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间隙连接蛋白 37(Cx37)rs1764391 基因多态性与多囊卵巢综合征不孕患者辅助生殖技术结局的关系

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【摘要】目的 分析连接蛋白 37(Cx37) rs1764391 基因多态性在多囊卵巢综合征 (PCOS) 患者中对控制性超促排卵的反应性及其妊娠结局的影响。方法 选择经辅助生殖技术 (ART) 治疗的 98 例 PCOS 不孕女性,使用 Taqman 技术分析 rs1764391 基因多态性分布,随后评估 rs1764391 基因型、等位基因型 对超促排卵的反应性以及 ART 妊娠结局的相关性。结果 PCOS 患者组 TT 基因型、等位基因 T 的频率 (18.4%,31.6%) 显著高于正常组 (9.6%,P=0.03;22.3%,P=0.04); LH 浓度、窦卵泡数、hCG 注射日雌激素水平、获卵数在基因型为 TT 的 PCOS 患者中要显著高于其它基因型 (P<0.05); 此外,受精率在不同的 rs1764391 基因型间无统计学差异,而 TT 基因型患者的种植率 (27.5%) 与临床妊娠率 (30.7%) 显著低于 CC、CT 基因型患者 (47.2%,52.3%,P=0.02;57.4%,69.6%,P=0.03);等位基因型 T 患者的临床妊娠率 (45.1%) 均显著低于 C 等位基因型 (66.8%,P=0.04)。结论 在 PCOS 不孕患者中 Cx37 rs1764391 基因多态性与 ART 结局密切相关。

【关键词】多囊卵巢综合征 (PCOS); 连接蛋白 37(Cx37); rs1764391; 基因多态性; 辅助生殖技术 (ART)

[Abstract] Objective To investigate whether Connexin 37 (Cx37) rs1764391 polymorphism could predict ovarian stimulation and reproductive outcomes in patients with polycystic ovary syndrome (PCOS). **Methods** A total of 98 PCOS patients undergoing assisted reproductive technology (ART) were included in the present study. The genotype of rs1764391 was detected using Taqman PCR method. Then the relationship of rs1764391 polymorphism with controlled ovarian hyperstimulation, reproductive outcomes were assessed. **Results** The frequencies of TT genotype (18.4%) and T allele (31.6%) were significantly higher in patients with PCOS (9.6%, P=0.03; 22.3%, P=0.04). LH concentration, estradiol level and the number of retrieved oocytes were significantly higher in PCOS patients with TT genotype when compared with other genotypes. Besides, embryo implantation rate (27.5%) and clinical pregnancy rate (30.7%) were significantly lower in PCOS patients with TT genotype than in patients with CC and CT genotypes (47.2%, 52.3%, P=0.02; 57.4%, 69.6%, P=0.03). Similarly, the low rate of clinical pregnancy was observed in PCOS patients with T allele (45.1%) than in patients with C genotype (66.8%, P=0.04). **Conclusion** In PCOS patients, Cx37 rs1764391 polymorphisms were significantly associated with reproductive outcomes.

[Key words] Polycystic ovary syndrome (PCOS); Connexin 37 (Cx37); rs1764391; Polymorphism; Assisted reproductive technology (ART)

博洛尼亚标准卵巢低反应者在促排卵体外 受精/卵胞质内单精子注射周期中的卵巢 反应性

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【摘要】目的 了解博洛尼亚标准卵巢低反应者在促排卵体外受精/卵胞质内单精子注射(IVF/ICSI)周期中的卵巢反应性。方法 本回顾性研究 2011 年 1 月—2016 年 12 月期间于本院行常规促排卵 IVF/ICSI,符合博洛尼亚标准的所有卵巢低反应(POR)患者,并分析这些患者在促排卵周期中出现POR的情况。结果 年龄》40岁且窦卵泡数(AFC)<5 的患者在首次促排卵 IVF/ICSI 周期中低反应的发生率为 98.7% (75/76),这些患者在后续促排卵周期中低反应的发生率明显下降。首次促排卵周期低反应且年龄》40岁的患者,第二周期促排卵出现低反应的几率为 67.2%(45/67)。首次促排卵周期低反应且 AFC<5 的患者,第二周期促排卵出现低反应的几率为 69.5%(57/82)。两次大剂量促排卵周期(促性腺激素用量每日至少 450 IU)均出现低反应的患者,再次促排卵发生低反应的几率为 71.4%(10/14)。结论 博洛尼亚标准中"预期的卵巢低反应者"在首次促排卵 IVF/ICSI 周期出现低反应的可能性极大,我们应该给予足够的重视,制定个性化的促排卵方案以改善患者的卵巢反应性。有过低反应史的博洛尼亚标准卵巢低反应者,也不应该放弃再次促排卵的机会,因为很大一部分患者在后续的促排卵周期中不再出现低反应。

【关键词】卵巢低反应 (POR); 博洛尼亚标准; 体外受精/卵胞质内单精子注射 (IVF/ICSI); 卵巢刺激; 卵巢储备

Ovarian responsiveness of poor responders diagnosed according to the Bologna criteria in ovarian stimulation *in vitro* fertilization/intracytoplasmic sperm injection cycles *Ke Hui, Yan Lizheng*

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[Abstract] Objective To explore the ovarian responsiveness of poor ovarian responders diagnosed according to the Bologna criteria in ovarian stimulation *in vitro* fertilization/intracytoplasmic sperm injection (IVF/ICSI) cycles. **Methods** This present retrospective study included all poor ovarian responders diagnosed according to the Bologna criteria and cycles with conventional stimulation protocol between January 2011 and December 2016 in our IVF center. We studied the incidence of poor ovarian response (POR) in these stimulation cycles. **Results** The incidence of POR for patients aged ≥ 40 years with antral follicle count (AFC)<5 in the first stimulation IVF/ICSI cycle was 98.7% (75/76), but it decline obviously in subsequent cycles. The incidence of POR in the second cycle for patients aged ≥ 40 years with POR in the first stimulation cycle was 67.2% (45/67). The incidence of POR in the second cycle for patients with AFC<5 and POR in the first stimulation cycle was 69.5% (57/82). The incidence of POR in the third cycle after two episodes of POR after maximal stimulation (at least 450 IU/d FSH) was 71.4% (10/14). **Conclusion** The incidence of POR in the first stimulation cycle for "expected poor ovarian responders" diagnosed according to the Bologna criteria is very high, so we should pay more attention to these patients, formulate personalized stimulation protocol to improve their ovarian responsiveness. Poor ovarian responders diagnosed according to the Bologna criteria with previous POR shouldn't give up subsequent stimulation cycles, because of many patients without POR in subsequent cycles.

