

• 实验研究 •

## 康普瑞汀磷酸钠对大鼠胚胎发育毒性的研究

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**【摘要】**目的: 探讨抗肿瘤药物康普瑞汀磷酸钠(combretastatin A-4 disodium phosphate, CA4P)对SD孕鼠胚胎发育的毒性作用。方法: 80只孕鼠随机分为低剂量(0.15 mg/kg)组、中剂量(0.50 mg/kg)组和高剂量(1.50 mg/kg)组及对照组(生理盐水), 每组20只, 给药容积均为10 mL/kg。于妊娠第6~15日尾静脉注射给药, 每日1次。妊娠第20日解剖孕鼠, 检查母体妊娠与胎鼠畸形情况。结果: 与对照组比较, 高剂量组的着床率、胚胎吸收率均有显著升高, 活胎率降低, 差异均有统计学意义( $P<0.05$ ); 妊娠后期高剂量组孕鼠体质量增长显著低于对照组, 差异有统计学意义( $P<0.05$ ); 中、高剂量组的胎盘质量、活胎体质量、活胎顶臀长以及尾椎数、掌骨数、枕骨数、胸骨数均显著减少( $P<0.05$ ); 各剂量组未见胎鼠外观及内脏畸形。结论: 本实验条件下, CA4P对亲代孕鼠未观察到不良反应的剂量水平(NOEL)为0.50 mg/kg, 对胚胎、胎仔发育的NOEL为0.15 mg/kg, 对胎仔致畸作用的NOEL为1.50 mg/kg。

**关键词:** 抗肿瘤药; 康普瑞汀磷酸钠(CA4P); 大鼠; 胚胎毒性; 致畸性

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• 实验研究 •

## Embryotoxicity study of combretastatin A-4 disodium phosphate (CA4P) in rats

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**【ABSTRACT】 Objective:** To investigate the embryotoxicity of combretastatin A-4 disodium phosphate (CA4P) in pregnancy SD rats. **Methods:** Eighty SD rats were randomly divided into 4 groups ( $n=20$  for each group). Three experimental dosages (0.15 mg/kg, 0.50 mg/kg, 1.50 mg/kg) were chosen, SD rats were injected intravenously with experimental agent or normal saline as control. The injection was conducted from the 6th to 15th day of gestation, once a day. Pregnancy rats were sacrificed on the 20th day of gestation and pregnancy results and embryonic malformation were examined. **Results:** There were significant differences in the rate of implantation, living and absorbed fetus in 1.50 mg/kg dosage group compared with negative control ( $P<0.05$ ), moreover, the weight gain of the pregnancy rats slowed down in the late gestation stage, which indicated maternal toxicity. Under both 0.50 mg/kg and 1.50 mg/kg dosages group, there were significant differences in placenta weight, living fetus weight body length and number of caudal vertebra, metacarpal bone, occipital bone and breast bone in comparison with control group. All dosage groups did not induce any embryonic teratogenic effect on the appearance or organs. **Conclusion:** Under these experimental conditions, the no observed adverse effect level (NOAEL) of CA4P on pregnancy rats and embryonic development were 0.50 mg/kg and 0.15 mg/kg, respectively, while the NOAEL on teratogenicity effect was 1.50 mg/kg.

**Key words:** combretastatin A-4 disodium phosphate (CA4P); rats; embryotoxicity; teratogenicity

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# 中药补肾调冲方对卵巢早衰大鼠激素水平和卵巢 Bcl-2/Bax 表达的影响

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**【摘要】**目的: 探讨补肾调冲方对雷公藤多苷片(GTW)致卵巢早衰(POF)的治疗作用。方法: 雌性SD大鼠42只, 随机分为正常组、模型组、结合雌激素片(雌激素组)和补肾调冲方治疗高、中、低剂量组。运用酶联免疫吸附试验(ELISA)法检测血清中雌二醇(E<sub>2</sub>)、卵泡刺激素(FSH)、抑制素B(INHB)水平。Western blotting法和RT-PCR法检测卵巢组织中Bcl-2、Bax蛋白及mRNA的表达水平。结果: 正常组和各给药组E<sub>2</sub>的含量均高于模型组( $P < 0.01$ )。正常组和各给药组FSH含量均低于模型组( $P < 0.01$ ); 正常组和各给药组INHB含量均高于模型组( $P < 0.01$ )。低剂量组INHB的含量与雌激素组比较, 差异有统计学意义( $P < 0.05$ )。模型组大鼠卵巢中Bcl-2蛋白和mRNA水平的表达显著低于正常组( $P < 0.05$ ); 各给药组Bcl-2蛋白和mRNA水平的表达显著高于模型组( $P < 0.01$ )。模型组大鼠卵巢中Bax蛋白和mRNA水平的表达显著高于正常组( $P < 0.05$ ); 各给药组Bax蛋白和mRNA水平的表达显著低于模型组( $P < 0.01$ )。低剂量组Bax蛋白的表达与雌激素组比较, 差异有统计学意义( $P < 0.05$ )。结论: 中药补肾调冲方对卵巢性激素水平具有调节作用, 能提高卵巢对性激素的敏感性, 促进卵巢排卵; 通过上调Bcl-2和下调Bax的表达, 抑制卵巢中颗粒细胞的过度凋亡, 减少卵泡闭锁, 促进卵巢功能的恢复。

