factor-like factor)——双调蛋白(amphiregulin, Areg)、上皮调节蛋白(epiregulin, Ereg)和细胞调节素(betacellulin, BTC)通过旁分泌和自分泌方式介导黄体生成素(luteinizing hormone, LH)峰效应, 从而诱导卵母细胞减数分裂恢复、卵丘扩展以及排卵。

关键词: 黄体生成素(LH)峰; 双调蛋白(Areg); 上皮调节蛋白(Ereg); 细胞调节素(BTC)

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Role of EGF-like Factors in LH Surge Effect and Its Clinical Research Progress

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【ABSTRACT】 Epidermal growth factor-like factors —— amphiregulin (Areg), epiregulin (Ereg) and betacellulin (BTC) play an essential role in mediating luteinizing hormone (LH) surge effect through paracrine and autocrine ways, resulting in oocyte meiotic resume, cumulus expansion and ovulation.

Key words: luteinizing hormone (LH) effect; amphiregulin (Areg); epiregulin (Ereg); betacellulin (BTC)

• 临床报道 •

硫氧还蛋白和硫氧还蛋白结合蛋白-2 在子宫内膜异位症的表达及意义

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【摘要】 目的: 探讨血清和腹水中硫氧还蛋白(thioredoxin, TRX)及硫氧还蛋白结合蛋白-2(Trx-binding protein-2, TBP-2)的含量与子宫内膜异位症(endometriosis, EMs)的相关性。方法: 应用病例-对照研究的方法, 分别收集34例EMs患者(病例组)和32例非EMs妇女(对照组)的外周血清和腹水样本, 通过酶联免疫吸附法(ELISA)测定血清及腹水中TRX、TBP-2的水平。结果: TRX在病例组血清、腹水中的表达量均高于对照组, 差异有统计学意义($P < 0.05$)。TBP-2在病例组血清、腹水中的表达量均明显低于对照组, 差异有统计学意义($P < 0.05$)。结论: EMs患者血清和腹水中TRX及TBP-2表达的变化可能与EMs的发生、发展有关。

关键词: 子宫内膜异位症(EMs); 硫氧还蛋白(TRX); 硫氧还蛋白结合蛋白-2(TBP-2); 血清; 腹水

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Expression and Significance of Thioredoxin and Trx-binding Protein-2 in Patients with Endometriosis (EMs)

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【ABSTRACT】 Objective: To explore the correlation between thioredoxin and Trx-binding protein-2 with endometriosis (EMs). **Methods:** The expressions of TRX and TBP-2 in serum and peritoneal fluid were detected by ELISA method in 34 patients with EMs (case group) and 32 patients without EMs (control group). **Results:** The expressions of TRX in serum and peritoneal fluid of case group were higher than those of the control ($P<0.05$). The expressions of TBP-2 in serum and peritoneal fluid of (651.12 ± 23.58 , 342.50 ± 14.81) were contrast to the results of TRX ($P<0.05$). **Conclusion:** The changes of expression of TRX and TBP-2 in serum and peritoneal fluid in patients with EMs may be related to the pathogenesis of EMs.

Key words: endometriosis (EMs); thioredoxin (TRX); trx-binding protein-2 (TBP-2); serum; peritoneal fluid

米非司酮药物流产后绒毛蜕膜细胞凋亡 的相关研究

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【摘要】 目的: 探讨米非司酮对早孕绒毛蜕膜细胞凋亡、增殖的作用机制。方法: 以20例药物流产患者为研究组, 以20例非意愿妊娠要求行人工流产负压吸引刮宫术的患者为对照组, 分别收集绒毛和蜕膜标本, 应用原位末端标记法(TUNEL)检测细胞凋亡, 并采用免疫组织化学方法检测bcl-2、bax、fas、fasL、增殖细胞核抗原(PCNA)5种蛋白在绒毛和蜕膜中的分布与表达强度, 同时应用原位杂交法测定fas与fasLmRNA的分布与表达强度。结果: 凋亡细胞在正常早孕绒毛合体滋养细胞中少量存在, 蜕膜中偶见; 绒毛、蜕膜中bcl-2、bax、fas、fasL、PCNA均有表达。采用米非司酮药物流产的绒毛合体滋养细胞及蜕膜间质及腺上皮细胞的凋亡显著增多, 同时伴有促凋亡bax、fas、fasL蛋白及fasLmRNA含量的增加, 而PCNA蛋白含量与C组比没有变化。结论: 米非司酮不仅能促进早孕绒毛合体滋养细胞、蜕膜间质及腺上皮细胞的凋亡, 而且主要通过Fas与FasL转录及翻译途径介导, bax表达增加也其也有一定的相关性, 此可能为其抗早孕机制之一。

关键词: 绒毛; 蜕膜; 米非司酮; 凋亡

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Apoptosis and Expression of Related Genes in Early Pregnant Chorionic Villi and Decidua