【Key words 】 Poor ovarian response (POR); Bologna criteria; *In vitro* fertilization/intracytoplasmic sperm injection (IVF/ICSI); Ovarian stimulation; Ovarian reserve

输卵管积水不同处理方式对体外受精-胚胎移植结局的影响:一项回顾性队列研究

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【摘要】目的 探讨输卵管积水的不同手术处理方式及术后积水复发对体外受精-胚胎移植 (in vitro fertilization and embryo transfer,IVF-ET) 临床结局的影响。方法 采用非随机分组数据,回顾性分析2012—2014 年期间因输卵管因素在本中心行常规 IVF-ET 治疗的 939 例不孕患者的资料,按 IVF-ET 前每位患者的输卵管积水处理方式分为手术组 (A组, n=533) 和未处理组 (B组, n=406)。手术组又分为输卵管近端结扎组 (A1组, n=311)、输卵管造口组 (A2组, n=113) 和输卵管切除组 (A3组, n=109),每例患者仅纳入本研究时间段内第一个新鲜胚胎移植周期的效果,比较积水患者不同手术方式对 IVF-ET 临床结局的影响。结果 A组的临床妊娠率 (50.7%) 和活产率 (91.1%) 均高于 B组 (40.4%, 77.4%)(P<0.05); A组的异位妊娠率 (3.7%) 明显低于 B组 (12.8%)(P<0.05); 控制性超促排卵 (COH) 过程中的获卵数、获胚胎数、优质胚胎数 A、B组间均无统计学差异 (P>0.05)。A1组、A2组及 A3组间 IVF-ET 的临床妊娠率、活产率、流产率均无统计学差异 (P>0.05),COH过程中获卵数、获胚胎数、优质胚胎数 3个亚组间亦均无统计学差异 (P>0.05)。结论 输卵管积水通过手术处理可以提高其 IVF-ET 的临床妊娠率、活产率、降低异位妊娠率,并且进行输卵管造口、结扎、切除的不同处理对于 IVF-ET 结局和卵巢储备功能均无统计学影响。

【关键词】 输卵管积水; 手术方式; 体外受精-胚胎移植 (IVF-ET)

基金项目: 卫生公益性行业科研专项 (201402004)

Effects of different operation managements on *in vitro* fertilization and embryo transfer outcome: a retrospective cohort study Wu Sheling, Tang Rong, Fan Xiuling, Ding Lingling, Yan Lei, Chen Zijiang Center for Reproductive Medicine, Shandong University, National Research Center for Assisted Reproductive Technology and Reproductive Genetics, the Key Laboratory for Reproductive Endocrinology of Ministry of Education, Shandong Provincial Key Laboratory of Reproductive Medicine, Jinan 250021, China (Wu SL, Tang R, Fan XL, Ding LL, Yan L, Chen ZJ)

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[Abstract] Objective To evaluate and compare the clinical impact of different operation methods of hydrosalpinges when performed before in vitro fertilization and embryo transfer (IVF-ET) in patients with hydrosalpinges. **Methods** The data of 939 of infertile patients through tubal factors undergoing IVF-ET from 2012 to 2014 were analyzed retrospectively. All patients were divided into two groups according to the management of hydrosalpinx per person, 533 patients with hydrosalpinx in group A who were treated with operation while 406 patients with hydrosalpinx in group B were untreated. Group A were divided into three subgroups according to surgical methods, 311 patients with hydrosalpinx in group A1 who were treated with proximal tubal ligation, 113 patients with hydrosalpinx in group A2 who were treated with salpingostomy, 109 patients with hydrosalpinx in group A3 who were treated with salpingectomy. The clinical outcome of IVF-ET was evaluated. **Results** The clinical pregnancy rate (50.7%) and the live birth rate (91.1%) in group A were significantly higher than those in group B (40.4%, 77.4%, respectively) (P<0.05). The ectopic-pregnancy rate (3.7%) in group A was significantly lower than that in group B (12.8%) (P<0.05). There were no significant differences among group A1, group A2 and group A3. Conclusion Surgical of the fallopian tube, when performed in women with unilateral or bilateral hydrosalpinges before their IVF treatment, represents potential benefits—significantly increasing the clinical pregnancy rate and significantly decreasing the ectopic pregnancy rate. There is no significant difference of the ovarian reserve and IVF-ET outcome after salpingostomy, proximal tubal ligation or salpingectomy of the fallopian tube.

[Key words] Hydrosalpinges; Surgical methods; *In vitro* fertilization and embryo transfer (IVF-ET) **Fund program**: Science Research Foundation Item of No-earnings Health Vocation (201402004)