**关键词:** 补肾调冲方; 卵巢早衰(POF); 性激素; 雌二醇(E<sub>2</sub>); 卵泡刺激素(FSH); 抑制素B(INHB); Bcl-2; Bax; 大鼠

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## Effects of Bushen Tiaochong prescription on the expression of sex hormone and Bcl-2/Bax in rat ovaries with premature ovarian failure

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**【ABSTRACT】 Objective:** To study the therapeutic action of Bushen Tiaochong prescription for premature ovarian failure (POF). **Methods:** Forty-two healthy female SD rats were randomly divided into normal group, model group, estradiol (E<sub>2</sub>) group, Bushen Tiaochong prescription high dosage group, medium dosage group, and low dosage group. Serum levels of E<sub>2</sub>, follicle-stimulating hormone (FSH), and inhibin B (INHB) were detected by enzyme-linked immunosorbent assay (ELISA). Expression levels of Bcl-2, Bax protein and mRNA in rat ovarian tissue were also detected by Western blotting and RT-PCR method. **Results:** The E<sub>2</sub> level in normal group and each administered group was higher than that in model group ( $P<0.01$ ). The FSH level in normal group and each administered group was lower than that in model group ( $P<0.01$ ). The INHB level in normal group and each administered group was higher than that in model group ( $P<0.01$ ). The difference of INHB level in low dosage group and estrogen group, was statistically significant ( $P<0.05$ ). Bcl-2 protein and mRNA expression levels in model group were significantly lower than those in normal group ( $P<0.05$ ), while Bcl-2 protein and mRNA expression levels in normal group and each administered group were significantly higher than those in model group ( $P<0.05$ ). Bax protein and mRNA expression levels in model group were significantly higher than those in normal group ( $P<0.05$ ), while Bax protein and mRNA expression levels in normal group and each administered group were significantly lower than those in model group ( $P<0.01$ ). The difference of Bax protein expression in low dosage group and estrogen group, was statistically significant ( $P<0.05$ ). **Conclusion:** Bushen Tiaochong prescription can regulate the sex hormone levels, and increase the sensitivity of sex hormone to promote ovulation. Bushen Tiaochong prescription can improve the function of ovaries by up-regulating the expression of Bcl-2 and down-regulating the expression of Bax mRNA in ovaries, inhibit the excessive apoptosis of granulosa cells, promote the recovery of ovarian function.

**Key words:** Bushen Tiaochong prescription; premature ovarian failure (POF); sex hormone; estradiol (E<sub>2</sub>); follicle-stimulating hormone (FSH); inhibin B (INHB); Bcl-2; Bax; rat

• 临床研究 •

## 月经期取卵在卵巢低储备患者 IVF-ET中的应用

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**【摘要】**目的: 探讨月经期取卵在卵巢低储备(diminished ovarian reserve, DOR)患者体外受精-胚胎移植(IVF-ET)中应用的可行性。方法: 回顾性分析70例DOR行IVF/卵胞质单精子注射(ICSI)-ET治疗的不孕症患者的临床资料, 比较其73个月经期取卵和270个非月经期取卵的结局。若月经2~4 d阴道超声提示优势卵泡直径 $\geq 14$  mm且 $E_2$ 水平 $>200$  ng/L则行月经期取卵, 若无优势卵泡按常规促排卵方案行IVF/ICSI, 观察其临床结局。结果: 月经期组获卵数、成熟卵数和可用胚胎数分别为 $1.0 \pm 0.4$ 个、 $0.8 \pm 0.4$ 个、0(0, 1)个, 非月经期组分别为 $1.6 \pm 1.2$ 个、 $1.4 \pm 1.1$ 个、1(0, 1)个, 组间有统计学差异( $P < 0.05$ )。月经期组周期取消率为72.6%, 显著高于非月经期组43.0%( $P < 0.05$ )。月经期组获卵率、卵裂率、卵子利用率分别为83.1%、94.7%和34.5%, 非月经期组分别为70.6%、96.7%和51.7%, 组间无统计学差异( $P > 0.05$ )。结论: 尽管月经期取卵的获卵数、成熟卵数、可用胚胎数小于非月经期取卵, 但获卵率、卵裂率和卵子利用率组间无统计学差异, 为反复周期取消、高基础雌激素的DOR不孕症患者节约了治疗时间, 提供了新的方法。

**关键词:** 卵巢低储备(DOR); 月经期取卵(OPU); 卵子利用率; 周期取消率

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• 临床研究 •

## Ovum pick-up (OPU) in menstruation is feasible for diminished ovarian reserve women underwent IVF-ET

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**【ABSTRACT】 Objective:** To investigate the feasibility of ovum pick-up (OPU) in menstruation for diminished ovarian reserve (DOR) women by comparing *in-vitro* fertilization/intracytoplasmic sperm injection and embryo transfer (IVF/ICSI-ET) outcomes with non-menstruation OPU cycles. **Methods:** Totally 70 women diagnosed with DOR underwent 73 OPU cycles in menstruation and 270 non-menstruation OPU. Patients were programmed for OPU in menstruation if dominant follicle was monitored by transvaginal ultrasound and high estrogen level >200 ng/L. And they were programmed regular IVF/ICSI protocols if not. The IVF/ICSI outcomes were compared between the two groups. **Results:** The number of oocytes retrieved, mature oocytes and viable embryos in menstruation group were  $1.0 \pm 0.4$ ,  $0.8 \pm 0.4$ , 0 (0, 1), respectively, while in non-menstruation group were  $1.6 \pm 1.2$ ,  $1.4 \pm 1.1$ , 1 (0, 1), respectively ( $P < 0.05$ ). There were no significant differences in oocyte retrieval rate, cleavage rate, and oocyte utilization rate between menstruation group (83.1%, 94.7%, 34.5%) and non-menstruation group (70.6%, 96.7%, 51.7%) ( $P > 0.05$ ). **Conclusion:** Although the number of oocytes retrieved, mature oocytes and viable embryos in menstruation group were lower than those in non-menstruation group, there were no significant differences with oocyte retrieval rate, cleavage rate, and oocyte utilization rate. The OPU in menstruation is feasible for DOR women with repeated cancellation and high basal estrogen level, saving treatment time and providing a new method for DOR patients.