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【ABSTRACT】 Objective: To investigate the mechanism of mifepristone on apoptosis and proliferation in early pregnant chorionic villi and decidua. **Methods:** The specimen of early pregnant chorionic villi and decidua was obtained from 20 cases of mifepristone contragestation (study group), 20 cases of requesting termination of pregnancy by curettage (the control). The paraffin sections were used to determine apoptotic cells by TdT-mediated dUTP-biotin nick and labeling method, to identify bcl-2, bax, fas, fasL and proliferating cell nuclear antigen (PCNA) by immunohistochemistry, to demonstrate *fas* and *fasL* mRNA by *in situ* hybridization. **Results:** In the control, apoptosis cells were mainly observed in syncytiotrophoblast, but not in cytotrophoblast cell, occasionally observed in decidua cells. The antigen of bax, fas, fasL were present in syncytiotrophoblast cells and decidua with lower amount. While bcl-2 antigen staining was strong in cytotrophoblastic cells and in decidua cells only. In study group, apoptotic cells were increased in syncytiotrophoblast cells of villi and visualized in decidua cells. The expression of fas, fasL and bax was also higher than that of the control. **Conclusion:** Mifepristone increased apoptosis in syncytiotrophoblast and decidua cells, but had no effect on the expression of bcl-2 and PCNA.

Key words: villi; decidua; mifepristone; apoptosis

基质细胞衍生因子-1(SDF-1)表达 与复发性流产的关系

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【摘要】 目的: 探讨复发性流产(recurrent spontaneous abortions, RSA)患者血清及滋养细胞中基质细胞衍生因子-1(stromal cell-derived factor 1, SDF-1)表达与流产的关系。方法: 应用酶联免疫吸附试验及荧光定量聚合酶链反应方法检测 RSA 患者血清及绒毛组织中 SDF-1 mRNA 的表达($n=36$), 同期选取因非意愿妊娠 7~9 周行人工流产患者的血清及绒毛($n=36$)作为对照组。结果: RSA 患者血清及滋养细胞中 SDF-1 蛋白及 mRNA 的表达均显著低于正常妊娠者, 差异有统计学意义($P < 0.01$)。结论: RSA 患者 SDF-1 蛋白及 mRNA 低表达与流产发生关系密切。

关键词: 基质细胞衍生因子-1(SDF-1); 复发性流产(RSA); 绒毛; 滋养细胞

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Relationship between the Expression of Stromal Cell-derived Factor 1 (SDF-1) and Recurrent Spontaneous Abortions

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【ABSTRACT】 Objective: To investigate the relationship between the expression of stromal cell-derived factor 1 (SDF-1) in serum or trophoblasts and recurrent spontaneous abortions (RSA). **Methods:** Samples of serum and villus tissues ($n=36$) were obtained from women undergoing RSA. Serum and villus tissue samples as the control ($n=36$) were collected from normal pregnant patients who accepted induced abortion in 7–9 weeks of pregnancy. The expressions of SDF-1 protein and mRNA in serum and trophoblasts were determined by enzyme linked immunosorbent assay (ELISA) and real-time reverse transcription polymerase chain reaction (Real-time RT-PCR). **Results:** SDF-1 protein and mRNA in serum and trophoblasts collected from recurrent spontaneous abortions patients had lower levels than those in normal pregnant patients' serum and trophoblasts ($P<0.01$). **Conclusion:** Lower expressions of SDF-1 protein and mRNA in serum and trophoblasts would be associated with recurrent spontaneous abortions.

Key words: stromal cell-derived factor 1 (SDF-1); recurrent spontaneous abortions (RSA); villi; trophoblasts

卵巢子宫内膜异位囊肿合并不孕患者 术后治疗探讨

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【摘要】目的: 探讨卵巢子宫内膜异位囊肿合并不孕的患者术后治疗策略。方法: 将腹腔镜下卵巢子宫内膜异位囊肿剥除术后要求妊娠的62例不孕患者随机分为期待组($n=31$)和GnRH-a组($n=31$)。期待组腹腔镜手术后随访观察, 避免使用激素类药物; GnRH-a组腹腔镜手术后月经第1日给予GnRH-a治疗: 达菲林3.75 mg皮下注射, 1次/28 d, 连用3次停药。所有患者随访24个月, 观察24个月内妊娠情况。结果: 期待组12个月内妊娠率为41.9%(13/31), 13~24个月内妊娠率为22.2%(4/31), 24个月累积妊娠率为54.8%(17/31)。GnRH-a组1年内妊娠率为48.4%(15/31), 13~24个月内妊娠率为18.8%(3/31), 24个月累积妊娠率为58.1%(18/31)。期待组与GnRH-a组比较, 12个月内妊娠率、24个月累积妊娠率组间均无统计学差异($P>0.05$)。结论: 初步临床观察, 卵巢子宫内膜异位囊肿剥除术后使用GnRH-a在提高EMs合并不孕患者妊娠率方面未显示出优势。