探讨经期内膜厚度及早卵泡期内膜搔刮对 冻融胚胎移植妊娠结局的影响

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【摘要】目的 探讨经期内膜厚度与冻融胚胎移植 (FET) 妊娠结局的关系,并对经期内膜厚度 >7 mm 的患者行早卵泡期子宫内膜搔刮,观察临床妊娠率,探讨内膜搔刮的时机及效果。方法 回顾性分析本中心 2014 年 11 月—2016 年 11 月期间行 FET 的 1 363 个周期,根据月经周期第 4~5 日内膜厚度分组: A 组为内膜厚度 <3 mm; B 组为内膜厚度 3~5 mm; C 组为内膜厚度 5~7 mm; D 组内膜厚度为 >7 mm; E 组为宫腔分离、内膜不清 (积液)。并对经期内膜厚度 >7 mm 的患者,在胚胎移植周期月经第 4~5 日行早卵泡期内膜搔刮,比较各组间的一般情况及临床妊娠率。结果 经期内膜厚度不同的 5 个组间患者的年龄、不孕年限、体质量指数 (BMI)、移植胚胎数、FET 内膜准备方式、双胎率及异位妊娠率均无统计学差异 (均 P>0.05); 5 组的平均经期内膜厚度及组间内膜增幅差异有统计学意义 (P<0.05),经期子宫内膜厚度 <7 mm(A 组、B 组及 C 组)平均的内膜增幅较 D 组显著增加 (P<0.05); 5 组组间的临床妊娠率、胚胎着床率差异有统计学意义 (P<0.05);组间两两比较结果提示,D 组的临床妊娠率、胚胎着床率较其他组显著下降 (P<0.005)。对经期内膜厚度 >7 mm 的患者行早卵泡期内膜搔刮,搔刮组的临床妊娠率为68.29%(56/82),明显高于未搔刮组的 53.26%(98/184),胚胎着床率 (52.67%) 显著高于未搔刮组 (36.34%),差异皆有统计学意义 (P<0.05)。结论 经期 4~5 d 内膜增厚 (>7 mm) 影响 FET 妊娠结局,对其行早卵泡期内膜搔刮,可改善子宫内膜容受性,提高 FET 的临床妊娠率及胚胎着床率。

【关键词】冻融胚胎移植 (FET); 经期内膜; 子宫内膜增幅; 早卵泡期内膜搔刮; 妊娠结局基金项目: 广州市科技计划项目 (201510010175)

Influence of menstrual endometrial thickness and endometrial scratching on pregnancy outcomes in frozen-thawed embryo transfer Liu Wenjuan, Nong Yingqi, Wang Yujiang, Chen Ye, Huang Li, Fan Lin, Liu Fenghua

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[Abstract] Objective To explore the influence of different endometrial thickness (EMT) during menstrual period on pregnancy outcomes in frozen-thawed embryo transfer (FET), and to evaluate the effect of endometrial scratching in patients whose EMT were more than 7 mm. **Methods** The data of 1 363 patients accepting FET were retrospectively analyzed. The patients were divided into five groups according to their EMT on the 4th or 5th day of menstruation. Group A: EMT < 3 mm; group B: EMT 3-5 mm; group C: EMT 5-7 mm; group D: EMT > 7 mm; group E: fluid within the endometrial cavity. Patients in group D were further divided into scratching group and non-scraping group. The general conditions, clinical pregnancy rate, implantation rate and ectopic pregnancy rate of patients were compared. **Results** There were no significant differences in general conditions among the five groups (P>0.05). The average EMT during menstruation and differences in inter-group endometrial growth of the five groups had statistical significances (P<0.05). The average endometrial growth of EMT < 7 mm (group A, group B and group C) was significantly higher than that in group D (P<0.005). The pregnancy rate and implantation rate of group D were significantly lower than those in other groups (P<0.005). While the clinical pregnancy rate and implantation rate in endometrial scratching group (68.29%, 52.67%, respectively) were higher than those in non-scraping group (53.26%, 36.34%, respectively) (P<0.05). Conclusion EMT during menstruation >7 mm can adversely influence pregnancy outcomes in FET. Endometrial scratching may improve the receptivity of endometrium and increase the rate of embryo implantation and pregnancy.

[Key words] Frozen-thawed embryo transfer (FET); Endometrial thickness during menstruation; Endometrial growth; Endometrial scratching; Pregnancy outcomes

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卵母细胞内滑面内质网聚集现象对其发育 潜能及临床结局的影响

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【摘要】目的 探讨卵胞质内单精子注射 (ICSI) 周期中卵母细胞滑面内质网聚集体 (SERC) 对胚胎发 育的影响及移植后的妊娠结局,判断是否有移植价值。方法 回顾性分析 2014 年 1 月—2015 年 12 月期间 768 个 ICSI 周期。根据所获 M II 期卵母细胞是否出现 SERC 分为 A 组 (n=681, 所获 M II 期卵母细胞均未出现 SERC) 和 B 组 (n=87, 至少有 1 枚 M π 期卵母细胞出现 SERC)。比较 A、B 两组患者的一般临床情况、 Gn 使用总量、Gn 使用时间、hCG 注射日雌激素 (E2)、孕酮 (P)、黄体生成素 (LH) 水平、子宫内膜厚度 以及获卵数、受精率、优质胚胎率、囊胚形成率、多囊卵巢综合征 (PCOS) 患者比例、中重度卵巢过度 刺激综合征 (OHSS) 发生率、临床妊娠率、种植率、流产率、活产率和胎儿畸形率。将 B 组再分为 3 个亚 组, SERC(+)组 (n=7), 所移植的胚胎均为 SERC(+) 卵子来源; SERC(+/-)组 (n=14), 所移植的胚胎 1 枚 为 SERC(+) 卵子来源的, 1 枚为 SERC(-) 卵子来源的; SERC(-) 组 (n=25), 所移植的胚胎均为非 SERC 卵 子来源的。比较其受精率、优质胚胎率和囊胚形成率。结果 B组 hCG 注射日 E2 水平 [(2 976.6±1 246.3) ng/L] 明显高于 A 组 [(2 323.4±871.4) ng/L](P<0.05), 而 P 和 LH 水平以及子宫内膜厚度均无统计学差异 (P>0.05); B 组受精率 (65.9%)、优质胚胎率 (28.6%)、囊胚形成率 (44.2%) 显著低于 A 组 (74.9%、33.4% 和 50.4%)(P<0.05), 而 B 组 Gn 用量 [(2 643.6±1 087.5) IU] 明显高于 A 组 [(2 256.6±976.4) IU](P<0.05)。 患者的年龄、Gn 使用时间、不孕年限、获卵数、PCOS 患者比例、中重度 OHSS 发生率、临床妊娠率、 种植率、流产率、活产率和胎儿畸形率方面组间均无统计学差异(P>0.05)。3个亚组间一般临床情况无统 计学有差异。SERC(+) 亚组卵母细胞的受精率 (59.6%)、囊胚形成率 (35.7%) 显著低于 SERC(-) 亚组 (68.6%, 48.1%)(P<0.05)。结论 卵母细胞 SERC 会影响早期胚胎的体外发育,但本研究未观察到 SERC 胚胎对妊 娠结局有不良影响,故需慎重对待 SERC 来源的胚胎。