**Key words:** diminished ovarian reserve (DOR); ovum pick-up (OPU); oocyte utilization rate; cancellation rate

# 长方案卵泡中 / 后期添加含活性 LH 的不同促性腺激素制剂的临床结局比较

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**【摘要】**目的: 探索经典长方案卵泡中 / 后期添加含活性黄体生成素(LH)的不同促性腺激素(Gn)制剂后行体外受精 / 卵胞质内单精子注射 - 胚胎移植(IVF/ICSI-ET)的最佳用药方案。方法: 回顾性分析采用长方案行IVF/ICSI的1441个周期患者的临床资料, 根据中 / 后期所添加的Gn制剂不同, 分为3组, A组为重组LH(r-LH)组, B组为人绝经期促性腺激素(hMG)组, C组为高纯hMG(HP-hMG)组。比较3组患者的Gn使用总量、Gn使用天数、获卵数、优质胚胎数、顶级优质胚胎数、临床妊娠率、活产率、早期流产率等。结果: C组Gn使用天数显著低于A组及B组, B组Gn使用总量显著高于A组及C组, A组和C组双原核(2PN)数、卵裂数、优质胚胎数、可利用胚胎数显著高于B组( $P < 0.05$ ), 但A组与C组比较无统计学差异( $P > 0.05$ ); C组的顶级优质胚胎数高于A组及B组, 差异有统计学意义( $P < 0.05$ )。种植率A组为44.0%, B组为38.2%, C组为42.5%, 各组间无统计学差异( $P > 0.05$ )。临床妊娠率和活产率A组为62.5%和50.6%, B组为59.8%和44.0%, C组为65.3%和52.3%, A组和C组高于B组, 但各组间比较无统计学差异( $P > 0.05$ ); 早期流产率各组间相似。结论: 长方案卵泡中后期添加LH制剂可获得较好的临床结局, 但添加HP-hMG与r-LH可以减少Gn使用天数和总量, 增加顶级优质胚胎数, 临床妊娠率和活产率有增高的趋势, 总体临床结局均优于国产hMG。

**关键词:** 体外受精 / 卵胞质内单精子注射 - 胚胎移植(IVF/ICSI-ET); 促黄体生成素(LH); 顶级优质胚胎

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## Comparison of the clinical outcomes of supplementation with different Gn (different LH preparations) in the middle- and late-follicular phase in the standard long down-regulation protocol

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**【ABSTRACT】 Objective:** To compare the impact of supplementation with different luteinizing hormone (LH) preparations in the middle- and late-follicular phase of ovarian stimulation on clinical outcomes in the standard gonadotropin releasing hormone agonist (GnRH-a) long protocol and to explore the optimized treatment method. **Methods:** Retrospective analysis was performed on clinical data of 1 441 *in vitro* fertilization/intracytoplasmic sperm injection-embryo transfer (IVF/ICSI-ET) cycles. Patients were divided into three groups according to the supplementation of different LH preparations. Patients of group A were added with recombinant LH (r-LH), group B were added with human menopausal gonadotropin (hMG) and group C were added with high pure (HP-hMG). Clinical outcomes of the three groups, including the amount of gonadotropin (Gn), duration of Gn stimulation, the number of oocytes retrieved, high-quality embryos and top-quality embryos, clinical pregnancy rate, live birth rate, early abortion rate, etc. were analyzed. **Results:** The duration of Gn stimulation was much fewer in group C than in group A and group B, and the total dosage of Gn used was much higher in group B than in group A and group C. The number of cleavage, good-quality embryos and available embryos in group A was significantly higher than that in group B, but there was no statistical difference between group A and group C. The number of top-quality embryos in group C was significantly higher than that in the other two groups. The implantation rate was 44.0% in group A, 38.2% in group B and 42.5% in group C, the clinical pregnancy rate and the live birth rate were 62.5% and 50.6% in group A, 59.8% and 44.0% in group B, 65.3% and 52.3% in group C, respectively, but there was no statistical significance. The early abortion rate was similar in three groups. **Conclusion:** LH preparations supplemented in the middle- and late-follicular phase in the standard long down-regulation protocol obtains good clinical outcomes. The clinical outcomes of HP-hMG and r-LH supplemented were better than that of hMG, which not only reduced the duration and doses of Gn used, but also increased the number of top-quality embryos, and there was an increasing tendency in clinical pregnancy rate and live birth rate.

