

• 实验研究 •

长期进食高糖饲料对雌性小鼠卵泡超微结构的影响

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【摘要】目的: 探讨长期进食高糖饲料对雌性小鼠卵泡超微结构的影响。方法: 将40只4周龄的C57BL/6J的雌性小鼠随机分为正常饲料组20只和高糖饲料组20只, 分别连续喂养180 d后, 测量雌性小鼠体质量、血清性激素、糖代谢指标、动情周期和各级卵泡数目。应用电子显微镜观察雌性小鼠卵泡的超微结构。结果: 长期进食高糖饲料的雌性小鼠体质量明显增加($P<0.05$), 血清雌二醇(E_2)水平升高(82.05 ± 15.62 ng/L vs 68.25 ± 4.90 ng/L, $P<0.05$), 空腹胰岛素显著升高(64.11 ± 39.97 mIU/L vs 14.25 ± 7.33 mIU/L, $P<0.05$), 动情周期延长(10.3 ± 1.5 d vs 6.0 ± 0.9 d, $P<0.01$), 其中动情前期(2.3 ± 0.6 d vs 1.3 ± 0.4 d, $P<0.05$)、动情后期(3.0 ± 0.8 d vs 1.0 ± 0.3 d, $P<0.001$)及动情间期延长(2.7 ± 0.9 d vs 1.3 ± 0.5 d, $P<0.01$)更显著, 窦前卵泡和窦卵泡数目均显著减少($P<0.05$)。长期进食高糖饲料的小鼠卵泡颗粒细胞发生凋亡; 部分卵母细胞核染色质排列紊乱; 卵母细胞内线粒体增生水肿; 高尔基体结构异常; 透明带形态及厚度异常; 卵母细胞微绒毛明显减少。结论: 长期进食高糖饲料小鼠体质量增加, E_2 水平升高, 动情周期延长, 卵泡中的卵母细胞和颗粒细胞超微结构受损。

关键词: 饮食; 高糖; 卵泡; 超微结构

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Influence of long-term exposure to high sugar diet on follicle ultrastructure of female mice

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【ABSTRACT】 Objective: To investigate the effect of long-term exposure to high sugar (HS) diet on follicle ultrastructure of female mice. **Methods:** Forty C57BL/6J female mice with 4 weeks old were divided into normal diet group and HS diet group, with twenty female mice per group. All mice were fed continuously for 180 d. The body weight, sex hormones, indexes of glucose metabolism, estrus cycle and numbers of follicles at all levels were detected. The ultrastructure of oocytes and granulosa cells (GCs) were observed by electron microscope. **Results:** The female mice with HS diet for 180 d showed significantly heavier body weight ($P<0.05$), higher serum E_2 level (82.05 ± 15.62 ng/L vs 68.25 ± 4.90 ng/L, $P<0.05$) and higher fasting insulin (64.11 ± 39.97 mIU/L vs 14.25 ± 7.33 mIU/L, $P<0.05$) compared with normal diet group. They also exhibited an extended estrous cycle (10.3 ± 1.5 d vs 6.0 ± 0.9 d, $P<0.01$) and prolonged proestrus (2.3 ± 0.6 d vs 1.3 ± 0.4 d, $P<0.05$), metestrus (3.0 ± 0.8 d vs 1.0 ± 0.3 d, $P<0.001$) and diestrus (2.7 ± 0.6 d vs 1.3 ± 0.5 d, $P<0.01$) phases significantly. The numbers of preantral follicles and antral follicles were significantly decreased ($P<0.05$). The follicle ultrastructure in the mice with HS diet showed GCs apoptosis, nucleus chromatin of part oocyte disordered arrangement, mitochondria hyperplasia and edema, Golgi structural abnormalities. The zona pellucid had abnormal shape or thickness, and the microvillous on the luminal surface of the oocyte and GCs were rare or completely disappeared. **Conclusion:** The body weight was heavier, the serum concentration of E_2 was increased, and the ultrastructure of oocytes and GCs were damaged in the mice with a long-term exposure to HS diet compared with normal diet group.

Key words: diet; high sugar (HS); follicle; ultrastructure

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Girdin 蛋白在小鼠受精卵微丝聚集 调控作用的初步研究

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【摘要】目的: 探讨 Girdin 蛋白在调控小鼠受精卵早期发育微丝聚集中的作用。方法: 采用免疫荧光染色观察 Girdin 蛋白和 F-actin 在小鼠受精卵中的共定位情况。激光共聚焦显微镜观察 Girdin 表达敲低后小鼠受精卵分裂形态及分裂率。结果: 在小鼠受精卵中存在 Girdin 蛋白并且 Girdin 蛋白与 F-actin 存在共定位。敲低 Girdin 蛋白的表达, 小鼠受精卵出现不规则分裂, 10 $\mu\text{mol/L}$ Girdin siRNA 处理组小鼠受精卵有 28.93% 到达 2- 细胞期, 而注射 20 $\mu\text{mol/L}$ Girdin siRNA 组小鼠受精卵只有 15.1% 到达 2- 细胞期。并且 Girdin 表达敲低的受精卵微丝不能正确聚集。结论: Girdin 蛋白在调控小鼠受精卵早期分裂微丝聚集中发挥作用。