【关键词】 卵母细胞;滑面内质网;卵胞质内单精子注射 (ICSI)

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Effect of smooth endoplasmic reticulum clusters in human oocytes on the embryo development and

pregnancy outcomes Zhao Jing, Zhao Junda, Hu Bo, Gong Xiaoyun, Wang Peng, Wang Zhihui, Zhu Yuejie, La Xiaolin Reproduction Center, the First Affiliated Hospital of Xinjiang Medical University, Urumqi 830054, China (Zhao J, Zhao JD, Hu B, Gong XY, Wang P, Wang ZH, Zhu YJ, La XL)

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[Abstract] Objective To investigate the effect of smooth endoplasmic reticulum clusters (SERC) in human oocytes on the embryo development and pregnancy outcomes during intracytoplasmic sperm injection (ICSI) cycles and discuss the reason for it and the value of SERC-positive [SERC(+)] embryos. Methods Seven hundred and sixty-eight ICSI cycles during January 2014 to December 2015 were retrospectively analyzed and were divided into two groups: 681 cycles in which no SERC occurred in any M_{II} oocyte as group A, while 87 cycles in which at least one M_{II} oocyte was found with SERC in each cycle as group B. The concentrations of estradiol (E₂), progesterone (P) and luteinizing hormone (LH) as well as thickness of endometrium were measured on hCG injection day. Comparisons were made on the patients' age, disease course, the concentrations of basal hormones, dosage of Gn used, duration of stimulation, the number of oocytes retrieved, fertilization rates, goodquality embryo rates, available blastocyst rates, the occurrence of polycystic ovary syndrome (PCOS) patients, occurrence rate of moderate and severe ovarian hyperstimulation sydrome (OHSS), clinical pregnancy rate per cycle, implantation rate, miscarriage rate, live-birth rate and malformation rate. Group B was further divided into three subgroups: group SERC(+) (n=7) with all SERC(+) oocytes, group SERC(+/-) (n=14) consisting of one SERC(+) oocyte and one SERC(-) oocyte, group SERC(-) (n=25) with all SERC(-) oocytes. The comparison of fertilization rates, good-quality embryo rate and available blastocyst rate were made among these three subgroups. **Results** The concentration of E_2 in group B [(2 976.6 \pm 1 246.3) ng/L] was significantly higher than that in group A [(2 323.4±871.4) ng/L] (P<0.05), while no significant differences were found on endometrium thickness as well as the concentrations of P and LH (P>0.05). Additionally, there were significantly lower fertilization rates (65.9%), good-quality embryo rate (28.6%) and available blastocyst rates (44.2%) (P<0.05), a significantly higher dosage of Gn used [(2.643.6 \pm 1.087.5) IU] (P<0.05) in group B than those in group A (74.9%, 33.4% and 50.4%) [(2 256.6 ± 976.4) IU], while no significant difference on the age, disease course, duration of stimulation, the number of oocytes retrieved, the occurrence of PCOS patients, occurrence rate of moderate and severe OHSS, clinical pregnancy rate per cycle, implantation rate, miscarriage rate, live-birth rate and malformation rate (P>0.05) were found. Furthermore, within group B, the fertilization rate (59.6%) and available blastocyst rate (35.7%) from SERC(+) oocytes was significantly lower than that from SERC(-) oocytes (68.6%, 48.1%) (P<0.01). Conclusion During ICSI cycles, SERC in human oocytes adversely influence the early embryo development, but can develop into a healthy baby.

[Key words] Oocyte; Smooth endoplasmic reticulum; Intracytoplasmic sperm injection (ICSI)

Fund program: Research Fund of National Health and Family Planning Commission of China: the Research of Establishing Human Assisted Reproductive Technological Quality Control System (201402004)

·实验研究 ·

氨基双吡酮对小鼠卵母细胞成熟的影响

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【摘要】目的 研究氨基双吡酮(氨力农)对体外和体内小鼠卵母细胞成熟的抑制作用,检测磷酸二酯酶 (PDE)3 抑制剂氨力农能否作为一个潜在的避孕药。方法 将不同浓度药物作用于体外培养的不成熟小鼠卵母细胞,以及注射于小鼠体内,观察其对卵母细胞成熟的阻滞作用并找出合适的浓度。卵母细胞成熟后进行卵胞质内单精子注射 (ICSI),并进行移植,观察其受精率、胚胎形成情况以及出生后代比较。并监测体内注射组小鼠的不良反应情况。结果 ①随着浓度的增加,氨力农导致减数分裂阻滞呈剂量依赖性,体外有效浓度为 1 μmol/L,而在体内为 300 mg/kg。② 其作用是可逆的。药物去除后,减数分裂恢复,小鼠卵母细胞成熟,并呈正常染色体排列和纺锤体组织。③ 与对照组比较,ICSI 受精后,卵母细胞表现出正常的形态、受精率、卵裂、囊胚形成。④ 其出生后代表现出相似的体质量和生育能力。⑤ 在体内,注入一定浓度药物后小鼠表现为不孕,停药后恢复。结论 氨力农可以抑制体外和体内小鼠卵母细胞的成熟,并且是可逆的;交配实验证明氨力农可能可作为一种避孕药物。

【关键词】 磷酸二酯酶 (PDE)3 抑制剂; 氨力农; 小鼠卵母细胞成熟; 纺锤体和染色体排列

•实验研究•

Effect of amrinone on the maturation of mouse oocytes *Li Xianping, Chen Taiting, Xie Liufang, Zhang Min, Qian Qinjia*

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[Abstract] Objective To examine the inhibitory effect of amrinone on the maturation of mouse oocytes *in vitro* and *in vivo*, and whether it is possible to detect the potential use of the inhibitor as a potential contraceptive. **Methods** The effects of different concentrations of amrinone on immature mouse oocytes were observed. After oocyte maturation, intracytoplasmic sperm injection (ICSI) was carried out, and the fertilization rate, embryo formation and the comparison of the offspring were observed. The adverse reaction of mice in *in vivo* injection group was monitored. **Results** 1) With the increase of the concentration, the ammonia induced meiosis was dose-dependent. The effective concentration was 1 μmol/L *in vitro*, but was about 300 mg/kg *in vivo*. 2) Its function was reversible. After the removal of the drug, the meiosis recovered gradually and mouse oocyte matured with normal chromosome alignment and spindle organization. 3) Compared with control group, after fertilization, oocytes showed normal morphology, fertilization rate, cleavage and blastocyst formation. 4) The birth offspring showed similar body weight and fertility. 5) *In vivo*, a certain concentration of drug injected into mice exhibited infertility till discontinuation. **Conclusion** *In vitro* and *in vivo* mouse oocytes can be inhibited by amrinone and maturation is reversible, and mating experiments have proved that it may be used as a contraceptive drug.