**Key words:** *in vitro* fertilization/intracytoplasmic sperm injection-embryo transfer (IVF/ICSI-ET); luteinizing hormone (LH); top-quality embryo

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# 氧浓度对体外培养胚胎发育的影响

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**【摘要】**目的: 探讨体外受精/卵胞质内单精子注射(IVF/ICSI)后移植前胚胎在不同氧浓度培养条件下的发育情况。方法: 将接受IVF或ICSI的患者随机分组为常氧组(体积分数20%的氧浓度, 包括IVF卵裂期胚胎患者150例, IVF囊胚期胚胎患者51例, ICSI卵裂期胚胎患者81例, ICSI囊胚期胚胎患者39例)和低氧组(体积分数5%的氧浓度, 包括IVF卵裂期胚胎患者108例, IVF囊胚期胚胎患者56例, ICSI卵裂期胚胎患者79例, ICSI囊胚期胚胎患者45例), 观察各组胚胎在受精后第3日的卵裂胚和第5日的囊胚发育情况以及临床妊娠结局。结果: 在患者年龄、不孕年限、基础FSH值、Gn用量、获卵数和M<sub>II</sub>卵率组间均无统计学差异的基础上, ①与常氧组相比, 低氧组的胚胎IVF或ICSI后的受精率、卵裂率以及第3日形成的优质胚胎率无统计学差异( $P>0.05$ ), 临床妊娠率和着床率组间也无统计学差异( $P>0.05$ ); ②低氧组胚胎IVF或ICSI后形成的V级囊胚多于常氧组( $P<0.05$ ), 总囊胚形成率组间有显著的统计学差异( $P<0.01$ ), 临床妊娠率和着床率组间无统计学差异( $P>0.05$ )。结论: 与常氧培养条件相比, 低氧培养条件并不能显著促进IVF/ICSI后卵裂期胚胎的发育, 但能够促进囊胚的形成, 特别是囊胚的孵出, 因此低氧培养可以作为囊胚培养的首选条件, 但不是卵裂期胚胎培养的必要条件。

**关键词:** 胚胎培养; 氧浓度; 体外受精(IVF); 卵胞质内单精子注射(ICSI)

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## Effect of different concentrations of oxygen on the development of embryos cultured *in vitro*

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**【ABSTRACT】 Objective:** To investigate the development of pre-implantation embryos under different concentrations of oxygen after *in vitro* fertilisation/intracytoplasmic sperm injection (IVF/ICSI). **Methods:** The embryos of IVF or ICSI were randomly divided into normal oxygen group (20% oxygen, including 150 cases in IVF ongoing cleavage embryo culture, 51 cases in IVF ongoing blastula culture, 81 cases in ICSI ongoing cleavage embryo culture and 39 cases in ICSI ongoing blastula culture) and low oxygen group (5% oxygen, including 108 cases in IVF ongoing cleavage embryo culture, 56 cases in IVF ongoing blastula culture, 79 cases in ICSI ongoing cleavage embryo culture and 45 cases in ICSI ongoing blastula culture) and then the development of cleavage embryos on day 3 and blastula on day 5 were compared between the two groups. **Results:** On the basis of no statistical difference in age, duration of infertility, basal FSH value, Gn used dosage and M<sub>II</sub> oocyte rate between normal oxygen group and low oxygen group, 1) there were no statistical difference in the rates of fertilization, cleavage and good-quality embryo cultured on day 3 between the two groups both in IVF and ICSI and no statistical difference existed on the clinical pregnancy rate and the implantation rate; 2) the number of grade V blastula formed in low oxygen group was statistically higher than that in normal oxygen group both after IVF and ICSI ( $P < 0.05$ ) and the total blastula formation rate in low oxygen group was significantly higher than that in normal oxygen group ( $P < 0.001$  and  $P < 0.01$ , respectively). Although the clinical pregnancy rate and the implantation rate were higher in low oxygen group than in normal oxygen group, the difference between them was not statistically significant. **Conclusion:** Compared with normal oxygen culture, low oxygen culture can't significantly improve the development of cleavage embryos, but can enhance the formation of blastula, especially the hatching of blastocysts. All these findings indicate that low oxygen culture is prior in blastula culture but not in cleavage embryo culture.

**Key words:** embryo culture; oxygen concentration; *in vitro* fertilization (IVF); intracytoplasmic sperm injection (ICSI)

# 左炔诺孕酮宫内缓释系统治疗子宫腺肌病的临床疗效研究

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**【摘要】**目的: 探讨左炔诺孕酮宫内缓释系统(LNG-IUS)治疗子宫腺肌病(AM)的临床疗效。方法: 对67例AM患者子宫内放入LNG-IUS, 检测放置前、放置后1、3、6、12、24个月的月经量、痛经情况、子宫内膜厚度、子宫体积以及血清中的血红蛋白(Hb)、促卵泡生成素(FSH)、黄体生成素(LH)、雌二醇(E<sub>2</sub>)等指标的变化。结果: 放置LNG-IUS后, 患者的月经量在3个月后较放置前明显减少( $P<0.05$ ), 痛经在放置3个月后较放置前明显减轻( $P<0.05$ ), 子宫内膜厚度在放置1个月后较放置前明显变薄( $P<0.05$ ), 子宫体积在放置1年后明显缩小( $P<0.05$ ), 血清Hb水平在放置6个月后较放置前明显上升( $P<0.05$ ), 血清FSH、LH、E<sub>2</sub>水平放置前、后无统计学差异( $P>0.05$ )。结论: LNG-IUS能有效缓解AM患者痛经、减少月经量、改善子宫内膜厚度并在一定程度上缩小子宫体积、提高血清Hb水平, 且不会影响患者卵巢功能, 是治疗AM的一种有效方法。

**关键词:** 左炔诺孕酮宫内缓释系统(LNG-IUS); 子宫腺肌病(AM); 临床疗效

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## Clinical observation of levonorgestrel intrauterine system in the treatment of adenomyosis