关键词: Girdin 蛋白; F-actin; 小鼠受精卵; 激光共聚焦显微镜

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Girdin is essential for rearrangement of the F-actin cytoskeleton and the development of mouse fertilized eggs

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【ABSTRACT】 Objective: To investigate the role of Girdin protein in the regulation of aggregation of actin filaments in mouse fertilized eggs. **Methods:** We used double-labeled eggs for both Girdin and F-actin to examine their colocalization by immunofluorescence confocal microscopy. The functions of Girdin on the remodeling of the actin cytoskeleton and the development of mouse fertilized eggs were examined. RNA mediated interference (RNAi) was used to knockdown the expression of Girdin in mouse fertilized eggs and Laser confocal scanning was used to observe the morphology and percentage of division. **Results:** Our data demonstrated for the first time the expression and localization of Girdin protein and its colocalization with F-actin in the mouse fertilized eggs. Staining of F-actin-rich structures with phalloidin revealed that F-actin was disrupted in the Girdin siRNA-transfected mouse fertilized eggs. Moreover, F-actin rich structures lost their shape and formed rugged boundaries that gave rise to the formation of multiple protrusions. **Conclusion:** Girdin is essential for rearrangement of F-actin filaments.

Key words: Girdin; F-actin; mouse fertilized eggs; laser confocal scanning microscopy

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• 临床研究 •

克罗米芬联合高孕激素促排卵抑制早发 LH 峰 的临床结局研究

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【摘要】目的: 探讨在控制性超促排卵中克罗米芬(CC)联合高孕激素促排卵方案抑制早发 LH 峰的临床效果。方法: 回顾性分析 126 名行体外受精/卵胞质内单精子显微注射(IVF/ICSI)取卵周期的患者, 分为 CC 联合高孕激素促排卵组(试验组, $n=63$)和短方案治疗组(对照组, $n=63$)。观察过早 LH 峰发生率、促排卵中 Gn 用量和用药天数、获卵数、成熟卵数、内分泌及胚胎试验室结果。结果: 试验组获卵数、成熟卵数、有效胚胎数、生化妊娠率、临床妊娠率、胚胎种植率与对照组比较均无统计学差异($P<0.05$)。所有对象在促排卵过程中未监测到早发 LH 峰, 试验组月经第 9~10 日和诱发排卵日 LH 水平与基础值间无统计学差异($P<0.05$)。试验组 Gn 用量和用药天数均高于对照组($P<0.05$)。结论: CC 联合高孕激素促排卵方案可以有效抑制早发 LH 峰, 促排卵过程中 LH 水平平稳, 且可以获得有发育潜能的胚胎。

关键词: 安宫黄体酮(MPA); 早发 LH 峰; 克罗米芬(CC); 控制性超促排卵(COH);
冻融胚胎移植(FET)

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Effect of progestin-primed ovarian stimulation in combination with clomiphene citrate to prevent LH surges in normal ovulatory women undergoing IVF/ICSI-FET treatments

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【ABSTRACT】 Objective: To explore whether progestin-primed ovarian stimulation (PPOS) in combination with clomiphene citrate (CC) can be used clinically to prevent LH surges in controlled ovarian hyperstimulation (COH) for *in vitro* fertilization/intercytoplasmic sperm injection (IVF/ICSI) cycle. **Methods:** A retrospective study was performed in 136 patients with normal ovarian reserve. They were divided into two groups according to the protocol used: group A with human menopausal gonadotropin (hMG) + medroxyprogesterone 17-acetate (MPA)+CC ($n=63$); group B with the short protocol ($n=63$). The incidence of premature LH surge, dosage and durations of hMG administered, the number of oocytes retrieved, the number of mature oocytes, the number of fertilization and cleavage, hormone profiles and pregnancy outcomes from FETs were compared between the two groups. **Results:** The number of oocytes retrieved, the number of mature oocytes, the number of fertilization and cleavage in group A were similar to those in group B. No premature LH surges were detected in both groups. In group A, LH levels on menstruation day 9–10 and on the trigger day during the stimulation were not significantly different from the basic level. The dosage and the duration of hMG administered were higher in group A than in group B. **Conclusion:** PPOS in combination with CC can effectively prevent premature LH surge, and the LH levels change smoothly and developmental potential embryos can be obtained during ovarian stimulation.