[Key words] Phosphodiesterase (PDE)3 inhibitor; Amrinone; Oocytes maturation of mouse; Spindle and chromosome

解冻周期序贯移植在反复种植失败患者中的应用

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【摘要】目的 探讨胚胎序贯移植法是否能够提高反复种植失败 (recurrent implantation failure, RIF) 患者的临床妊娠率。方法 回顾性分析 128 例行常规体外受精或卵胞质内单精子注射 - 胚胎移植 (IVF/ICSI-ET) 的 RIF 患者,按不同的移植法分为 3 组: 解冻周期序贯移植 36 例,卵裂期移植 45 例,囊胚期移植 47 例。分析比较 3 组患者一般资料及胚胎和妊娠结局。结果 解冻周期序贯移植组临床妊娠率 (72.2%) 及持续妊娠率 (69.4%) 明显高于卵裂期胚胎移植组 (44.4%,37.8%) 及囊胚期胚胎移植组 (48.9%,44.7%),差异有统计学意义 (P<0.05)。结论 解冻周期序贯移植法能够有效提高 RIF 患者的妊娠率,对于RIF 患者序贯移植可作为一种有效的可供选择的移植手段,该方案避免了取消移植的可能性并对有较多移植胚胎数的患者有效。

【关键词】反复种植失败 (RIF);囊胚移植;解冻周期;体外受精/卵胞质内单精子注射-胚胎移植 (IVF/ICSI-ET);序贯移植

Application of Sequencing embryo transfer in frozen-thawed cycles of patients with recurrent implantation failure Zhang Yinfeng, Yao Ruqiang, Han Ying, Zhang Yunshan

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[Abstract] Objectives To evaluate whether the sequencing embryo transfer in frozen period can improve the clinical pregnancy rate in patients with recurrent implantation failure (RIF) compared with simple cleavage embryo transfer and blastocyst stage embryo transfer. Methods A retrospective matched case—control study was conducted and the outcomes of 128 patients with a history of RIF were analysed, of which 36 women underwent sequential embryo transfer, 45 women underwent day-3 embryo transfer only and 47 women underwent day-5/6 embryo transfer only. General information and embryo and pregnancy outcome were analyzed among three groups. Results The clinical pregnancy rate (72.2%) and the ongoing pregnancy rate (69.4%) of sequential embryo transfer group were higher than those of the day 3 group (44.4%, 37.8%) and of the day 5/6 groups (48.9%, 44.7%). The difference was statistically significant. Conclusion Sequencing embryo transfer of thawing cycle can effectively improve the pregnancy outcome of RIF patients. Sequential transplantation of patients with repeated implantation failure can be used as an effective alternative transplantation method, which avoids the possibility of eliminating transplantation and is effective for patients with more transplanted embryos.

Key words Repeated implantation failure (RIF); Blastocyst transfer; Frozen-thawed cycle; *In vitro* fertilization/intracytoplasmic sperm injection-embryo transfer (IVF/ICSI-ET); Sequencing embryo transfer

经阴道途径与经腹部途径体外受精-胚胎移植多胎妊娠减胎术后妊娠结局的分析

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【摘要】目的 比较体外受精-胚胎移植 (IVF-ET) 多胎妊娠在早孕早期 (6~8 孕周) 经阴道减胎与早孕晚期 (11~13⁺⁶ 孕周) 经腹部减胎术后的妊娠结局,探讨多胎妊娠合适的减胎时机。方法 2014 年 1 月一2016 年 12 月期间于本院经超声波诊断的多胎妊娠拟行减胎手术患者,6~8 孕周经阴道减胎组 110 例,11~13 孕周经腹部减胎组 78 例,比较两组间早产率、流产率、低出生体质量率、胎儿体质量、孕周等。结果 比较流产率、低出生体质量率、流产孕周、分娩孕周、平均胎儿体质量组间均无统计学差异。与经腹减胎组 (5.13%,6.12%) 比较,经阴道减胎组 34~37 孕周早产率明显升高 (17.27%)、减胎个数分层显示 6~8 孕周双胎减一胎后早产率升高 (19.40%)。结论 与 11~13⁺⁶ 孕周经腹部减胎比较,6~8 孕周经阴道减胎组 34~37 孕周的早产率升高、双胎减一胎后的总体早产率升高。

【关键词】 多胎妊娠; 减胎术; 经阴道减胎; 经腹部减胎; 妊娠结局

Comparison of the outcomes between transvaginal and abdorminal multifetal reduction achieved by *in vitro* fertilization-embryo transfer

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[Abstract] Objective To investigate the outcomes of fetal reduction for multifetal pregnancies between transvaginal and abdominal approach. **Methods** Multifetal pregnancies were enrolled from our hospital during Jan. 2014 to Dec. 2016. Totally 110 transvaginal and 78 abdormianl reduciton were included, the rate of abortion, preterm birth, birth weight, birth week were analyzed between the two groups. **Results** Compared with abdormianl group (5.13%, 6.12%), transvaginal group had higher preterm rate (17.27%), higher preterm rate in reduced twins (19.40%). **Conclusion** Compared with abdominal group, transvaginal reduction group had higher preterm rate for 34–37 weeks of gestation, especially in reduced tiwns.