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**【ABSTRACT】 Objective:** To investigate the clinical efficacy of levonorgestrel intrauterine system (LNG-IUS) on the treatment of adenomyosis (AM). **Methods:** LNG-IUS was placed in 67 patients with AM. Menstrual flow, dysmenorrhea, uterine endometrial thickness, uterine volume, level of hemoglobin, follicle-stimulating hormone (FSH), luteinizing hormone (LH), estradiol (E<sub>2</sub>) were compared between before treatment and 1 month, 3 months, 6 months, 12 months, 24 months after treatment. **Results:** The parameters of menstrual flow and dysmenorrhea at 3 months after treatment, uterine endometrial thickness at 1 month after treatment, uterine volume at 12 months after treatment were lower than those before treatment with statistically significant differences ( $P < 0.05$ ). Level of hemoglobin at 6 months after treatment was higher than that before treatment with a statistically significant difference ( $P < 0.05$ ). Levels of FSH, LH, E<sub>2</sub> after treatment were similar to those before treatment with no statistical difference ( $P > 0.05$ ). **Conclusion:** LNG-IUS has an effect on relieved dysmenorrhea, reduced menstrual flow, uterine endometrial thickness and uterine volume, increased level of hemoglobin, but didn't affect the ovarian function, which is an effective method to cure AM.

**Key words:** levonorgestrel intrauterine system (LNG-IUS); adenomyosis (AM); clinical efficacy

# 人工流产术后即刻放置依托孕烯植入剂 避孕的可行性研究

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**【摘要】**目的: 探讨人工流产术后是否可即刻放置依托孕烯植入剂进行避孕。方法: 要求避孕的66例因非意愿妊娠行人工流产术后妇女即刻放置依托孕烯植入剂为研究组, 另同期征集84例健康妇女于月经期放置该植入剂作为对照组, 术后1、6、12个月随访, 随访阴道出血情况, 植入剂取出原因, 并在放置12个月时进行满意度调查。结果: 在放置12个月期间所有对象均未怀孕。研究组闭经/出血稀发发生率为53.0%, 出血频发/出血延长发生率为15.1%, 对照组闭经/出血稀发发生率为58.4%, 出血频发/出血延长发生率为27.3%; 满12个月时, 研究组取出20例, 续用率为69.7%, 满意度为69.6%; 对照组取出22例, 续用率为73.8%, 满意度为72.6%。结论: 人工流产术后即刻放置依托孕烯植入剂与月经期放置效果相同, 人工流产术后妇女即刻放置依托孕烯植入剂进行避孕也是一个较合适的放置时机。

**关键词:** 依托孕烯植入剂; 阴道出血模式; 续用率; 满意度

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## Feasibility analysis of the etonogestrel implants in women undergoing postabortion immediate placement

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**【ABSTRACT】 Objective:** To estimate the vaginal bleeding pattern, discontinuation rate and satisfaction of the etonogestrel implants in women with immediate postabortion placement. **Methods:** Totally 66 women who required of contraception and received the etonogestrel implants immediately after postabortion were treated as research group, 84 women undergoing menstrual placement of the etonogestrel implants during the same period were treated as control group. Follow-up of 1, 6, 12 months after implantation were performed. The 12-month vaginal bleeding pattern, discontinuation rate and satisfaction for the etonogestrel implants were compared between the two group. **Results:** Over the study period in 12 months, pregnancy rate in two groups was 0%. In the research group, amenorrhea/infrequent bleeding occurred in 53.0%, and frequent/prolonged bleeding occurred in 15.1%. In control group the rate of amenorrhea/infrequent bleeding and frequent/prolonged bleeding was 58.4% and 27.3%. After 12 months of implantation, 20 cases were removed in the research group, the continuation rate was 69.7%, and satisfaction rate was 69.6%; in control group, 22 cases were removed, the continuation rate was 73.8%, and satisfaction rate was 72.6%. **Conclusion:** Women who undergo immediate postabortion placement of the etonogestrel implants have high rates of continuation that are equivalent to women undergoing menstrual insertion. Maybe, the time immediately after the postabortion with etonogestrel implants is a more appropriate time.

**Key words:** etonogestrel implants; bleeding pattern; discontinuation rate; satisfaction

• 综述 •

## 卵巢源雌性生殖干细胞增殖分化 及其通路的研究进展

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**【摘要】** 雌性生殖干细胞的发现打破了传统的“固定卵泡理论”。研究表明, 在人和小鼠卵巢中, 该类细胞定位于卵巢表面上皮, 并可在其中检测到 Oct4、Sox-2、Nanog、Vasa 等生殖细胞和干细胞特异性标志物的存在; 且 2 条重要的信号途径——Notch 和 Hippo 在雌性生殖干细胞增殖与分化的过程中发挥重要的作用。

**关键词:** 雌性生殖干细胞; Hippo 信号通路; Notch 信号通路

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• 综述 •

## Research progress in proliferation, differentiation and pathway of ovary female germline stem cells

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**【ABSTRACT】** The discovery of female germline stem cells has broken the traditional view that the mammalian females produce a finite number of oocytes at birth. Researchers have isolated the germline stem cells from the ovary that are mainly located in the ovarian surface epithelium and detected of the positive expressions of the specific markers (Oct4, Sox2, Nanog, Vasa). According to our research, Notch and Hippo signaling pathway plays an important role in the process of proliferation and differentiation.