Key words: medroxyprogesterone 17-acetate (MPA); premature LH surge; clomiphene citrate (CC); controlled ovarian stimulation (COS); frozen-thawed embryo transfer (FET)

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PCOS 患者移植冻融胚胎后妊娠结局

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【摘要】目的: 探讨多囊卵巢综合征(PCOS)患者在优质冻融胚胎移植(FET)后是否有更高的妊娠丢失率。方法: 回顾性分析诊断为PCOS并初次接受体外受精-胚胎移植(IVF-ET)或卵胞质内单精子注射(ICSI)FET的患者, 选择移植冻融胚胎中含有卵裂期优质胚胎且生化妊娠阳性的157个周期的临床资料为PCOS组, 同期年龄、体质量指数(BMI)、不孕年限与PCOS组匹配的、因单纯输卵管因素接受IVF-ET助孕治疗并生化妊娠阳性的389个FET周期的临床资料为对照组, 比较组间的生化妊娠丢失率、早期流产率、晚期流产率、活产率。结果: 在接受优质卵裂期FET的PCOS患者妊娠后, 生化妊娠丢失率、早期流产率、晚期流产率、活产率与对照组相比(8.28% vs 5.14%、7.64% vs 8.13%、6.94% vs 5.15%、79.86% vs 84.28%), 差异无统计学意义($P>0.05$)。结论: 在固定胚胎质量这个重要的影响妊娠早期丢失的影响因子的基础上, 排除年龄、BMI、自然流产次数、是否多胎妊娠、移植日内膜厚度等影响因素的干扰, 患PCOS并不增加IVF/ICSI的生化妊娠丢失率和临床妊娠流产率。

关键词: 多囊卵巢综合征(PCOS); 优质胚胎; 冻融胚胎移植(FET); 妊娠丢失

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Pregnancy outcome after transplantation of frozen-thawed high-quality embryo in PCOS patients

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【ABSTRACT】 Objective: To observe whether polycystic ovary syndrome (PCOS) patients have higher pregnancy loss rate than non-PCOS patients after transplantation of frozen-thawed high-quality embryos. **Methods:** A retrospective analysis was performed among the PCOS patients who accepted the *in vitro* fertilization/intracytoplasmic sperm injection and embryo transfer (IVF/ICSI-ET) and received frozen-thawed high-quality embryo transplantation for the first time. A total of 157 PCOS women who were transplanted with frozen-thawed high-quality cleavage embryos and got positive biochemical pregnancy were included. And 389 cases who received IVF because of tubal obstructive infertility simply and got positive biochemical pregnancy over the same period were as controls whose age, body mass index (BMI), infertility duration matched with the PCOS group. The biochemical pregnancy loss rate, early abortion rate, late abortion rate and live birth rate between the two groups were compared. **Results:** After transplantation of high-quality frozen-thawed day 3 embryos, there were no significant differences in biochemical pregnancy loss rate, early abortion rate, late abortion rate and live birth rate between PCOS group and control group (8.28% vs 5.14%, 7.64% vs 8.13%, 6.94% vs 5.15%, 79.86% vs 84.28%)($P>0.05$). **Conclusion:** Conditioned by fixed embryo quality which was the important index influencing abortion rate, and excluded the interference of age, BMI, number of spontaneous abortion, multiple pregnancies, endometrial thickness on transplantation day and so on, PCOS does not increase biochemical pregnancy rate and clinical abortion rate after transplantation of frozen-thawed embryo during IVF/ICSI.

Key words: polycystic ovary syndrome (PCOS); high-quality embryo; frozen-thawed embryo transfer (FET); pregnancy loss

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控制性超促排卵周期多囊卵巢综合征患者生长分化因子-9和骨形成蛋白-15的初步研究

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【摘要】目的: 探讨控制性超促排卵(COH)周期多囊卵巢综合征(PCOS)患者卵巢颗粒细胞生长分化因子-9(GDF-9)、骨形成蛋白-15(BMP-15)的表达及其与体外受精-胚胎移植(IVF-ET)治疗结局的关系。方法: 选择接受IVF-ET治疗的PCOS患者45例, 同期输卵管因素不孕患者103例作为对照组。应用免疫组织化学、Real-time PCR技术检测患者卵巢颗粒细胞GDF-9、BMP-15蛋白和mRNA的表达, 并分析与IVF-ET的临床结局关系。结果: GDF-9、BMP-15蛋白在PCOS组和对照组患者卵巢颗粒细胞胞质均呈阳性表达, PCOS患者颗粒细胞GDF-9 mRNA、BMP-15 mRNA的表达水平低于对照组, 差异有统计学意义($P < 0.01$)。多元线性回归分析显示, 颗粒细胞GDF-9 mRNA、BMP-15 mRNA表达水平与优质胚胎数呈正相关关系($P < 0.05$)。临床妊娠组的颗粒细胞GDF-9 mRNA、BMP-15 mRNA表达水平高于未妊娠组($P < 0.05$)。结论: COH周期PCOS患者颗粒细胞GDF-9 mRNA、BMP-15 mRNA表达水平可能与胚胎发育潜能存在相关性。

关键词: 生长分化因子-9(GDF-9); 骨形成蛋白-15(BMP-15); 多囊卵巢综合征(PCOS); 控制性超促排卵(COH); 胚胎发育

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Expression of growth differentiation factor 9 and bone morphogenetic protein 15 in patients with polycystic ovary syndrome during controlled ovarian hyperstimulation cycles