[Key words] Multifeal pregnancies; Fetal reduction; Transabdominal reduction; Abdominal reduction; Pregnancy outcome

血小板反应蛋白-1等血管相关因子在复发性流产中的表达及临床研究

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【摘要】目的 探讨血小板反应蛋白 -1(TSP-1)、血管内皮生长因子 (VEGF) 及其可溶性受体 -1(sflt-1) 在复发性流产 (RSA) 患者血清和绒毛组织中的表达及意义。方法 以 57 例 RSA 患者为研究对象,其中 RSA 早孕停育组 30 例,RSA 未孕组 27 例,以同期接诊的 64 例正常妇女为对照,其中正常早孕组 36 例,正常健康未孕组 28 例。采用 ELISA 法对所有入组患者血清中 TSP-1、VEGF 及 sflt-1 水平进行检测,采用免疫组织化学法对 RSA 早孕停育组及正常早孕组流产后绒毛组织中 TSP-1、VEGF 及 sflt-1 的表达情况进行定性和定量分析。结果 RSA 妇女血清中 sflt-1 水平高于正常妇女,TSP-1、VEGF 水平低于正常妇女;绒毛组织中 TSP-1、VEGF 和 sflt-1 的阳性表达率及表达强度均高于正常妇女,差异有统计学意义 (P<0.05)。结论 RSA 的发生可能与 TSP-1、VEGF 及 sflt-1 的异常表达相关。血清和绒毛组织中 sflt-1 蛋白的过度表达可能拮抗 VEGF 的促血管生成功能、影响胎盘绒毛血管网络的正常建立;绒毛中 TSP-1 蛋白的高表达可能直接抑制 VEGF 的分泌、抑制绒毛组织中血管的新生,导致流产的发生。

【关键词】 血小板反应蛋白 -1 (TSP-1); 血管内皮生长因子 (VEGF); 可溶性血管内皮生长因子受体 -1 (sflt-1); 复发性流产 (RSA)

·临床报道。

Study of the expression and clinical value of thrombospondin-1 and other vascular related factors in recurrent spontaneous abortion Liu Meimei, Wang Shan, Li Xiaoxiao, Yu Caihong, Wang Shiyuan, Yang Wei Department of Obstetrics and Gynecology, the Second Affiliated Hospital of Harbin Medical University, Harbin 150086, China (Liu MM, Wang SY, Yang W); Xinxiang Center Hospital Department of Reproductive Medicine, Xinxiang 453000, China (Wang S); Affiliated Hospital of Jining Medical College Obstetrics and Gynecology, Jining 272029, China (Li XX); Department of Obstetrics and Gynecology, the Fourth Hospital of Shijiazhuang, Shijiazhuang 050000, China (Yu CH)

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[Abstract] Objective To explore the expression and significance of thrombospondin-1 (TSP-1), vascular endothelial growth factor (VEGF) and soluble fms-like tyrosine kinase-1 (sflt-1) in serum and villi of recurrent spontaneous abortion (RSA) patients. Methods Fifty-seven patients with RSA were selected as the experimental group, including RSA early pregnancy group (n=30) and RSA non-pregnancy group (n=27). And 64 normal women were treated as control group, including normal early pregnancy group (n=36) and non-pregnancy group (n=28). The levels of TSP-1, VEGF and sflt-1 in serum of all were determined by enzyme-linked immunosorbent assay (ELISA). The expressions of VEGF, sflt-1 and TSP-1 in the villi of RSA early pregnancy group and normal early pregnancy group were detected by immunohistochemistry for histological localization and quantitative The level of sflt-1 in the serum of RSA group was higher than that of control group, the level of TSP-1 and VEGF was lower than that of control group. The positive expression rate and expression intensity of TSP-1, VEGF and sflt-1 in villous tissues were significantly higher than those in control group, the difference was statistically significant (P<0.05). Conclusion The occurrence of RSA may be associated with abnormal expression of TSP-1, VEGF and sflt-1. Overexpression of sflt-1 protein in serum and villous tissue may antagonize the angiogenic function of VEGF and affect the normal establishment of placental villous blood vessels. The high expression of TSP-1 protein in villi may directly inhibit the secretion of VEGF and inhibit the angiogenesis in villous tissue, leading to the occurrence of miscarriage.

【Key words】 Thrombospondin-1 (TSP-1); Vascular endothelial growth factor (VEGF); Soluble fms-like tyrosine kinase-1 (sflt-1); Recurrent spontaneous abortion (RSA)

·现场调查 ·

输精管结扎术对中老年男性血脂代谢的远期影响

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【摘要】目的 评估输精管结扎术对中老年男性血脂代谢的远期影响。方法 以社区为单位分层整群抽取遵义市 40 岁及以上成年男性 474 例行生殖健康现状调查和体格检查,空腹抽取肘静脉血检测甘油三脂 (TG)、总胆固醇 (TCH)、高密度脂蛋白 (HDL) 和低密度脂蛋白 (LDL)。结果 ①结扎组 261 人,未结扎组 213 人,结扎平均年限为 (30.1 ± 7.8) 年;结扎组 TG[(1.22 ± 1.02) mmol/L] 低于未结扎组 [(1.59 ± 1.27) mmol/L],HDL[(1.17 ± 0.39) mmol/L]和 LDL[(2.31 ± 0.70) mmol/L]高于未结扎组 [(0.90 ± 0.36) mmol/L、(2.17 ± 0.83) mmol/L](均 P < 0.05)。②年龄与 TG 呈负相关,与 HDL、LDL 呈正相关;体质量指数 (BMI)与 TG、TCH 呈正相关,与 HDL 呈负相关;FPG 与 TG 呈正相关,与 HDL、LDL 呈负相关;收缩压和舒张压分别与 TG 呈正相关,HDL 呈负相关(均 P < 0.05)。③校正相关因素后,结扎组与未结扎组相比,TG(β : 0.041,95% CI: -0.111 < 0.301)、TCH(β : 0.015,95% CI: -0.184 < 0.253)、LDL(β : -0.063, 95% CI: -0.242 < 0.050) 差异无统计学意义 (P > 0.05),HDL(β : -0.236, 95% CI: -0.258 < -0.119) 有统计学差异 (P < 0.05);结扎 10 < 19 年组、20 < 29 年组和 30 < 39 年组的 HDL 水平均高于对照组(均 P < 0.01),结扎 \geq 40 年组的 HDL 水平与对照组比较无统计学差异 (P > 0.05)。结论 输精管结扎术对中老年男性的TG、TCH和LDL无不良远期影响,但早期可能影响 HDL 水平。

