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· 临床研究 ·

子宫内膜异位症相关性不孕卵泡液代谢物组初筛及其与卵母细胞质量的关系

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【摘要】目的 探讨与子宫内膜异位症(EMS)相关性不孕患者卵母细胞发育潜能相关的代谢物组。**方法** 利用超高效液相色谱-质谱(HPLC-MS)对接受体外受精(IVF)的 EMS 相关性不孕患者即 EMS 组($n=27$)和同期因男方因素行体外受精的健康妇女即对照组($n=28$)进行卵泡液代谢组学分析。**结果** 共观察到与 EMS 相关性不孕密切相关的差异代谢物 28 种, 主要有脂类、核苷酸类、蛋白降解片段及其它等四大类, 其中上调的代谢物主要有 Valyl-Arginine、Methyl-15-cyanopentadecanoate、4-Oxo-13-cis-retinoate 等 15 种; 下调的代谢物主要有 Menadiol dibutyrate、3-hydroxynonanoyl carnitine、Phytosphingosine 等 13 种。**结论** 本研究发现并描绘出两组卵泡液差异性代谢物谱, 这 28 种代谢物组可能成为预测 EMS 妇女卵母细胞早期发育潜能的重要生物标志物。然而, 并未见其与随后的胚胎质量、累积妊娠率以及活产率间明显的相关性。

【关键词】 子宫内膜异位症(EMS); 不孕症; 卵泡液代谢组学; 卵母细胞质量

基金项目: 国家自然科学基金(面上项目)(81373676, 81674018)

· 临床研究 ·

Preliminary screening of metabolites of follicular fluid in endometriosis-related infertility and its relationship with oocyte quality

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【Abstract】Objective To investigate metabolites associated with oocyte developmental potential in infertile patients with endometriosis (EMS). **Methods** The metabolic analysis of follicular fluid was performed on 27 EMS-related infertility patients receiving *in vitro* fertilization (observation group) and 28 healthy women who underwent IVF due to male factor (control group) by ultra performance liquid chromatography-mass spectrometry (HPLC-MS). **Results** There were 28 metabolites, which were closely related to infertility associated with EMS. They were divided into four categories, including lipids, nucleotides, protein degradation fragments and the others. Fifteen metabolites such as Valyl-Arginine, Methyl-15-cyanopentadecanoate and 4-Oxo-13-cis-retinoate were up-regulated; Menadiol dibutyrate, 3-hydroxy pentanoyl carnitine, Phytosphingosine and other 13 metabolites were down-regulated. **Conclusions** In this study, we found and mapped the differential metabolite profiles of follicular fluid in the two groups, which may be an important biomarker for predicting the early developmental potential of EMS women oocytes. However, we did not find a significant correlation between subsequent embryonic quality, cumulative pregnancy rate and live birth rate.

【Key words】 Endometriosis; Infertility; Follicular fluid metabolomics; Oocyte quality

Fund program: National Natural Science Foundation of China (Surface project) (81373676, 81674018)

· 临床研究 ·

米非司酮顿服后不同时间对早孕蜕膜形态及类固醇受体表达的影响

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【摘要】目的 探讨药物流产中缩短米非司酮用药时间的可行性。**方法** 将 80 例因非意愿妊娠自愿要求终止早孕的女性随机分为 4 组: 对照组(直接负压吸宫术)、用药后 12 h 组、24 h 组、48 h 组, 3 个用药组顿服米非司酮 150 mg, 于不同时间行负压吸引术, 留取各组蜕膜组织。应用光学显微镜、透射电子显微镜观察 4 组蜕膜组织的形态学改变, 应用免疫组织化学方法和计算机图像分析系统检测四组蜕膜组织中类固醇受体的表达。**结果** 3 个用药组蜕膜细胞变性、坏死, 间质水肿、出血, 毛细血管扩张充血。对照组蜕膜组织中雌激素受体(ER)和孕激素受体(PR)阳性染色位于大部分蜕膜细胞及少数腺上皮细胞, 用药后 12 h 组、24 h 组、48 h 组蛋白表达均低于对照组, 差异有统计学意义($P < 0.05$), 而这 3 组之间无统计学差异($P > 0.05$)。**结论** 米非司酮用药后 12 h 蜕膜组织变性坏死, 蛋白表达受到抑制, 为临床缩短药物流产用药时间提供了一定的理论参数。

【关键词】 米非司酮; 不同时间; 蜕膜组织; 类固醇受体; 超微结构

基金项目: 2017 年河北省医学科学研究重点课题计划(20170254)

· 临床研究 ·

Effects of shortening the time of mifepristone on the ultrastructure and the expression of steroid receptors in human decidua tissue in early pregnancy Han Hua, Li Yanli, Zhao Hongwei, Wang Jie, Yan Ping

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【Abstract】 Objective To explore the feasibility of shortening the time of mifepristone in abortion. **Mehtods** Eighty women who desired to terminate the early pregnancy were divided into four groups: control group, 12 h group, 24 h group, 48 h group. The decidua tissues were collected after uterine aspiration. The morphological change of decidua tissue was observed by light microscope and transmission electron microscope. The expression of estrogen receptor (ER), progesterone receptor (PR) in decidua tissue were detected by immunohistochemistry technique and computer image analysis system. **Results** Three medication groups showed that the decidual cells degenerate, necrosis, interstitial edema and telangiectasis. In decidua tissue of control group, the expression of ER and PR was mainly in the decidual cell and a few in epithelial cells, which were significant lower in the three medication groups than in control group ($P<0.05$), and there was no difference among the three medication groups ($P>0.05$). **Conclusion** The decidua tissues have turned to dropsy, degenerate and necrosis by 12 h after oral mifepristone. And the expressions of ER and PR have already been inhibited. It is indicated that shortening the time of mifepristone in medical abortion provides a certain theoretical parameters.