**Key words:** female germline stem cells (FGSCs); Hippo signaling pathway; Notch signaling pathway

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# 卵巢生殖干细胞与卵巢表面生发上皮关系的研究进展

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**【摘要】** 雌性哺乳动物体内是否存在分裂活跃的生殖干细胞(GSCs), 依然存在争议。近年来研究证实, 在人类和小鼠卵巢中分离得到了具有分裂活性的 GSCs 样细胞。假定的雌性哺乳动物 GSCs 可能定位于卵巢表面生发上皮中。卵巢微环境对 GSCs 池的维持和分化至关重要, 而年龄增加和免疫系统退变可以通过改变卵巢微环境使 GSCs 无法获得足够的支持来形成新的卵子和卵泡。雌性 GSCs 的存在, 不仅可以为干细胞领域的研究提供新的来源, 对辅助生殖技术的未来发展也有着重要意义。

**关键词:** 卵巢生殖干细胞; 卵巢表面上皮细胞(OSE); 卵巢微环境

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## Relationship between ovarian germline stem cells and ovarian surface epithelium

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**【ABSTRACT】** Whether ovarian germline stem cells (GSCs) exist in female mammals has always been a controversial topic. Recent studies demonstrated that there are isolated putative GSCs from human and mouse ovaries. Evidences showed that these putative GSCs may reside in ovarian surface epithelium, which is an assembly of multipotent cells. What's more, signaling from ovarian surrounding microenvironment is vital for the maintenance and differentiation of GSCs. Aging and degeneration of immune system may influence surrounding microenvironment, thus cause inability of GSCs to generate new oocytes and follicles. The existence of GSCs can not only provide new study materials in stem cells researches, but also be of important significance for development of assisted reproductive technology.

**Key words:** ovarian germline stem cells (GSCs); ovarian surface epithelium; ovarian microenvironment

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# 始基卵泡活化的分子机制研究进展

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**【摘要】** 始基卵泡是哺乳动物整个生殖期限中各级卵泡及卵子发育的源头。始基卵泡的激活既需要卵母细胞内如 PI3K-PTEN-AKT-FOXO3、mTORC1 及 p27Kip1-CDK 体系等信号通路的正常激活, 也需要一些卵母细胞特异性的分子如 Nobox 和 Sohlh1 等的参与, 除此之外, 始基卵泡周围的前颗粒细胞也发挥巨大作用, 其首先在 mTORC1 等信号通路的调节下分化为立方形颗粒细胞, 改变自身形态, 启动始基卵泡活化, 其次可通过分泌 KITL 与卵细胞表面 KIT 结合后激活调节卵细胞生长的关键通路——PI3K 信号通路, 最终导致卵母细胞生长及始基卵泡的正常激活。了解始基卵泡活化过程有助于阐明卵子发生的分子机制, 为女性不孕提供新的治疗靶点。

**关键词:** 始基卵泡激活; 始基卵泡颗粒细胞(pfGCs); 雷帕霉素复合物 1(mTORC1)信号通路; 磷脂酰肌醇 3 激酶(PI3K)信号通路; KIT 配体(KITL)-KIT 信号通路

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## Current progress on the molecular mechanisms of the activation of primordial follicle

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**【ABSTRACT】** Primordial follicles serve the source of developing follicles and oocytes for the entire reproductive lifespan of the animal. In recent years, more and more molecular mechanisms of the activation of primordial follicles have been elucidated via genetically modified mouse models, in which several molecules and pathways operating in both the somatic primordial follicle granulosa cells (pfGCs) and oocytes, such as the phosphatidylinositol 3 kinase (PI3K-PTEN-AKT-FOXO3), the mechanistic target of rapamycin complex 1 (mTORC1) pathways and p27Kip1 cyclin dependent kinase systems are included. Furthermore, several factors expressed specifically in oocyte such as Nobox and Sohlh1 are also involved in this process. The functional roles of pfGCs in controlling the activation of primordial follicles are highlighted in this review, which showed that it firstly experience morphology change from flat to cube via the regulation of mTORC1 pathways, and then secrete KIT ligand (KITL) to combine with KIT receptor on oocyte and launch the activation of PI3K signaling pathways. Those process finally contributes to the activation of primordial follicles. Expounding those mechanisms will contribute to better treatments of female infertility.

**Key words:** primordial follicle activation; primordial follicle granulosa cells (pfGCs); phosphatidylinositol 3 (PI3) kinase signaling; the mechanistic target of rapamycin complex 1 (mTORC1) signaling; KIT ligand (KITL)-KIT signaling,

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# 子宫内膜异位症患者原位内膜异常改变的研究进展

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**【摘要】**子宫内膜异位症(endometriosis, EMS)是指子宫内膜组织(腺体和间质)出现在子宫腔以外的部位。EMS患者的原位内膜不同于正常子宫内膜,不仅在形态结构上发生了改变,在基因层面与分子生物学层面亦发生了多种改变,这些改变进而引起一系列在位子宫内膜功能上的变化,主要表现为EMS患者在位内膜细胞的黏附性、侵袭力、转移力、血管生成能力、细胞增殖能力增强,细胞凋亡能力与子宫内膜容受性下降,以及神经纤维分布异常,引发盆腔疼痛等。

**关键词:** 子宫内膜异位症(EMS); 原位内膜; 超微结构; 基因; 分子生物学

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## Research progress on abnormal changes in the eutopic endometrium of patients with endometriosis

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**【ABSTRACT】** Endometriosis (EMS) is defined as the presence of endometrial tissues, such as glands and mesenchyma, outside of the uterine cavity. The eutopic endometrium in patients with EMS is different from the normal endometrium, which not only changes in the morphological structure, but also has various changes at the genetic level and molecular biological level, then further causes a series of changes in the function of the eutopic endometrium. The main manifestations of the changes include the enhancement of adhesion, invasiveness, metastatic potential, angiogenesis ability, cell proliferation ability of the eutopic endometrial cell in patients with EMS, and the decrease of apoptotic ability and endometrial receptivity, and abnormal distribution of nerve fibers, and pelvic pain, and so forth.