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【ABSTRACT】 Objective: To explore the expression levels of growth differentiation factor 9 (GDF-9) and bone morphogenetic protein 15 (BMP-15) in granulosa cells of patients with polycystic ovary syndrome (PCOS) during controlled ovarian hyperstimulation (COH) cycles and the relationship between the expression levels of above two genes and the outcomes of *in vitro* fertilization and embryo transfer (IVF-ET). **Methods:** Totally 43 PCOS patients and 103 infertile cases due to tubal factors who underwent IVF-ET at the same period were recruited as the experimental group and control group, respectively. Immunocytochemistry and Real-time PCR were used to detect the expression levels of GDF-9, BMP-15 proteins and their mRNA in granulosa cells of the two groups, respectively. And their relationship with the outcomes of IVF-ET was analyzed. **Results:** Both GDF-9 and BMP-15 proteins were detected in the cytoplasm of granulosa cells in the two groups. The expression levels of *GDF-9*, *BMP-15* mRNA in granulosa cells in PCOS group were significantly lower than those in control group ($P<0.01$). Multivariate linear analysis discovered that *GDF-9*, *BMP-15* mRNA levels were positively associated with the number of high-quality embryos ($P<0.05$). The expression levels of *GDF-9* and *BMP-15* mRNA in pregnancy group were significantly higher than those in non-pregnancy group ($P<0.05$). **Conclusion:** *GDF-9*, *BMP-15* mRNA levels in granulosa cells of PCOS patients during COH cycles may be associated with embryo developmental potential.

Key words: growth differentiation factor 9 (GDF-9); bone morphogenetic protein 15 (BMP-15); polycystic ovary syndrome (PCOS); controlled ovarian hyperstimulation (COH); embryo development

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输卵管积液超声介入硬化治疗 对冻融胚胎移植结局的影响

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【摘要】目的: 探讨超声介入硬化治疗输卵管积液对冻融胚胎移植(frozen-thawed embryo transfer, FET)周期妊娠结局的影响。方法: 回顾性分析输卵管积液的输卵管性不孕接受体外受精-胚胎移植(IVF-ET)未妊娠或未移植且有冷冻胚胎的患者FET周期的临床资料, 按积液的处理方式分组: A组(观察组)121个周期, FET前行超声介入硬化治疗; B组(对照组)60个周期, FET前行输卵管近端结扎。结果: A、B组胚胎种植率(20.06% vs 20.63%)、临床妊娠率(40.50% vs 38.33%)、流产率(14.29% vs 13.04%)、异位妊娠率(6.12% vs 0.00%)组间差异均无统计学意义($P>0.05$)。结论: 输卵管积液超声介入硬化治疗可获得与输卵管近端结扎治疗近似的FET临床结局, 且简单、经济、基本无创。

关键词: 输卵管积液; 冻融胚胎移植(FET); 超声介入硬化治疗; 妊娠结局

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Effects of interventional ultrasound sclerotherapy on pregnancy outcomes of the women with hydrosalpinx in the frozen-thawed embryo transfer cycles

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【ABSTRACT】 Objective: To investigate the effects of interventional ultrasound sclerotherapy on the pregnancy outcomes of the women with hydrosalpinx in frozen-thawed embryo transfer (FET) cycles. **Methods:** The data of 181 FET cycles with tubal infertile women were analyzed retrospectively. All of the 181 cycles with hydrosalpinx under hysterosalpingography (HSG) and ultrasonography were divided into two groups. Group A (study group, 121 cycles) were pretreated with interventional ultrasound sclerotherapy, and group B (control group, 60 cycles) were pretreated with proximal tubal ligation / distal tubal ostomy. **Results:** There were no significant differences in the embryo implantation rate (20.06% vs 20.63%), the clinical pregnancy rate (40.50% vs 38.33%), the abortion rate (14.29% vs 13.04%) and the ectopic pregnancy rate (6.12% vs 0.00%) between groups A and B ($P>0.05$). **Conclusion:** Interventional ultrasound sclerotherapy could obtain similar pregnancy outcomes as proximal tubal ligation / distal tubal ostomy in FET cycles with the advantage of simple, lower cost and less invasion.

Key words: hydrosalpinx; frozen-thawed embryos transfer (FET); interventional ultrasound sclerotherapy; pregnancy outcome

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• 循证医学 •

激光辅助孵化对胚胎移植妊娠结局影响的 Meta 分析

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【摘要】目的: 探究激光辅助孵化(LAH)对行胚胎移植不孕患者妊娠结局的影响。方法: 计算机检索 PubMed、OvidSP、Medline、Cochrane Library、CNKI、CBM、万方和维普等数据库, 纳入 LAH 与其他多种辅助孵化方法和不作任何处理组比较的随机对照试验(RCT), 检索年限截至 2015 年 10 月, 语言不限, 按照 Cochrane 协作组建议对纳入文献行质量评价和异质性分析, 数据分析采用 RevMan 5.3.5 软件。结果: 纳入 25 个 RCT; 激光组分别与酸化组、机械组和对照组(不作任何处理)进行比较, 继续妊娠率、流产率、活产率等差异均无统计学意义($P>0.05$); 对选择行冻融胚胎移植(FET)的患者, 激光组较对照组有较高的种植率及临床妊娠率, 差异有统计学意义($P<0.000\ 01$; $P<0.05$); 但多胎率显著增加($P<0.05$)。结论: 对选择行 FET 的患者, LAH 较不做任何处理更有优势, 可以提高种植率和临床妊娠率, 值得推广及应用, 但 LAH 会增加多胎发生的风险。