【Key words】 Mifepristone; Different time; Decidua; Steroid receptors; Ultrastructure

Fund program: Key Project of Hebei Medical Science Research Project in 2017 (20170254)

· 临床研究 ·

记忆滤泡性辅助 T 细胞与原因不明复发性流产的关联研究

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【摘要】目的 探讨原因不明复发性流产(unexplained recurrent spontaneous abortion, URSA)的发生与记忆滤泡性辅助 T(memory Tfh)细胞表达异常是否存在关联。**方法** 收集 15 例染色体正常的 URSA 为流产组, 并以 15 例正常人工流产患者为正常对照组。分离所有患者外周血单个核细胞及蜕膜组织免疫细胞, 用流式细胞术(FCM)检测上述细胞中 CD4⁺CXCR5⁺memory Tfh 以及 CD4⁺CXCR5⁺PD-1⁺memory Tfh 细胞水平。**结果** 流产组蜕膜局部 CD4⁺CXCR5⁺memory Tfh 以及 CD4⁺CXCR5⁺PD-1⁺memory Tfh 细胞水平显著高于正常对照组($P<0.05$)。流产组外周血 CD4⁺CXCR5⁺memory Tfh 以及 CD4⁺CXCR5⁺PD-1⁺memory Tfh 细胞水平与正常对照组无明显差异 ($P>0.05$)。**结论** 早孕妇女蜕膜局部 memory Tfh 细胞数量增多可能与 URSA 发生有关, 母-胎界面的免疫异常可能导致 URSA 的发生。

【关键词】 原因不明复发性流产(URSA); 记忆滤泡性辅助 T(memory Tfh)细胞; 外周血; 蜕膜; 流式细胞术(FCM)

· 临床研究 ·

Relationship between memory Tfh cells and unexplained recurrent spontaneous abortion

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【Abstract】 Objective To discuss the relationship between memory Tfh cells and unexplained recurrent spontaneous abortion (URSA). **Methods** The peripheral blood and deciduas of 15 URSA patients were got, and 15 normal patients early pregnancy women were taken as the control. The CD4⁺CXCR5⁺memory Tfh cells and CD4⁺CXCR5⁺PD1⁺memory Tfh cells were assessed by flow cytometry. **Results** The CD4⁺CXCR5⁺memory Tfh cells and CD4⁺CXCR5⁺PD1⁺memory Tfh cells were both significantly increased in deciduas of the URSA patients compared with the control ($P<0.05$). While there were no statistical differences of CD4⁺CXCR5⁺memory Tfh cells and CD4⁺CXCR5⁺PD1⁺memory Tfh cells in peripheral blood between the two groups ($P>0.05$). **Conclusion** The up-regulation of decidual memory Tfh cells in human early pregnancy led to the failure of the pregnancy, abnormal activation of the immune maternal-fetal interface may cause the occurrence of URSA, which provides a basis for further study.

【Key words】 Unexplained recurrent spontaneous abortion (URSA); Memory Tfh; Peripheral blood mononuclear cell (PBMC); Decidua; Flow cytometry (FCM)

· 临床研究 ·

宫腔灌注自体外周血单个核细胞治疗对反复种植失败患者妊娠结局的影响及相关机制

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【摘要】目的 探讨宫腔灌注自体外周血单个核细胞(PBMCs)治疗对反复种植失败(RIF)患者妊娠结局的影响及相关机制。**方法** 36 名 RIF 患者于冻融胚胎移植(FET)前 24 h 行自体 PBMCs 宫腔灌注, 随访妊娠结局; 酶联免疫吸附试验(ELISA)检测宫腔灌注前、后外周血及宫颈分泌物中白细胞介素 -6(IL-6)、肿瘤坏死因子 - α (TNF- α)水平。**结果** RIF 患者经宫腔灌注自体 PBMCs 治疗后得到了较高的临床妊娠率(47.22%); 宫颈分泌物中 IL-6、IL-6/TNF- α 均显著升高 ($P<0.05$), TNF- α 水平无统计学差异($P>0.05$), 外周血中 IL-6、TNF- α 水平均无统计学差异($P>0.05$)。**结论** 宫腔灌注自体 PBMCs 治疗能提高 RIF 患者宫腔局部 IL-6 水平及 IL-6/TNF- α 比值, 有效改善 RIF 患者临床妊娠率。

【关键词】 反复种植失败(RIF); 外周血单个核细胞(PBMCs); 宫腔灌注; 白细胞介素 -6(IL-6); 肿瘤坏死因子 - α (TNF- α)

· 临床研究 ·

Effect of intrauterine administration of autologous peripheral blood mononuclear cells on pregnancy outcomes in patients with recurrent implantation failure and the related mechanism *Liu Yanghong, Zhang Jing, Liu Lian, Shi Xiaobo*

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【Abstract】 Objective To investigate the effect of intrauterine administration of autologous peripheral blood mononuclear cells (PBMCs) on pregnancy outcomes in patients with recurrent implantation failure (RIF) and the related mechanism. **Methods** Thirty-six RIF patients received intrauterine administration of PBMCs 24 h before the frozen-thawed embryo transfer, with observation of their pregnancy outcomes. Enzyme-linked immunosorbent assay (ELISA) was performed to detect the concentration of interleukin-6 (IL-6) and tumor necrosis factor- α (TNF- α) in peripheral blood and cervical secretions before and after the treatment. **Results** Following the PBMC intrauterine administration, this cohort of women with RIF received a higher clinical pregnancy rate (47.22%). The concentration of IL-6 and the ratio of IL-6/TNF- α in the cervical secretions were significantly higher than before ($P < 0.05$), while no change in TNF- α ($P > 0.05$). No significant change was found in the concentrations of IL-6 and TNF- α in peripheral blood ($P > 0.05$). **Conclusion** Intrauterine administration of autologous PBMCs increases the concentration of IL-6 and the ratio of IL-6/TNF- α in the uterine cavity, and this method can effectively improve the clinical pregnancy rate in patients with RIF.