【关键词】 输精管结扎; 中老年男性; 血脂代谢

·现场调查 ·

Long-term effects of vasectomy on lipid metabolism in aging males Xiong Shimin, Zhou Yuanzhong, Liu Fangwei, Shi Yongjun, Yu Qin, Dai Lulu, Shen Xubo

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[Abstract] Objective To evaluate the long-term impact of vasectomy on serum lipids in middleaged and elderly men. **Methods** In the community as a unit, 474 adult men aged ≥ 40 years in Zunyi were investigated by stratified cluster sampling and physical examination was performed, fasting venous blood test triglycerides (TG), total cholesterol (TCH), high density lipoprotein (HDL) and low density lipoprotein (LDL). Results (1) There were 261 patients in vasectomy group and 213 in non-vasectomy group. The average length of vasectomy was (30.1 ± 7.8) years. In vasectomy group, TG level $[(1.22\pm1.02) \text{ mmol/L}]$ was lower than that in non-vasectomy group [(1.59 ± 1.27) mmol/L], HDL [(1.17 ± 0.39) mmol/L] and LDL [(2.31 ± 0.70) mmol/L] levels were higher than those of non-vasectomy group $[(0.90\pm0.36) \text{ mmol/L}, (2.17\pm0.83) \text{ mmol/L}]$ (P<0.05). (2) Age was negatively correlated with TG, and positively correlated with HDL and LDL; body mass index (BMI) was positively correlated with TG and TCH, and negatively correlated with HDL; FPG was positively related to TG and negatively correlated with HDL and LDL; FPG was positively correlated with TG, and negatively correlated with HDL and LDL; systolic and diastolic blood pressure were positively correlated with TG, and negatively correlated with HDL (P<0.05). (3) After adjustment for relevant factors, there were no statistically significant differences between the non-vasectomy and vasectomy group in TG (β: 0.041, 95% CI: -0.111-0.301), TCH (β: 0.015, 95% CI: -0.184-0.253) and LDL (β: -0.063, 95% CI: -0.242-0.050)(P>0.05), but HDL (β: -0.236, 95% CI: -0.258--0.119) had a statistically significant difference (P<0.05). The level of HDL in vasectomy of 10-19 years, 20-29 years and 30-39 years groups was higher than that of control group (P < 0.01), there was no statistically significant difference between the vasectomy of more than 40 years and control group in HDL level (P < 0.05). Conclusion Vasectomy has no adverse long-term effect on TG, TCH and LDL in middle-aged and elderly men, but early may affect HDL levels.

Key words Vasoligation; Aging male; Lipidmetabolism

· 综 述 ·

辅助生殖中薄型子宫内膜治疗的研究进展

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【摘要】在辅助生殖技术 (ART) 中,通常认为内膜厚度≤7 mm 可称为薄型子宫内膜,约占体外受精周期的2.4%,其显著降低临床妊娠率。薄型子宫内膜病因以宫腔操作和炎症最多见,另有部分病因以及机制尚不明了。目前,治疗薄型内膜的方法众多,但尚无公认确切有效的治疗方法。本文主要以激素相关治疗、改善血流灌注治疗、促进内膜增殖和再生治疗等为分类,详细介绍治疗方法、分析其作用机制、评价其效果及前景,对治疗方法的最新研究进展加以总结,旨在为临床治疗薄型内膜提供思路和启示。

【关键词】薄型子宫内膜;辅助生殖技术(ART);机制;治疗

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 $\textbf{Research advances in the treatment of thin endometrium in assisted reproductive technology} \quad \textit{Luo Zhuoye},$

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【Abstract】 The endometrial thickness of ≤ 7 mm is considered thin endometrium in assisted reproductive technology (ART). Thin endometrium occurs in 2.4% of the *in vitro* fertilization cycles and it is linked to a lower probability of pregnancy. The most common cause of thin endometrium lies in inflammatory and iatrogenic. And some of the causes remain unknown. It has numerous treatments, but so far none of them has been widely accepted. Treatments are classified into hormone related therapy, improving blood flow therapy, improving endometrium proliferation therapy and so on. And the detail methods, mechanism and effects of the treatments were presented. This review starts from mechanism and summarizes the research advances in treatments of thin endometrium, aiming to provide new ideas to treat thin endometrium.

[Key words] Thin endometrium; Assisted reproductive technology (ART); Mechanism; Treatment **Fund program**: Merck Serono China Research Fund for Fertility (2015)

人绒毛膜促性腺激素影响子宫内膜容受性的研究进展

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【摘要】良好的子宫内膜容受性是胚胎植入的重要因素,人绒毛膜促性腺激素 (hCG) 是与胚胎植入最为密切的物质分子信号之一,hCG对子宫内膜容受性具有调控作用,可以刺激子宫内膜细胞生长成熟、促进子宫内膜血管形成、调节子宫内膜对胚胎的免疫耐受和调控子宫内膜细胞因子的分泌。本文回顾总结了 hCG 及其受体对子宫内膜的作用机理及临床研究,旨在对 hCG 与子宫内膜容受性的研究进展作一综述。

【关键词】 人绒毛膜促性腺激素 (hCG); 子宫内膜容受性; 体外受精 - 胚胎移植 (IVF-ET) 基金项目: 甘肃省卫生行业项目 (GSWSKY-2015-47)

・综述・

Research progress on the effect of human chorionic gonadotropin on the receptivity of endometrium

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【Abstract】 Good endometrial receptivity is an important factor for embryo implantation. Human chorionic gonadotropin (hCG) is one of the closest molecules in embryo implantation. hCG can improve the receptivity of endometrium, including stimulating the growth of endometrial cells' mature, promoting endometrial vascular formation, regulating the immune tolerance and secretion of cytokines in maternal-fetal interface, etc. We reviewed the mechanism and clinical research about hCG and its receptor on the receptivity of endometrium in this paper.