**Key words:** endometriosis (EMS); eutopic endometrium; ultrastructure; genes; molecular biology

• 临床报道 •

## IVF-ET中卵巢低反应患者拮抗剂方案中应用生长激素的研究

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**【摘要】**目的: 研究卵巢低反应(POR)患者采用拮抗剂方案加用生长激素(GH)对子宫内膜容受性及妊娠结局的影响。方法: 对采用拮抗剂方案促排卵行体外受精-胚胎移植(IVF-ET)助孕的188例POR患者的资料进行回顾性分析。以加用GH者为研究组( $n=98$ ), 其余不加用GH者为对照组( $n=90$ ), 比较组间的临床资料、实验室数据及妊娠结局, 以评估GH治疗对POR患者的临床疗效。结果: 研究组的Gn使用时间、GnRH-A使用时间及总Gn使用量显著少于对照组, 而获卵数、M<sub>II</sub>卵子数、受精卵数、优质胚胎数、hCG注射日血E<sub>2</sub>水平均显著高于对照组, 差异均有统计学意义( $P<0.05$ ); hCG注射日子宫内膜厚度组间比较差异无统计学意义( $P>0.05$ ), 但研究组子宫内膜血流改善显著, 差异有统计学意义( $P<0.05$ ); 研究组生化妊娠率、临床妊娠率、种植率、活产率略高于对照组, 但差异无统计学意义( $P>0.05$ )。结论: 对于POR患者, GH改善了子宫内膜血流, 可能提高了子宫内膜容受性, 但对妊娠结局没有改善。

**关键词:** 拮抗剂方案; 生长激素(GH); 体外受精-胚胎移植(IVF-ET); 卵巢低反应(POR); 子宫内膜容受性

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• 临床报道 •

## Application of growth hormone to the poor ovarian responders during *in vitro* fertilization and embryo transfer antagonist protocol

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**【ABSTRACT】 Objective:** To investigate the influence of applying the growth hormone (GH) to the endometrial receptivity and the outcome of pregnancy to the poor ovarian responders during *in vitro* fertilization and embryo transfer (IVF-ET) antagonist protocol. **Methods:** A total of 188 patients undergoing IVF-ET were collected and analyzed who all had poor ovarian response (POR) and antagonist protocol. Among them, 98 cases added GH were served as research group, other 90 patients without addition of GH were acted as control group. **Results:** The duration of gonadotropin treatment, duration of GnRH antagonist treatment, and dose of gonadotropin were significantly lower in research group than in control group, while the mean E<sub>2</sub> levels on the day of hCG administration, number of retrieved oocytes, number of metaphase II oocytes, numbers of fertilized oocytes and high-quality embryos were significantly higher in research group than in control group; there was no significant difference between the two groups with regard to endometrial thickness on injection day, but the endometrial blood flow was significantly improved in research group, the difference was statistically significant; the biochemical pregnancy rate, the clinical pregnancy rate, the implantation rate and the live birth rate in research group were higher than those in control group, but the difference was not statistically significant. **Conclusion:** GH can improve the endometrial blood flow and maybe increase the endometrial receptivity, but the outcome of pregnancy is not improved in poor ovarian responders.

**Key words:** antagonist protocol; growth hormone (GH); *in vitro* fertilization and embryo transfer (IVF-ET); poor ovarian response (POR); endometrial receptivity

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本课题为广西医疗卫生重点项目(体外受精与胚胎移植相关研究), 项目号: 重200101  
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## 2 294 例生殖异常者的染色体核型分析

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**【摘要】**目的: 探讨生殖异常者与染色体核型异常的关系。方法: 对 2 294 例生殖异常者的外周血进行培养并行常规 G 显带、核型分析。结果: 2 294 例生殖异常者中检出 221 例染色体核型异常, 核型异常率为 9.63%, 其中常染色体结构异常 33 例, 性染色体数目异常 26 例, 性染色体结构或功能异常 6 例, 染色体多态性核型 156 例。结论: 染色体核型异常是导致生殖异常的重要原因。

**关键词:** 染色体; 生殖异常; 核型; 染色体多态

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## **Analysis of chromosome karyotype of 2 294 cases with reproduction abnormalities**

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**【ABSTRACT】 Objective:** To discuss the relationship between reproduction abnormality and chromosome karyotype. **Methods:** Chromosome karyotypes and clinical data of 2 294 patients with reproduction abnormalities during the last four years were analyzed. **Results:** In 2 294 patients with reproduction abnormality, 221 cases were of abnormal chromosome karyotype, the abnormal chromosome karyotype rate was 9.63%. Among 221 cases, 33 cases were of abnormal euchromosome structure, 26 cases were of abnormal sex chromosome number, 6 cases were of abnormal sex chromosome structure or function, and 156 cases were of chromosome polymorphism karyotype. **Conclusion:** Chromosome karyotype abnormality is one of the important factors in patients with reproduction abnormality. It is necessary for patients with reproduction abnormality to take chromosome karyotype examination.