【Key words】 Recurrent implantation failure (RIF); Peripheral blood mononuclear cells (PBMCs); Intrauterine administration; Interleukin-6 (IL-6); Tumor necrosis factor- α (TNF- α)

· 临床研究 ·

脱氢表雄酮在卵巢储备功能低下高龄患者体外受精 / 卵胞质内单精子注射 - 胚胎移植中的应用研究

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【摘要】目的 探讨口服脱氢表雄酮(DHEA)辅助治疗在卵巢储备功能低下(DOR)高龄患者体外受精 / 卵胞质内单精子显微注射 - 胚胎移植(IVF/ICSI-ET)中的临床疗效。**方法** 选取行 IVF/ICSI 助孕治疗的 DOR 患者 152 例, 所有患者均行 2 次及以上助孕周期, 前一周期为未加用药周期(治疗前组), 本次为用药周期(治疗后组), 进行自身用药前后对照分析。比较口服 DHEA 后卵巢储备功能的变化情况, 同时比较是否加用 DHEA 患者 IVF/ICSI-ET 的临床治疗参数、实验室参数及临床结局。**结果** ①口服 DHEA 后患者血清抗苗勒管激素(AMH)、硫酸脱氢表雄酮(DHEA-s)、睾酮(T)及窦卵泡计数(AFC)较用药前升高, 卵泡刺激素(FSH)较前下降, 差异有统计学意义($P<0.05$); ②治疗后组 hCG 注射日 E_2 及孕酮(P)水平、获卵数、受精率、可移植胚胎数、胚胎种植率及临床妊娠率高于治疗前组, Gn 总用量、Gn 使用时间、周期取消率低于治疗前组, 差异有统计学意义($P<0.05$)。**结论** DOR 的高龄患者在进入 IVF/ICSI 周期前口服 DHEA 可改善其卵巢储备功能及助孕结局。

【关键词】 脱氢表雄酮(DHEA); 卵巢储备功能低下(DOR); 抗苗勒管激素(AMH); 临床妊娠率

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· 临床研究 ·

Application of DHEA to advanced aged patients with diminished ovarian reserve in *in vitro* fertilization or intracytoplasmic sperm injection and embryo transfer Ye Yaping, Ou Qizhi, Qin Aiping

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【Abstract】 Objective To investigate the effects of dehydroepiandrosterone (DHEA) supplementation on *in vitro* fertilization or intracytoplasmic sperm injection and embryo transfer (IVF/ICSI-ET) outcomes and changes in ovarian reserve among patients with diminished ovarian reserve (DOR). **Methods** The study enrolled 152 treatment cycles in 152 couples who accepted IVF/ICSI. All patients had repeated IVF/ICSI-ET cycles. The last cycle without DHEA supplementation were taken as before treatment group and this time received DHEA supplementation were taken as after treatment group, as self-control study. The ovarian reserve in after treatment group were compared between before and after oral DHEA subgroup. Also the IVF treatment parameters and outcomes were compared. **Results** 1) In after treatment group, serum anti-Müllerian hormone (AMH), testosterone (T), dehydroepiandrosterone sulfate (DHEA-s), and the number of antral follicle count (AFC) were increased and basic follicle-stimulating hormone (FSH) value was reduced after DHEA treatment which had a statistical significant ($P<0.05$). 2) Serum estradiol (E_2) and progesterone (P) levels on the day of human chorionic gonadotropin (hCG) injection, the number of retrieved oocytes and available embryos, fertilization rate, embryo implantation rate, clinical pregnancy rate were significantly higher in after treatment group than in before treatment group. The dosage and duration of gonadotropin (Gn) used, cycle cancellation rate were significantly lower in after treatment group than in before treatment group. **Conclusion** DHEA supplementation can improve ovarian reserve and outcome of IVF/ICSI in aged patients with DOR.

【Key words】 Dehydroepiandrosterone (DHEA); Diminished ovarian reserve (DOR); Anti-Müllerian hormone (AMH); Clinical pregnancy rate

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· 临床研究 ·

精子顶体精氨酸酰胺酶测定在体外受精 - 胚胎移植妊娠结局中的价值研究

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【摘要】目的 研究精子顶体精氨酸酰胺酶在体外受精 - 胚胎移植(IVF-ET)中的应用价值。**方法** 选择 349 个 IVF 治疗周期, 其中精氨酸酰胺酶高值组 162 个周期, 精氨酸酰胺酶低值组 187 个周期。比较两组间的受精率、正常受精率、卵裂率、优质胚胎率以及新鲜移植周期的生化妊娠率、临床妊娠率、流产率及活产率等指标。**结果** 精子精氨酸酰胺酶高值组的受精率(78.74%)高于低值组(76.07%, $P < 0.05$), 而卵裂率高值组(98.24%)低于低值组(99.58%, $P < 0.05$)。两组间正常受精率和优质胚胎率比较无统计学差异。高值组新鲜移植周期的临床妊娠率(58.75%)及活产率(52.50%)均明显高于低值组(44.00%, $P < 0.05$; 33.00%, $P < 0.01$)。两组间生化妊娠率和流产率比较无统计学差异($P > 0.05$)。**结论** 精子精氨酸酰胺酶活性与 IVF-ET 精卵结合有一定关系, 并对妊娠结局有一定的指导作用。

【关键词】 精子; 精氨酸酰胺酶; 体外受精; 胚胎移植; 妊娠

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· 临床研究 ·

Predictive value of sperm arginine amidase enzyme in the outcome of *in vitro* fertilization-embryo transfer

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【Abstract】 Objective To examine the effects of arginine amidase activity variations to the *in vitro* fertilization-embryo transfer (IVF-ET) cycles. **Methods** The arginine amidase activity was analyzed for 349 IVF-ET cycles, there were 162 cycles with high arginine amidase activity and 187 cycles with low arginine amidase activity. We evaluated the rates of fertilization, cleavage, quality embryos of IVF, and biochemical pregnancy, clinical pregnancy, abortion and live birth of fresh embryos transfer cycles. **Results** The fertilization rate was significantly higher in high arginine amidase activity group (78.74%) than low activity group (76.07%, $P < 0.05$), while the cleavage rate was lower in high arginine amidase activity group (98.24%) than low activity group (99.58%, $P > 0.05$). There were no significant difference in the rates of normal fertilization and quality embryos. The rates of clinical pregnancy (58.75%) and live birth (52.50%) were significantly higher in high arginine amidase activity group than in low group (44.00%, $P < 0.05$; 33.00%, $P < 0.01$). There was no significant difference in the rates of biochemical pregnancy and abortion between two groups ($P > 0.05$). **Conclusion** The sperm arginine amidase activity may affect the fertilization of IVF-ET. It helps predicting the outcome of fresh embryos transfer cycles.