关键词: 激光辅助孵化(LAH); 妊娠; 种植率; 临床妊娠率; Meta 分析

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Impact of laser-assisted hatching on pregnancy outcome: a Meta-analysis

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【ABSTRACT】 Objective: To evaluate the impact of laser-assisted hatching (LAH) on pregnancy outcome of infertile patients. **Methods:** Well-known databases at home and abroad were searched, then randomized controlled trials (RCTs) concerning the impact of LAH and non-LAH on pregnancy outcome were analyzed. Quality and heterogeneity of the articles were screened, and then relative risk (*RR*) was served as effective size to merge the studies. **Results:** Twenty-five relevant RCTs studies were included. There were no significant differences in the ongoing pregnancy rate, the miscarriage rate and the live birth rate ($P>0.05$). But for the frozen-thawed embryo of patients, LAH group could significantly improve the implantation rate and the clinical pregnancy rate ($P<0.000\ 01$; $P<0.05$) compared with control group. In addition, LAH can increase the incidence of multiple pregnancies ($P<0.05$). **Conclusion:** For the frozen-thawed embryo of patients, LAH was worthy to be popularized and applied and LAH can increase the incidence of multiple pregnancies.

Key words: laser-assisted hatching (LAH); pregnancy; implantation rate; clinical pregnancy rate; Meta-analysis

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卵巢生殖干细胞的研究进展

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【摘要】 越来越多的研究表明, 从雌性哺乳动物和人卵巢表面上皮细胞中能够分离出少量端粒酶活性高、表达干性标志且能被诱导发育成为卵母细胞样的卵巢干细胞, 即生殖干细胞(GSCs)。体内移植后, 可使不孕小鼠产生排卵, 生育后代。GSCs可能在维持出生后卵泡的再生与修复中发挥重要作用。然而, GSCs的研究还存在一些缺陷和存在性的直接证据。本文主要对卵巢GSCs的研究进展和潜在的应用前景进行了综述。

关键词: 生殖干细胞 (GSCs); 卵巢; 卵巢表面上皮; 卵母干细胞

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Research progress of ovarian germline stem cells

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【ABSTRACT】 Studies have shown that a bit of ovary stem cells were isolated from female mammal and human epithelial cells of the ovary surface. These ovary stem cells have high telomerase activity, and express some of stemness markers. The ovary stem cells can be induced to develop into oocyte-like *in vitro*. After the oocyte-like cells were transplanted, infertile mice could cause ovulate, then produced offspring. Researchers believe that the kind of ovary stem cells precisely is germline stem cells (GSCs). They may play an important role in maintain of follicle's regeneration and repairmen after birth. Nevertheless, there are still have some deficiencies and lack of more direct evidence *in vivo* about the existence of GSCs. This article review some of research progress and application prospect on ovary GSCs.

Key words: germline stem cells (GSCs); ovary; ovarian surface epithelium; oocyte stem cells

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线粒体疾病的诊疗策略——生殖细胞基因治疗

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【摘要】线粒体疾病是由基因突变导致电子传递链损伤而引起的疾病, 其诊断需要结合临床与实验多方面综合评估, 包括实验室检查、影像学检查、病理组织检查、生物化学检测及基因检测。目前为止, 对线粒体疾病的治疗仅限于症状的缓解和对可治疗症状的治疗, 例如癫痫, 心脏疾病以及糖尿病的早期发现, 包括饮食疗法、抗氧化剂治疗、对症治疗、药物治疗及基因治疗。近年来, 线粒体置换技术越来越受到关注, 该技术包括卵胞质移植(OT)、原核移植(PNT)、中期染色体移植(CT)、生发泡移植(GVT)技术以及极体移植(PBT)等。

关键词: 线粒体疾病; 线粒体 DNA(mtDNA); 线粒体置换; 治疗

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Diagnosis and treatment for mitochondrial diseases

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【ABSTRACT】 Mitochondrial diseases (MD) are caused by genetic mutations that determine an impairment of the electron transport chain functioning. The diagnosis requires a combination of clinical and experimental aspects of the comprehensive evaluation, it includes laboratory test, imaging, histopathologic examination, biochemistry examinations and genetic testing. So far, the treatment of mitochondrial diseases are limited to relieve the symptoms and early detection the treatable symptoms (such as epilepsy, heart disease and diabetes). Therefore, the prevention of mitochondrial disease is particularly important. Recently mitochondrial replacement technology has been attracted more and more attention. The technology includes ooplasmic transfer (OT), pronuclear transfer (PNT), metaphase chromosome transfer (CT), germinal vesicle transfer (GVT) and the polar body transplant (PBT). At present, research on mitochondrial disease is getting more and more attention. The purpose of this review is to introduce the diagnosis and treatment for mitochondrial diseases and various mitochondrial replacement techniques.