关键词: 子宫内膜异位症(EMs); 不孕; 腹腔镜; GnRH-a; 妊娠率

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Treatment of Endometriosis Associated with Infertility Patients

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【ABSTRACT】 Objective: To explore the strategy for the treatment of endometriosis (EMs) complicated with infertility patients. **Methods:** A total of 62 cases were randomly divided into expect group ($n=31$) and GnRH-a group ($n=31$). The patients in expect group were followed up after operation without hormonal drugs. The patients at day 1 of menstruation after operation in GnRH-a group received diphereline 3.75 mg subcutaneous injection, once every 28 d for 3 times. All patients were followed up for 2 years, the pregnancy outcomes were observed during this period. **Results:** In 12 months, 13 cases were pregnant in expect group, the pregnancy rate was 41.9%, 4 cases were pregnant during 13–24 months, the pregnancy rate was 22.2%, 24-month cumulative pregnancy rate was 54.8%. In 12 months, 15 cases were pregnant in GnRH-a group, the pregnancy rate was 48.4%, 3 cases were pregnant during 13–24 months, the pregnancy rate was 18.8%, 24-month cumulative pregnancy rate was 58.1%. There was no significant difference of the pregnancy rate within 12 months and 24-month cumulative pregnancy rate between expect group and GnRH-a group ($P>0.05$). **Conclusion:** According to the preliminary clinical observation, postoperative use of GnRH-a showed no advantage in pregnancy rate of EMs with infertility patients.

Key words: endometriosis (EMs); infertility; laparoscopy; GnRH-a; pregnancy rate

输卵管阻塞性不孕症宫、腹腔镜术后 治疗方法的探讨

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【摘要】目的:探讨输卵管阻塞性不孕症宫、腹腔镜术后阻止再次粘连和阻塞的诊疗方法。方法:将宫、腹腔镜术后至少一侧输卵管通畅的不孕症患者随机分为治疗组和对照组,治疗组和对照组分别术后第1次月经干净后3~7 d应用欣可貯或注射体积分数20%甲硝唑氯化钠注射液进行彩色B超监测下腹腔镜输卵管插管通液;观察术后1年的妊娠情况,术后1年未孕者,于月经干净后3~7 d行子宫输卵管碘佛醇造影检查,了解输卵管通畅度。结果:术后1年治疗组妊娠率(68.75%)高于对照组(51.25%),差异有统计学意义($\chi^2=5.104$, $P=0.024$);异位妊娠差异无统计学意义($P>0.05$);未孕者治疗组双侧输卵管通畅率(40.9%)高于对照组(14.2%),差异有统计学意义($\chi^2=5.168$, $P=0.023$)。结论:输卵管阻塞性不孕症宫、腹腔镜术后第1次月经干净后3~7 d用欣可貯注射液进行彩色B超监测下腹腔镜输卵管插管通液,可以降低盆腔的再次粘连,维持输卵管的通畅,提高受孕率,值得临床推广应用。

关键词: 输卵管通液;欣可貯注射液;宫腔镜;输卵管阻塞性不孕症

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Discussion about the Follow-up Treatment on Salpinx Obstructive Infertility Postoperation of Hysteroscopy Combined Laparoscopy

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【ABSTRACT】 Objective: To evaluate about the follow-up treatment methods on salpinx obstructive infertility postoperation of hysteroscopy combined laparoscopy. **Methods:** The infertility patients postoperation by hysteroscopy combined laparoscopy with at least one side fallopian tube patency were randomly divided into two groups. The study group will be clean application hin can ceruminous injection under hysteroscopic tubal intubation fluid after 3–7 d after the first menstrual cycle of postoperation, control group with 20% metronidazole and sodium chloride injection, observation of postoperative pregnancies a year. The unpregnancy patients were given Ioversol check to observe the influence of Fallopian tube. **Results:** The pregnancy rate after one year was 68.75% in study group, which was higher than that in the control (51.25%), the difference was statistically significant ($\chi^2=5.104$, $P=0.024$). Ectopic pregnancy had no statistically significant difference ($P>0.05$). Bilateral fallopian tube patency rate of unfertilized cases was 40.9%, which was higher than that in the control (14.2%), the difference was statistically significant ($\chi^2=5.168$, $P=0.023$). **Conclusion:** Hin ceruminous injection with salpinx obstructive infertility postoperation of hysteroscopy combined laparoscopy for the first time can be 3–7 d after menstruation for color B ultrasonic monitoring under hysteroscopic tubal intubation liquid, can reduce pelvic adhesion, again to maintain tubal patency and improve the conception rate. It's useful for the follow-up treatment on salpinx obstructive infertility postoperation of hysteroscopy combined laparoscopy.

Key words: hydrotubation; Hin ceruminous injection; hysteroscopy; second trimester; salpinx obstructive infertility