【Key words】 Sperm; Arginine amidase; *In vitro* fertilization; Embryos transfer; Pregnancy

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· 临床研究 ·

剖宫产手术史对体外受精 - 胚胎移植患者临床结局的影响

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【摘要】目的 探讨剖宫产手术史对体外受精 - 胚胎移植(IVF-ET)患者临床结局的影响。**方法** 回顾性分析 2013 年 1 月—2015 年 12 月行 IVF-ET 且有剖宫产手术史的 144 例患者的助孕情况、妊娠及分娩结局, 对照组为同期行 IVF-ET 且既往仅有阴道分娩史的 166 例患者。**结果** 与对照组比较, 剖宫产史组基础卵泡刺激素水平(bFSH)、人绒毛膜促性腺激素(hCG)注射日雌二醇(E₂)水平、子宫内膜厚度、促性腺激素(Gn)用量、Gn 刺激时间, 获卵率、受精率、卵裂率、优质胚胎率、胚胎移植数、多胎妊娠率、流产率、异位妊娠率差异均无统计学意义($P>0.05$); 但剖宫产手术史组胚胎移植困难比例(6.25%)高于阴道分娩史组(0.00%), 胚胎种植率(24.01%)及临床妊娠率(40.28%)明显低于阴道分娩史组(分别为 34.98% 和 54.82%), 差异均有统计学意义($P<0.05$); 剖宫产史组双胎妊娠者较对照组双胎妊娠发生前置胎盘、产后出血比例增加($P<0.05$); 无论是剖宫产手术史组还是阴道分娩史组, 双胎分娩较单胎分娩新生儿出生孕周、体质量明显降低($P<0.01$)。**结论** 剖宫产手术史可能降低 IVF-ET 患者的胚胎种植率和临床妊娠率, 增加胚胎移植难度。对疤痕子宫妇女应严格控制移植胚胎数目, 妊娠后加强孕期监管。

【关键词】 剖宫产; 体外受精 - 胚胎移植(IVF-ET); 妊娠率; 并发症

· 临床研究 ·

Effect of prior cesarean section on clinical outcomes of *in vitro* fertilization and embryo transfer

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【Abstract】 Objective To investigate the influence of prior cesarean section on the pregnancy outcome of *in vitro* fertilization and embryo transfer (IVF-ET). **Methods** A retrospective analysis was performed on 144 patients with prior cesarean section during January 2013 to December 2015. The pregnancy, delivery, and neonatal outcomes of patients who had previous cesarean scar and received IVF-ET were analyzed. A total of 166 patients with only previous vaginal delivery receiving IVF-ET in the same period were included as control group. **Results** The basal follicle stimulating hormone (FSH) level, estradiol (E₂) level on human chorionic gonadotrophin (hCG) injection day, endometrial thickness, dosage and duration of gonadotrophin (Gn) stimulation, rate of retrieved oocytes, fertilization rate, cleavage rate, high-quality embryo rate, number of transfer embryos, multiple birth rate, abortion rate, ectopic pregnancy rate were similar between the previous cesarean section group and the previous vaginal delivery group ($P>0.05$). But the ratio of embryo difficulty transfer in previous cesarean section group (6.25%) was higher than that of previous vaginal delivery group (0.00%) while implantation rate (24.01%) and pregnancy rates (40.28%) in previous cesarean section group were significantly lower than those of previous vaginal delivery group (34.98%, 54.82%) ($P<0.05$). The risk of twin pregnancy complication with pernicious placenta previa and postpartum hemorrhage in previous cesarean section group were significantly higher than that in previous vaginal delivery group ($P<0.05$). Twin deliveries had significantly lower gestational age and neonatal birth weight compared with singleton deliveries in both groups ($P<0.01$). **Conclusions** The existence of cesarean section scar maybe impact embryo implantation and clinical pregnancy outcome, increase difficulty of embryo transfer. We should limit the number of transferred embryos to avoid multiple pregnancy and strengthening gestational supervision in patients with cesarean scar.

【Key words】 Cesarean section scars; *In vitro* fertilization and embryo transfer (IVF-ET); Pregnancy rate; Complication

· 临床研究 ·

三核苷酸重复引物 PCR 和甲基化特异性多重连接探针扩增技术在脆性 X 综合征产前诊断中的应用

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【摘要】目的 探讨脆性 X 综合征(FXS)产前基因诊断的方法。**方法** 采用三核苷酸重复引物 PCR 法(TP-PCR)及甲基化特异性多重连接探针扩增技术(MS-MLPA)检测 2 个 FXS 家系及 30 例正常对照胎儿样本 *FMR1* 基因 CGG 重复数、AGG 排布及 *FMR1* 基因 CpG 岛甲基化状态。**结果** 正常对照 *FMR1* 基因(CGG)_n 重复数介于 23~40 之间, 频数最大的重复数为 29, AGG 排布式以 9A9A9 最为常见。2 个 FXS 家系中前突变等位基因向子代遗传过程中均发生了 CGG 扩展。正常对照及前突变携带者 *FMR1* 基因 CpG 岛均为低甲基化状态, 全突变患者 CpG 岛为高甲基化状态。**结论** TP-PCR 和 MS-PCR 联合应用能够检出胎儿 *FMR1* 基因 CGG 重复数和 CpG 岛甲基化状态, 从而判断胎儿是否为脆性 X 综合征患儿, 为优生干预提供可靠的依据。

【关键词】 脆性 X 综合征(FXS); 产前基因诊断; *FMR1* 基因; CGG 重复数; AGG 排布式

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· 临床研究 ·

Application of triplet repeat-primed-PCR and methylation specific multiplex ligation-dependent probe amplification in prenatal diagnosis of fragile X syndrome He Wenzhi, Li Shaoying, Wang Xiaoman, Wang Yanchao, Ma Xiaoyan, Xian Jiajia, Liu Haibo, Wang Ding, Li Qing

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【Abstract】Objective To explore the application value of triplet repeat-primed (TP)-PCR and methylation specific multiplex ligation-dependent probe amplification (MS-MLPA) for prenatal diagnosis of Fragile X syndrome. **Methods** The CGG repeat number and AGG interruption pattern were analyzed using TP-PCR and methylation status of CpG islands was detected by MS-MLPA from 2 FXS family members and 30 unrelated fetuses. **Results** The range of alleles was 23–40 CGG repeats in fetuses, and the most frequent allele and AGG interruption pattern were 29 CGG repeats and 9A9A9, respectively. CGG expansion was observed in both of the two permutation alleles during transmission. CpG islands of *FMR1* were observed hypermethylated in patients with full mutation, while 30 controls and premature carriers were hypomethylation. **Conclusion** TP-PCR, in combination with MS-MLPA, represents a reliable diagnostic protocol in the prenatal diagnosis of FXS.