Key words: mitochondrial disease; mitochondrial DNA (mtDNA); mitochondrial replacement; treatment

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范可尼贫血基因调节生殖细胞发育的研究进展

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【摘要】从原始到成熟生殖细胞的发育过程中, 生殖细胞是处于DNA复制、链间交换和重组的活跃期, 也是DNA损伤的高峰期。范可尼贫血(*FA*)基因是一组在同源重组修复DNA链间交联损伤中起核心作用的分子。*FA*基因通过促进原始生殖细胞增生, 调控生殖细胞减数分裂的同源重组DNA损伤修复, 抑制减数分裂中交叉形成和促进霍利迪交叉的解除等方面来调节生殖细胞发育。此外, *FA*基因表达影响胚胎质量和参与卵巢衰老的调节; 这些功能的正常运行对保持哺乳动物生殖细胞基因组的稳定性起着至关重要的作用。

关键词: 范可尼贫血(*FA*); DNA 修复; 生殖细胞; 发育

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Current progress in germ cell development regulated by fanconi anemia gene

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【ABSTRACT】 Germ cells are active in DNA replication, strand exchange and recombination from primordial to mature germ cells, which is also the peak of DNA damage. Fanconi anemia (*FA*) gene is a group of molecules that play a key role in the homologous recombination repair of DNA strand damage. *FA* genes regulate germ cell development by promoting the primordial germ cell proliferation, regulating homologous recombination repair of DNA damage in the process of meiosis, inhibiting meiotic crossover formation and promotion of Holliday junction termination. In addition, the expression of *FA* gene affects the quality of the embryo and regulation of ovarian ageing. The normal functions of *FA* gene play an important role in maintaining the stability of the genome of mammalian germ cells.

Key words: fanconi anemia (FA); DNA repair; germ cell; development

多囊卵巢综合征患者的辅助生殖治疗结局

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【摘要】多囊卵巢综合征(PCOS)是育龄期妇女常见的内分泌紊乱性疾病,发病率达6%~10%。由于稀发排卵或无排卵,常常伴发不孕的问题。近年来,辅助生殖技术(ART)越来越多地应用于此类患者。研究表明不同类型的PCOS患者,如肥胖、高促黄体生成激素(LH)、高雄激素及胰岛素抵抗(IR),其ART助孕结局均较非PCOS患者差,虽然发生机制各有特点,但不同的病理生理异常相互作用,最终多反映为卵子质量下降,表现为PCOS患者ART治疗的临床妊娠率低、早期自然流产率高。本文就不同类型的PCOS患者的辅助生殖治疗结局以及影响其结局的因素进行论述,并探讨能够改善PCOS患者辅助生殖治疗结局的措施。

关键词: 多囊卵巢综合征(PCOS); 辅助生殖治疗; 肥胖; 高促黄体生成激素(LH); 高雄激素; 胰岛素抵抗(IR)

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Assisted reproductive technology outcome in women with polycystic ovary syndrome (PCOS)

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【ABSTRACT】 Polycystic ovary syndrome (PCOS) is the most common female endocrine disorder, affecting 6%–10% of women of childbearing age. Due to the dilute ovulation or anovulation, PCOS often associated with infertility problems. In recent years, assisted reproductive technology (ART) is increasingly used in such patients. Studies have shown that different types of PCOS patients, such as obesity, high uteinizing hormone (LH), hyperandrogenism and insulin resistance (IR) in patients with PCOS. The ART outcomes of assisted reproduction were poorer than those in non PCOS patients. Although the mechanisms are variant, different pathophysiological abnormal interactions, which ultimately performance the decline of oocytes quality, the low clinical pregnancy rate, the high rate of early spontaneous abortion of PCOS patients treated with ART. This article will make a review about the ART outcomes of those types of PCOS and explore the way to improve the poor pregnancy rate.

Key words: polycystic ovary syndrome (PCOS); assisted reproductive technology (ART); obesity; high luteinizing hormone (LH); hyperandrogenism; insulin resistance (IR)

• 临床报道 •

多重连接依赖性探针扩增技术在脊髓性肌萎缩症产前诊断中的应用

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【摘要】目的: 探讨多重连接依赖性探针扩增(MLPA)技术在脊髓性肌萎缩症(SMA)产前诊断中的应用价值。方法: 收集3个SMA家系(10例), 采集患儿及其父母的外周血及妊娠11~13⁺6周的绒毛, 提取基因组DNA, 运用MLPA技术进行产前诊断。结果: 3例胎儿均为运动神经元存活基因(SMN)1杂合缺失, SMN2拷贝数正常; 家系I先证者为SMN1纯合缺失及SMN2杂合重复; 3个家系父母均有SMN1杂合缺失, 部分还有SMN2杂合缺失或重复。结论: MLPA技术对SMA的产前诊断具有重要意义, 可为遗传咨询提供可靠信息。