**Key words:** chromosome; reproduction abnormality; karyotype; chromosome polymorphism

# 交互式群组管理对 IVF-ET 患者 精神健康的影响

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**【摘要】**目的: 探讨交互式群组管理对体外受精-胚胎移植(IVF-ET)患者精神健康的影响。方法: 将接受 IVF-ET 的 80 例患者随机分为试验组和对照组, 各 40 例, 试验组接受交互式群组管理, 对照组接受常规护理。采用焦虑自评量表(SAS)、抑郁自评量表(SDS)及生活质量评定量表(SF-36)测评患者的精神健康状态。结果: 在促排卵和移植术后 15 d 内的 SAS、SDS 量表评分, 试验组明显低于对照组( $P < 0.05$ ), 而 SF-36 量表评分, 试验组明显高于对照组( $P < 0.05$ )。结论: 交互式群组管理可以对 IVF-ET 患者的精神健康产生重大影响, 降低焦虑、抑郁水平, 提高患者的生活质量和健康水平。

**关键词:** 交互式群组管理; 体外受精-胚胎移植(IVF-ET); 精神健康

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## Effects of interactive group visits of mental health in patients with IVF-ET

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**【ABSTRACT】Objective:** To explore effects of interactive group visits on mental health in patients with *in vitro* fertilization and embryo transfer (IVF-ET). **Methods:** Eighty patients with IVF-ET were assigned to two groups according to the computer-generated random numbers. The patients in experimental group ( $n=40$ ) received interactive group visits while the patients in control group ( $n=40$ ) received routine health education. **Results:** Patients in experimental group had significantly lower SAS/SDS scale score than those in control group ( $P<0.05$ ). The SF-36 scale score, however, was significantly higher in experimental group than in control group during ovarian stimulation and 15 d after embryo transplantation ( $P<0.05$ ). **Conclusion:** Interactive group visits can be effective for IVF-ET patients' mental health, reduce the level of anxiety or depression, and improve the patient's quality of life and health level.

**Key words:** interactive group visits; *in vitro* fertilization and embryo transfer (IVF-ET); mental health

# 体外受精 - 胚胎移植患者心理因素 与妊娠结局的调查

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**【摘要】**目的: 探讨体外受精 - 胚胎移植(IVF-ET)患者心理因素与妊娠结局的关系。方法: 以康奈尔医学指数(CMI)为效标对 180 名 IVF-ET 患者进行心理评估。结果: CMI 得分与妊娠结局分析具有统计学意义( $P < 0.05$ ), Logistic 回归分析结果提示, IVF-ET 患者经济收入及 CMI 测评得分是患者妊娠成功的主要影响因素。结论: 通过对患者心理状态评估, 给予适当的护理、医疗干预, 可以提高患者身心治疗的积极性和依从性, 最终提高妊娠成功率。

**关键词:** 体外受精 - 胚胎移植(IVF-ET); 心理因素; 评估

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## A survey of psychological factors and pregnancy outcomes in *in vitro* fertilization-embryo transfer patients

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**【ABSTRACT】 Objective:** To investigate the association between psychological factors and successful pregnancy rate among *in vitro* fertilization and embryo transfer (IVF-ET) patients. **Methods:** Cornell medical index (CMI) was used as the criterion indicator to assess the psychological risk in 180 patients undergoing IVF-ET. Data were analyzed by  $\chi^2$  test and Logistic regression. **Results:** CMI scores had a significant association with pregnancy outcomes ( $P<0.05$ ). Economic factor and CMI assessment score were the main factors affecting the success of the patients with pregnancy. **Conclusion:** Evaluating psychological state of patients undergoing IVF-ET and providing proper medical care and intervention can improve patients' the enthusiasm and compliance of patients, eventually improve the success rate of pregnancy.

**Key words:** *in vitro* fertilization-embryo transfer (IVF-ET); psychological factor; assessment

# 超声评价疤痕妊娠子宫动脉栓塞后的疗效

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**【摘要】**目的: 探讨彩色多普勒超声检查对子宫疤痕妊娠病例子宫动脉栓塞术疗效评估的价值。方法: 收集行子宫动脉栓塞术治疗的子宫疤痕妊娠病例 60 例, 通过二分类变量 Logistic 回归分析筛选出子宫动脉栓塞术后行刮宫术治疗效果的影响因素。结果: Logistic 回归分析显示: 妊娠物距浆膜层距离比数比(OR)为 0.162 及血管阻力指数(RI)OR<0.001 为影响子宫动脉栓塞术后行刮宫术疗效的因素。结论: 彩色多普勒超声检查是评估子宫疤痕妊娠行子宫动脉栓塞术合并刮宫术疗效的有效方法。

**关键词:** 彩色多普勒超声; 子宫动脉栓塞术; 剖宫产疤痕; Logistic 回归

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## Discussion on color Doppler flow imaging in treatment of caesarean scar pregnancy after uterine artery embolization

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**【ABSTRACT】 Objective:** To evaluate the effect of caesarean scar pregnancy treated after uterine artery embolization by color Doppler flow imaging. **Methods:** Sixty cases of pregnancy located at the uterine incision after cesarean section performed by uterine artery embolization were collected. The binary Logistic regression was used in the analysis of influence factors. **Results:** Two factors entered Logistic regression model. They were distance between mass and serosa ( $OR=0.162$ ) and resistant index (RI) ( $OR<0.001$ ). **Conclusion:** Ultrasound is valuable in judging the effect of uterine artery embolization combined with dilation and curettage in caesarean scar pregnancy.

**Key words:** color Doppler flow imaging; uterine artery embolization; cesarean section scar; Logistic regression