【Key words】 Fragile X syndrome (FXS); Prenatal diagnosis; *FMR1* gene; CGG repeat number; AGG interruption pattern

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· 实验研究 ·

枸杞多糖对生精障碍模型小鼠生精能力作用的研究

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【摘要】目的 研究枸杞多糖(LBP)对生精功能和生精干细胞的影响。**方法** 122 只雄性昆明小鼠中随机选取 92 只, 通过 35 mg/kg 白消安造模, 获得生精障碍动物模型, 另外 30 只小鼠为正常对照组。40 d 后对造模成功的小鼠随机分为自然恢复组($n=23$)和 LBP 低剂量组($n=16$, 75 mg/kg)、中剂量组($n=19$, 150 mg/kg)、高剂量组($n=16$, 300 mg/kg), 连续灌胃给药 70 d(小鼠 2 个生精周期)后进行观察, 并与正常对照组进行比较, 观察其生理状态和生殖功能变化。**结果** LBP 在造模动物的外观体征、机能和行为的表、动物正常发育状态(体质量)、生殖器官组织重量(睾丸、附睾和储精囊、前列腺-会阴复合体)、附睾精子质量、睾丸组织精子生成量、睾丸组织形态学和 c-kit 表达量、精曲小管直径和空泡化程度、生精上皮厚度和细胞层数、c-kit 阳性细胞数、H-score 评分、平均吸光度(LA)等系列指标均显示明显高于自然恢复组($P<0.05$, $P<0.01$), 并具有剂量效应关系, 但仍未达到正常对照动物的水平。**结论** LBP 具有明显促进白消安生精障碍模型小鼠的生精能力的作用, 可以显著增加生精干细胞、附睾精子质量和睾丸精子生成量。

【关键词】 枸杞子; 枸杞多糖(LBP); 白消安; 生精障碍; c-kit

· 实验研究 ·

Function of spermatogenic promotion of lycium barbarum polysaccharide on mice with spermatogenesis impairment

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【Abstract】 Objective To study the effect of lycium barbarum polysaccharide (LBP) on the function of spermatogenesis and spermatogonial stem cells. **Methods** Totally 92 of 120 male Kunming mice were randomly selected and treated with 35 mg/kg busulfan to build the animal model with spermatogenesis impairment. And 14 mice were selected as solvent control, 16 selected as normal control. After 40 d, the model animals were randomly divided into spontaneous recovery group ($n=23$), LBP low-dose group ($n=16$, 75 mg/kg), LBP middle-dose group ($n=19$, 150 mg/kg), LBP high-dose group ($n=16$, 300 mg/kg). After treatment for 70 d (two spermatogenic cycles), the changes of physiological status and reproductive function were observed. **Results** In terms of the appearance, behaviors, body weight, reproductive organs, sperm count in epididymis, sperm count in testis, histology and morphology of testis and expression of c-kit, three kinds dosages of LBP group were better than the spontaneous recovery group with dose-effect relationship, but still not achieve the level of normal control. **Conclusion** LBP can promote the spermatogenic function on the busulfan-treated infertile mouse, and increase the spermatogonial stem cells, quality of sperm in epididymis and sperm count in testis.

【Key words】 Medlar; Lycium barbarum polysaccharide (LBP); Busulfan; Spermatogenesis impairment; c-kit

· 临床报道 ·

辅助生殖技术单卵双胎相关因素分析及含单绒毛膜双胎三胎妊娠减除单绒毛膜双胎之一的临床结局比较

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【摘要】目的 探讨辅助生殖技术(ART)治疗后行多胎妊娠减胎术中单卵双胎(MZT)的发生和三胎妊娠行单绒毛膜双胎中一胎减胎术保留双胎者的临床结局。**方法** 回顾性分析 ART 治疗后行经阴道多胎妊娠减胎术的 196 例患者的临床资料, 分析比较 MZT 在不同分组中的发生情况, 同时比较其中伴单绒毛膜双胎的三胎妊娠减单绒毛膜双胎之一者(A组)与不伴单绒毛膜双胎的三胎妊娠减胎后保留双胎者(B组)的临床结局。**结果** ① 196 例患者中 MZT 所占比率为 44.39%(87/196)。MZT 占比率在体外受精(IVF)组(0.85%)、卵胞质内单精子显微注射(ICSI)组(0.66%)、冻融胚胎移植(FET)组(0.78%)和人工授精(AIH/AID)组(0.16%)间比较差异有统计学意义($P=0.001$); 在辅助孵化(AH)组(1.48%)和无AH组(0.44%)间比较差异亦有统计学意义($P=0.000$)。MZT 占比率在高龄(≥ 35 岁)和非高龄患者中($P=0.330$)及卵裂期胚胎移植组和囊胚期胚胎移植组间($P=0.950$)比较差异无统计学意义。② A组和B组患者的平均年龄、平均孕周、新生儿的平均胎龄、平均胎儿出生体质量、流产率、早期流产率、晚期流产率、早产率、足月产率、活产率、低出生体质量儿发生率、新生儿出生缺陷率和妊娠并发症率比较, 差异均无统计学意义($P>0.05$)。**结论** ART行多胎妊娠减胎术的患者中 MZT 所占几率很高, 为减少 MZT 的发生, 尽量选择单胚胎移植; A组和B组患者临床结局无统计学差异, 单绒毛膜双胎中一胎减胎术可能是安全而可行的。