关键词: 脊髓性肌萎缩(SMA); 运动神经元存活基因(SMN); 多重连接依赖性探针扩增(MLPA); 产前诊断; 基因诊断

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Application of multiple ligation-dependent probe amplification in molecular diagnosis and prenatal diagnosis of spinal muscular atrophy

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【ABSTRACT】 Objective: To investigate the application value of multiple ligation-dependent probe amplification (MLPA) technology in the prenatal diagnosis of spinal muscular atrophy (SMA), and then guide the genetic counseling. **Methods:** Peripheral blood samples and 11–13⁺⁶ weeks of pregnancy villi were collected from three pedigrees with SMA. DNA was extracted and then analyzed using MLPA. **Results:** Three fetuses had heterozygous deletion of the survival of motor neuron 1 (*SMN1*) gene and normal copy number of survival of motor neuron 2 (*SMN2*) gene. Proband of family I had homozygous deletion of *SMN1* and homozygous repeat of *SMN2*. All of the parents had heterozygous deletion of the *SMN1*, and part of them had heterozygous deletion or homozygous repeat of *SMN2*. **Conclusion:** MLPA technology is important for prenatal diagnosis of SMA, since it can provide reliable information for genetic counseling.

Key words: spinal muscular atrophy (SMA); survival of motor neuron (*SMN*) gene; multiple ligation-dependent probe amplification (MLPA); prenatal diagnosis; genetic diagnosis

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中药联合西药治疗排卵障碍性不孕症 及对妊娠结局的影响

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【摘要】目的: 探讨温肾活血法结合克罗米芬(CC)联合补佳乐在治疗排卵障碍性不孕症中的疗效。方法: 将排卵障碍性不孕症患者 89 例随机分为 A 组(CC+ 补佳乐)、B 组(温肾活血汤+CC+ 补佳乐)和 C 组(阿司匹林+CC+ 补佳乐) 3 种方案治疗。比较 3 组的排卵率、未破裂卵泡黄素化综合征(LUFS)发生率、妊娠率、流产率, 以经阴道彩色多普勒 B 超测量 3 组治疗前、后的排卵期子宫内膜厚度、子宫动脉阻力指数(RI), 观察内膜容受性。结果: A 组周期排卵率为 79.0%, 妊娠率为 23.3%, 流产率为 28.6%, LUFS 发生率为 14.8%。B 组周期排卵率达 87.6%, 妊娠率为 56.7%, 流产率为 0.0%, LUFS 发生率为 4.1%, C 组周期排卵率为 86.9%, 妊娠率为 44.8%, 流产率为 15.4%, LUFS 发生率为 8.7%, 3 组排卵率无统计学差异($P>0.05$), 3 组妊娠率、流产率比较差异有统计学意义($P<0.05$), 其中, B 组妊娠率最高, 流产率最低, 显著高于 A 组、C 组($P<0.05$), C 组妊娠率高于 A 组, 流产率低于 A 组, 但差异均无统计学意义($P>0.05$)。B 组及 C 组 hCG 注射日子宫内膜厚度及 A 型子宫内膜比例明显高于 A 组($P<0.05$), 子宫动脉 RI 明显低于 A 组($P<0.05$); LUFS 发生率 B 组明显低于 A 组($P<0.05$), C 组略低于 A 组, 但差异无统计学意义($P>0.05$)。结论: 温肾活血法能显著提高 CC 联合补佳乐治疗排卵障碍性不孕症的临床妊娠率, 降低流产率, 其效果好于阿司匹林。其机制主要与中药降低 LUFS 发生率、促进卵泡排出及改善 CC 对子宫内膜容受性的抑制作用有关, 其改善内膜容受性的效果好于阿司匹林。

关键词: 温肾活血法; 促排卵; 子宫内膜容受性; 阿司匹林; 补佳乐

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Clinical efficacy of the Traditional Chinese Medicine (Wenshenhuoxue Tang) with Western Medicine in the treatment of women with ovulation difficulty infertility and the effects on pregnancy outcome