【关键词】 辅助生殖技术(ART); 多胎减胎术; 单卵双胎(MZT); 含单绒毛膜双胎的三胎妊娠; 临床结局

· 临床报道 ·

Analysis of related factors of monozygotic twins in assisted reproductive techniques and the clinical outcomes of dichorionic triplet pregnancy which reduced one monochorionic twin Wang Xingling,

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【Abstract】 Objective To investigate the incidence of monozygotic twins (MZT) and the clinical outcomes of dichorionic triplet pregnancy which reduced one monochorionic twin after multifetal pregnancy reduction with assisted reproductive techniques (ART). **Methods** A retrospective analysis was performed in 196 patients who underwent vaginal multifetal pregnancy reduction after ART. The proportion of MZT in different groups was analyzed, and the clinical outcomes of dichorionic triplet pregnancy which reduced one monochorionic twin (group A) with trichorionic triplet pregnancy which reduced to twins (group B) were compared. **Results** 1) The proportion of MZT in 196 patients was 44.39% (87/196). There was a significant difference in the proportion of MZT among the *in vitro* fertilization (IVF) group, the intracytoplasmic sperm injection (ICSI) group, the frozen-thawed embryo transfer (FET) group and the artificial insemination (AIH / AID) group ($P=0.001$). There was also a significant difference between the assisted hatching (AH) group and the non-AH group ($P=0.000$). There was no significant difference in the proportion of MZT between the elderly (≥ 35 years) patients and non-elderly patients ($P=0.330$) and between the cleavage stage embryo transferred group and the blastocyst stage embryo transferred group ($P=0.950$). 2) The patients' average age, the mean gestational age, the mean gestational age of newborns and the mean birth weight were similar. There was no significant difference in abortion rate, early abortion rate, late abortion rate, preterm birth rate, term birth rate, live birth rate, low birth weight rate and the incidence of neonatal birth defects and pregnancy complications ($P>0.05$). **Conclusion** The proportion of MZT was high in ART patients with multifetal pregnancy reduction. It should transform to a single embryo transfer to reduce MZT incidence. There was no difference in clinical outcomes between group A and group B, multifetal pregnancy reduction of one monochorionic twin in dichorionic triplet pregnancy may be safe and feasible.

【Key words】 Assisted reproductive techniques (ART); Multifetal pregnancy reduction; Monozygotic twins (MZT); Dichorionic triplet pregnancy; Clinical outcome

· 临床报道 ·

沙眼衣原体感染与生殖道人乳头瘤病毒感染的关系及其与 宫颈病变发生的相关性研究

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【摘要】目的 研究女性生殖道人乳头瘤病毒(human papilloma virus, HPV)感染与沙眼衣原体(*Chlamydia trachomatis*, CT)感染的关系, 及其与宫颈癌前病变和宫颈癌发生的相关性。**方法** 以妇产科门诊患者 540 例为研究对象, 所有患者均行 HPV、CT 和宫颈细胞学检查。对疑似宫颈病变的患者进一步行宫颈活检。根据 HPV 检测结果, 将 HPV 检测阳性的患者 140 例设为观察组, HPV 检测阴性的患者 400 例设为对照组, 分析生殖道 HPV 感染与 CT 感染的相关性, 以及其与宫颈病变发生的相关性。**结果** 观察组宫颈病变发生率(21.4%)显著高于对照组(1.3%, $P<0.000\ 1$)。按照 HPV 感染分型, 进一步将观察组分为高危组(78 例)、低危组(32 例)和混合感染组(30 例)。高危组(25.6%)和混合感染组(26.7%)宫颈病变发生率均显著高于低危组(6.3%, $P=0.009$; $P=0.019$)。同时, 观察组 CT 感染率(27.1%)显著高于对照组(3.3%, $P<0.000\ 1$)。HPV 感染患者中, 高危组(33.3%)和混合感染组(36.7%)的 CT 感染率均显著高于低危组(3.1%, $P=0.021$; $P=0.019$)。依据是否存在 CT 感染将观察组患者分为 HPV 单纯感染组和 CT 混合感染组。结果显示后者宫颈病变率(57.8%)显著高于前者(25.5%, $P=0.046$)。且 CT 混合感染组, 高危 HPV 和混合 HPV 感染患者宫颈病变的发生率分别为 39.3% 和 50.0%, 均明显高于 HPV 单纯感染组中高危 HPV 和混合 HPV 感染患者, 其发生率分别为 16.0% 和 15.4%, 差异均具有统计学意义($P=0.026$ 和 $P=0.017$)。Logistic 回归分析显示高危型 HPV 感染($OR=2.180$, $P=0.018$)、HPV 和 CT 混合感染($OR=6.690$, $P=0.012$)是宫颈病变发生的风险因素。**结论** 女性生殖道 CT 感染与 HPV 感染密切相关, HPV 和 CT 混合感染是宫颈癌前病变和癌变的独立风险因素。通过早期筛查女性生殖道 HPV 感染和 CT 感染, 及时有效地治疗微生物混合感染, 对进一步降低宫颈癌前病变和宫颈癌的发病率, 提高临床治疗效果具有重要意义。

【关键词】 生殖道; 人乳头状瘤病毒(HPV); 沙眼衣原体(CT); 宫颈癌前病变; 宫颈癌

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· 临床报道 ·

Relationship between human papilloma virus infection and *Chlamydia trachomatis* infection and its correlation with cervical lesions Zhang Ying, Wang Youping, Huang Zhilan, Yin Na, Tang Haiting

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【Abstract】Objective To study the relationship between female genital human papilloma virus (HPV) infection and *Chlamydia trachomatis* (CT) infection, and its correlation with cervical precancerous lesions and cervical cancer. **Methods** A total of 540 female outpatients were recruited. All the patients were given HPV, CT and cervical scraping examination. Cervical biopsy was conducted in patients with suspected cervical lesions. According to the results of HPV examination, 140 patients with confirmed HPV infection were designated as the observation group, and 400 patients negative to HPV were designated as control group. The relationship between HPV infection and CT infection, and its correlation with cervical lesions was analyzed. **Results** The incidence of cervical lesions in the observation group (21.4%) was significantly higher than that in control group (1.3%, $P<0.000\ 1$). According to type of HPV infection, patients in the observation group were divided into the high-risk group (78 cases), low risk group (32 cases) and mixed infection group (30 cases). The incidence of cervical lesions in the high-risk group (25.6%) and mixed infection group (26.7%) was significantly higher than that in the low-risk group (6.3%, $P=0.009$; $P=0.019$). The incidence of CT infection in the observation group (27.1%) was significantly higher than that in control group (3.3%, $P<0.000\ 1$). The incidence of CT infection in the high-risk group (33.3%) and the mixed infection group (36.7%) was significantly higher than that in the low-risk group (3.1%, $P=0.021$; $P=0.019$). Based on the presence of CT infection, the patients in the observation group were divided into HPV infection group and CT mixed infection group. The incidence of cervical lesions in the latter (57.8%) was significantly higher than that in the former (25.5%, $P=0.046$). And in CT mixed infection group, the incidence of cervical lesions in patients with high risk of HPV infection and mixed HPV were 39.3% and 50.0%, it was significantly higher than that of pure HPV and mixed infection in patients with high-risk HPV infection group, the incidence rate was 16.0% and 15.4%, the differences were statistically significant ($P=0.026$, $P=0.017$). Logistic regression analysis showed that high-risk HPV infection ($OR=2.180$, $P=0.018$), mixed infection of HPV and CT ($OR=6.690$, $P=0.012$) were risk factors for cervical lesions. **Conclusion** CT infection in female genital tract is closely related to HPV infection. Mixed infection of HPV and CT is an independent risk factor of cervical precancerous lesion and cancer. It is of important significance to further reduce the incidence of cervical cancer and precancerous lesions through the early screening of female genital HPV infection and CT infection, timely and effective treatment of mixed microbial infections.

【Key words】 Genital tract; Human papilloma virus (HPV); *Chlamydia trachomatis* (CT); Cervical precancerous lesions; Cervical cancer

Fund program: Promotion Project of Chongqing Appropriate Health Technology (2016jstg027)

· 临床报道 ·

显微外环下治疗高位结扎术后复发精索静脉曲张

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【摘要】目的 探讨显微外环下手术处理高位精索静脉曲张结扎术后复发的应用价值。**方法** 对 26 例既往已行高位精索静脉曲张结扎术后复发患者采用显微外环下切口处理, 精索静脉曲张 III 度患者切口偏向阴囊, 以便提出睾丸, 同时处理精索外静脉。**结果** 术后 3~6 个月随访, 得到随访 23 例, 随访复查未见复发。**结论** 复发性精索静脉曲张适合采用显微技术治疗。

【关键词】 显微手术; 精索静脉曲张; 复发

· 临床报道 ·

Subinguinal microsurgical varicocelectomy of recurrent varicocele after high ligation Xie Sheng,

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【Abstract】Objective To investigate the value of microsurgical treatment on recurrent high ligation of spermatic vein. **Methods** Twenty-six patients with recurrent spermatic vein ligation underwent microsurgical incision, the incision on patients with grade III varicocele was toward to the scrotum in order to put the testicles, while dealing with spermatic vein. **Results** After 3–6 months follow-up, 23 cases were followed up and no recurrence was observed.

Conclusion Subinguinal microsurgery varicocelectomy is suitable for recurrent varicocele.

【Key words】 Microsurgery; Varicocele; Recurrence

· 个案报道 ·

单纯性染色体 18p 部分三体综合征患儿的产前遗传学诊断和文献回顾

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【摘要】目的 探讨单纯性染色体 18P 部分三体综合征患者的产前诊断特点。**方法** 联合运用传统染色体核型分析和染色体微阵列(chromosome microarray analysis, CMA)基因芯片技术对家系成员行染色体核型分析和基因组拷贝数变异检测。**结果** 胎儿羊水染色体核型结果为 46,XY,der(18), 父母双方染色体核型均未见异常; 胎儿基因芯片检测结果为 arr [hg19]18p11.31p11.21(3,521,718-15,099,116)×3, 即胎儿基因组 18 号染色体短臂 p11.31p11.21 区域存在 11.58 Mb 的片段重复, 父母双方基因芯片结果均为阴性, 提示该胎儿的 18 号染色体结构重排为新发生的。**结论** 在一个有不良生育史家系的胎儿中检出一个罕见新发的单纯性染色体 18p 部分三体变异, 这是世界少见的单纯性染色体 18p 部分三体综合征的产前病例报道。联合运用传统染色体核型分析和 CMA 基因芯片技术在预防不良产史家系中胎儿出生缺陷的产前诊断中具有重要的临床应用价值。

【关键词】 不良产史; 产前诊断; 单纯性染色体 18p 部分三体综合征; 染色体微阵列(CMA); 染色体微缺失微重复综合征

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· 个案报道 ·

Prenatal genetic diagnosis in a fetus with isolated partial trisomy 18p syndrome and literature

review Deng Linbei, Xiong Shiyi, Zhou Jia, Xing Ya, Sun Luming

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【Abstract】Objective To investigate the characteristics of prenatal diagnosis of isolated partial trisomy 18p syndrome. **Methods** Traditional chromosome karyotype and chromosome microarray analysis (CMA) was used to process karyotyping and genomic copy number variation analysis. **Results** The result of fetal amniotic fluid chromosome karyotype was 46,XY,der(18). Both parents had normal chromosome karyotype with 46,XY and 46,XX, respectively. The fetal CMA test result was arr [hg19]18p11.31p11.21 (3,521,718-15,099,116) × 3. That is to say, there was 11.58 Mb fragment duplication derived from the chromosome 18 short arm p11.31p11.21 region. CMA test results were negative for both parents, suggesting that the chromosome 18 structure variation of the fetus was de novo. **Conclusions** A rare novel isolated partial trisomy 18p variation was detected in a fetus whose mother with abnormal pregnancy history. This is world's infrequent prenatal case report of isolated partial trisomy 18p syndrome. Combined with traditional chromosome karyotype and CMA, gene chip technology has an important clinical value in the prevention of fetal birth defects of abnormal pregnancy history family in prenatal diagnosis.