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【ABSTRACT】 Objective: To study the clinical efficacy of the Traditional Chinese Medicine (TCM) (Wenshenhuoxue Tang) associated with clomiphene citrate (CC) and estradiol valerate on treatment for women with ovulation difficulty infertility. **Methods:** A total of 89 women with ovulation difficulty infertility were divided into 3 groups. Group A ($n=30$) was treated with CC (CC+ estradiol valerate), group B ($n=30$) was treated with (CC+TCM+estradiol valerate), group C ($n=29$) was treated with (CC+estradiol valerate+aspirin). The ovulation rate, occurrence of luteinized unrupture follicle syndrome (LUFS), pregnancy rate, miscarriage rate were compared among the three groups. Endometrial thickness and uterine artery resistant index (RI) detected by B ultrasound before and after ovulation were compared to evaluate the endometrial receptivity. **Results:** The ovulation rate, pregnancy rate, abortion rate and LUFS rate in groups A, B, C was 79.0% vs 87.6% vs 86.9%, 23.3% vs 56.7% vs 44.8%, 28.6% vs 0.0% vs 15.4%, and 14.8% vs 4.1% vs 8.7%, respectively. There was no significant difference in ovulation rate among the three groups ($P>0.05$), but there were significant differences in the pregnancy rate and the abortion rate among the three groups ($P<0.05$). In group B, the pregnancy rate was the highest and the abortion rate was the lowest compared with groups A and C ($P<0.05$). The pregnancy rate was higher and the abortion rate was lower in group C than those in group A, but with no significant difference ($P>0.05$). Endometrial thickness on hCG injection day and ratio of type A endometrium were significantly higher in groups B and C than those in group A ($P<0.05$). Uterine artery RI in groups B and C was significantly lower than that in group A ($P<0.05$). LUFS rate in group B was statistically significantly lower than that in group A ($P<0.05$), while LUFS rate in group C was lower than that in group A without no significant difference ($P>0.05$). **Conclusion:** The TCM therapy enhances the pregnant ability and improves an inadequate endometrial development during the course of ovulation induction using CC, and the effect is better than aspirin.

Key words: Traditional Chinese Medicine (TCM); ovulation induction; endometrial receptivity; aspirin; estradiol

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麒麟丸联合左卡尼汀治疗特发性少弱精子症 临床疗效观察

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【摘要】目的: 探讨麒麟丸联合左卡尼汀治疗特发性少弱精子症的效果。方法: 将特发性少弱精子症患者按照数学表法随机分为研究组与对照组各 50 例。对照组给予左卡尼汀口服溶液; 研究组给予麒麟丸联合左卡尼汀, 观察治疗前、后患者的精子质量。结果: 治疗前对照组与研究组精子浓度 $[(13.12 \pm 3.58) \times 10^6/\text{mL}$ vs $(12.34 \pm 3.59) \times 10^6/\text{mL}]$ 、a 级精子活动率 $(12.03\% \pm 5.21\%$ vs $12.31\% \pm 5.43\%)$ 、a+b 级精子比例 $(21.11\% \pm 5.32\%$ vs $22.56\% \pm 4.69\%)$ 相比较, 组间无统计学差异 $(P>0.05)$; 治疗后对照组与研究组精子浓度 $[(14.06 \pm 3.61) \times 10^6/\text{mL}$ vs $(19.18 \pm 6.19) \times 10^6/\text{mL}]$ 、精子活动率 $(68.13\% \pm 11.35\%$ vs $78.62\% \pm 18.37\%)$ 、a 级精子活动率 $(16.24\% \pm 7.98\%$ vs $24.67\% \pm 8.36\%)$ 、a+b 级精子比例 $(29.69\% \pm 8.15\%$ vs $45.27\% \pm 12.53\%)$ 相比较, 治疗组显著优于对照组 $(P<0.05)$ 。结论: 麒麟丸联合左卡尼汀对改善精子浓度、a 级精子活动率、a+b 级精子比例有更好的临床疗效。

关键词: 麒麟丸; 左卡尼汀; 特发性少弱精子症

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Effect of the Qilin pills combined with L-carnitine in the treatment of idiopathic oligoasthenospermia

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【ABSTRACT】 Objective: To investigate the effect of the combination of Traditional Chinese Medicine Qilin pills and L-carnitine on idiopathic oligoasthenospermia. **Methods:** Totally 100 cases of idiopathic oligoasthenospermia patients were divided into study group and control group with 50 cases each. L-carnitine oral solution was given to the control, and Qilin pills combined with L-carnitine was given to the treatment group. Sperm quality was detected between the two groups before and after treatment. **Results:** Before treatment, there were no differences in sperm concentration [$(13.12 \pm 3.58) \times 10^6/\text{mL}$ vs $(12.34 \pm 3.59) \times 10^6/\text{mL}$], a grade sperm rate ($12.03\% \pm 5.21\%$ vs $12.31\% \pm 5.43\%$), a+b grade sperm rate ($21.11\% \pm 5.32\%$ vs $22.56\% \pm 4.69\%$) between control group and treatment group ($P > 0.05$). After treatment, compared with control group, sperm concentration [$(14.06 \pm 3.61) \times 10^6/\text{mL}$ vs $(19.18 \pm 6.19) \times 10^6/\text{mL}$], sperm activity rate ($68.13\% \pm 11.35\%$ vs $78.62\% \pm 18.37\%$), a grade sperm rate ($16.24\% \pm 7.98\%$ vs $24.67\% \pm 8.36\%$), a+b grade sperm rate ($29.69\% \pm 8.15\%$ vs $45.27\% \pm 12.53\%$) in the study group were significantly higher than those in the control ($P < 0.05$). **Conclusion:** Qilin pills combined with L-carnitine to improve sperm concentration, sperm activity rate, a + b grade sperm rate has a better clinical curative effect.

Key words: Qilin pills; L-carnitine; idiopathic oligoasthenozoospermia