【Key words】 Abnormal pregnancy; Prenatal diagnosis; Isolated partial trisomy 18p syndrome; Chromosome microarray analysis (CMA); Chromosome microdeletion and microduplication syndrome

Fund program: Key Disciplines Group Construction Project of Pudong Health Bureau of Shanghai (PWZxq2014-02)

· 综述 ·

条件基因敲除技术在卵泡发育调控机制研究中的应用进展

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【摘要】 卵泡发育是受内分泌、旁分泌及基因调节的复杂生理过程。条件基因敲除能选择去除调控特定发育阶段特定细胞或器官的基因, 是在体基因功能研究的主要手段。近年来该技术被广泛应用于卵泡发育调控机制的研究。本文综述了条件基因敲除技术在始基卵泡激活、卵母细胞成熟、排卵、黄体形成及早期胚胎发育等机制研究中的应用进展。

【关键词】 条件基因敲除; 卵泡激活; 卵母细胞成熟; 排卵; 信号通路

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· 综述 ·

Application of conditional knockout technology in the research of follicular development

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【Abstract】 Follicular development is a complicated physiological processes regulated by endocrine, paracrine and gene. Conditional knockout approach can remove a gene at a specific cells or organs. This technology can help us to clarify gene functions *in vivo*. In recent years, the conditional knockout is widely applied to study the follicular regulatory mechanism. In this review, we have summarized recent progress in molecular mechanisms regulating activation of primordial follicles, oocyte meiotic maturation, ovulation, and luteinization as revealed by conditional knockout technology in the mouse ovary.

【Key words】 Conditional knockout; Follicle activation; Oocyte meiotic maturation ovulation; Signal pathway

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· 综述 ·

子宫自然杀伤细胞在胚胎着床期功能的研究进展

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【摘要】 子宫自然杀伤(uNK)细胞是存在于女性子宫中的一类特殊的免疫细胞, 表型主要为 CD56^{bright}CD16⁻, 在正常妊娠早期表现为强大的免疫调节功能及相对较弱的细胞毒性, 其在胚胎着床过程中有着重要的作用, 包括细胞因子及生长因子的分泌, 促进滋养层细胞入侵蜕膜以及蜕膜和胎盘的血管生成等。uNK 细胞功能及数量的异常被认为与多种妊娠相关疾病有关, 如复发性流产、子痫前期等。本综述目的在于汇总对子宫自然杀伤细胞的最新研究, 将有助于了解这些疾病的发病机制, 最终指导临床的预防与治疗。

【关键词】 子宫自然杀伤(uNK)细胞; 着床; 分泌作用; 血管生成作用; 复发性流产; 子痫前期

· 综述 ·

Study on development of the function of uterine natural killer cell during implantation Ma Xueqian,

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【Abstract】 Uterine natural killer (uNK) cell is a kind of immune cells located in female uterine, whose main phenotype is CD56^{bright}CD16⁻. It has a great immunomodulatory effect and relatively weak cytotoxicity during normal early pregnancy. It has played a significant role during the process of embryo implantation, including the secretion of cytokines and growth factors, promoting the invading of trophoblast cells into decidua as well as the angiogenesis of decidua and placenta, et al. It is considered that the abnormality of uNK cell's function and amount is related to many gestational diseases, such as repeated implantation failure, preeclampsia, et al. The objective of this review is to summarize the latest researches about uNK cell in order to understand more about the mechanism of the related diseases, and to guide the clinical prevention and treatment.

【Key words】 Uterine natural killer (uNK) cell; Implantation; Secretion; Angiogenesis; Recurrent spontaneous abortion; Preeclampsia

· 综述 ·

高龄影响卵母细胞及早期胚胎线粒体功能的研究进展

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【摘要】 线粒体是真核细胞中重要的细胞器, 为卵母细胞成熟、受精及胚胎生长提供充足的能量, 在卵母细胞和胚胎发育过程中起到关键作用。年龄的增长会引起线粒体功能降低, 进而影响卵母细胞及胚胎的质量, 不利于高龄女性的成功妊娠。本文将从高龄如何影响卵母细胞及早期胚胎线粒体功能, 以及怎样减少高龄对线粒体功能的损伤等方面进行探讨, 以期的高龄不孕不育患者提供理论指导。

【关键词】 女性高龄; 生育力减退; 线粒体功能

· 综述 ·

Progress of the effects of advanced age on mitochondrial function of oocytes and early embryos

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【Abstract】 Mitochondria are important organelles of eukaryotic cells, which provide energy for oocyte maturation, fertilization and embryo development. And they play a key role in the development of oocytes and embryos. The function of the mitochondria decreased with age, which influenced the quality of oocytes and embryos, as well as the pregnancy outcomes of aged women. In this article, we reviewed the effect of advanced age on mitochondrial function of oocytes and early embryos and its solution, which may provide theoretical guidance for aged women infertility.

【Key words】 Maternal advanced age; Declined fertility; Mitochondrial function

· 综述 ·

不孕症患者子宫内膜容受性的评估及改善研究

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【摘要】 在辅助生殖技术(assisted reproductive technology, ART)中, 优质的胚胎、良好的子宫内膜容受性(endometrial receptivity, ER)以及胚胎和子宫内膜的同步发育是影响胚胎成功植入的三个关键因素, 多项研究表明移植失败的主要原因是 ER 的欠缺, 而胚胎因素仅占三分之一, 因此如何提高胚胎着床率已成为辅助生殖领域讨论的焦点。本文对目前国内外在 ER 评估和改善这两方面的进展进行综述, 以期对临床决策有所帮助。

【关键词】 不孕症; 子宫内膜容受性(ER); 研究进展

· 综述 ·

Research for the assessment and improvement of endometrial receptivity in infertile women Wen Juan,

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【Abstract】 In assisted reproductive technology (ART), there are three critical factors which are high-quality embryos, good endometrial receptivity (ER) and the synchrony between the blastocyst and the endometrium largely affecting the successful implantation of embryos. A large number of studies indicate that the main cause of implantation failure is the defect of endometrial receptivity, and the embryos accounted for one third. Therefore, how to improve the implantation rate has been a focus issue in the assisted reproductive field. This paper mainly reviewed the latest progress in China and abroad about the assessment and improvement of endometrial receptivity, which is hoped to contribute to clinicians.

【Key words】 Infertility; Endometrial receptivity (ER); Research progress