【Key words】 Human chorionic gonadotropin (hCG); Receptivity of endometrium; *In vitro* fertilization-embryo transfer (IVF-ET)

Fund program: Gansu health industry project (GSWSKY-2015-47)

维生素 D 与多囊卵巢综合征

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【摘要】多囊卵巢综合征 (polycystic ovary syndrome, PCOS) 是妇科及生殖医学科常见的一种内分泌疾病,生殖功能障碍与糖脂代谢紊乱常同时存在,具有多起因、异质性。研究表明维生素 D 水平在 PCOS 患者中普遍低于正常值,且与 PCOS 人群的胰岛素抵抗 (insulin resistance, IR)、肥胖、高雄激素血症、生殖力下降、远期并发症、卵巢功能及抑郁症发生等相关,通过维生素 D 补充治疗及生活方式改变或许可以改善上述情况,进而提高 PCOS 患者的生殖力及生活质量。

【关键词】 多囊卵巢综合征 (PCOS);维生素 D;胰岛素抵抗 (IR);肥胖

Vitamin D and polycystic ovary syndrome Zheng Jiahua, Zhou Xiaojing, Li Lipeng, Huang Xianghua, Hao Guimin, Wang Wei

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[Abstract] Polycystic ovary syndrome (PCOS) is a kind of reproductive dysfunction and glucose and lipid metabolism disorder of endocrine disease, which has the characteristic of multiple causes and heterogeneity. Vitamin D deficiency is common in women with PCOS, which may be associated with insulin resistance, obesity, hyperandrogenism, reproductive dysfunction, the long-term complications, ovarian function and depressive disorder and so on. There may be a place for vitamin D supplementation to alleviate the above and improve well-being in women with PCOS.

[Key words] Polycystic ovary syndrome (PCOS); Vitamin D; Insulin resistance; Obesity

· 综 述 ·

髓系来源的抑制性细胞在母 - 胎界面的研究进展

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【摘要】 髓系来源的抑制性细胞 (myeloid derived suppressor cells, MDSCs) 是一类具有显著抑制 T 细胞功能的异质性细胞群体,能够促进机体免疫耐受形成。在妊娠建立过程中,母体免疫系统要对含有父系抗原的胎儿具有足够的免疫耐受,具有免疫抑制特性的细胞以及细胞因子在母 - 胎界面聚集是母 - 胎免疫耐受形成的机制之一。近年来,有研究表明 MDSCs 在母 - 胎界面聚集,促进母 - 胎免疫耐受的形成。本文就 MDSCs 的免疫抑制特性及其在妊娠中的研究进展作一综述。

【关键词】 髓系来源的抑制性细胞 (MDSCs);免疫抑制;母-胎耐受;妊娠基金项目:华中科技大学同济医学院重大疾病交叉创新团队培育计划资助 (5001519002)

Myeloid derived suppressor cells at the maternal-fetal interface Hu Xiaohui, Liao Aihua

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[Abstract] Myeloid-derived suppressor cells (MDSCs) are a heterogeneous group of myeloid cells that suppress immune responses through multiple mechanisms promoting the immune tolerance formation. The maintenance and establishment of normal pregnancy need enough maternal immune tolerance to fetus. Recent data have revealed that a large number of MDSCs accumulate at the maternal-fetal interface and promote the establishment of immune tolerance. In this review, we will focus on the mechanisms that regulate the expansion and function of MDSCs. In addition, meaningful questions that need further investigation and the various and potential roles of MDSCs at the maternal-fetal interface will be discussed.

[Key words] Myeloid-derived suppressor cells; Immunosuppression; Maternal-fetal tolerance; Pregnancy **Fund program**: Innovative Team for Major Human Diseases Program of Tongji Medical College, HUST (5001519002)

·综 述·

孕期糖皮质激素暴露对子代睾丸发育影响的研究进展

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【摘要】睾丸是雄性机体调控生殖内分泌功能的重要器官。孕期母体摄入的过量合成类糖皮质激素 (GC),或遭受内外环境剧变而产生的大量内源性 GC,可通过胎盘进入胎儿体内,而过量的 GC 对睾丸发育具有抑制作用并可延续到出生后。其发生主要与宫内神经内分泌系统和局部因子的调节不当有关,并与表观修饰改变密切相关。本综述概述了 GC 的睾丸发育毒性,为指导优生优育、生殖健康并制定调节生殖内分泌系统功能策略奠定了基础。

【关键词】糖皮质激素 (GC); 睾丸; 发育毒性

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Research progress on the effects of prenatal glucocorticoids exposure on testicular development of male offspring Liu Min, Zhang Qi, Pei Linguo, Wang Hui

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[Abstract] The testis plays an important role in regulating male reproductive endocrine function. Exposure of the fetus to increased levels of glucocorticoids, resulting from maternal integrated response to the sudden changes of internal and external environment or treatment with synthetic glucocorticoids, can lead to long-term suppression of the testicular development. This is mainly due to the improper regulation of neuroendocrine system and local factors in utero, and is related to the alteration of epigenetic modification closely. This review outlines the developmental toxicity of glucocorticoids in testis, we hope it could improve the eugenism and reproductive health, and establish a foundation for formulating the strategy of regulating reproductive endocrine function.

Key words Glucocorticoids (GC); Testis; Developmental toxicity

Fund program: National Natural Science Foundation of China (81430089, 81673524)

· 综 述 ·

哺乳动物胚胎着床分子机制综述的研究现状

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【摘要】 胚胎着床涉及到胚胎和子宫间复杂的关系,是胚胎能否继续发育的重要环节。胚胎发育到囊胚阶段以及子宫内膜同步分化到容受状态是成功着床的关键。着床过程涉及到许多信号通路分子的相互作用,但是其中同步胚胎和子宫状态的调控网络仍有很多谜题未解开。本文总结了目前对于着床的分子调控以及在这个领域中的研究进展,对着床机制的了解有助于阐明女性不明原因的不孕症并且帮助提高胚胎着床率和妊娠率。

【关键词】 胚胎着床; 子宫内膜容受性; 囊胚激活; 窗口期

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Research progress on the molecular mechanism of mammalian embryo implantation Lv Bo, Xue Jinfeng,

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[Abstract] Embryo implantation involves complex contact between embryo and endometrium cells, which determines the following development of embryo. Synchronization of blastocyst activation and endometrial receptivity is the key process for implantation. This process involves signaling pathways regulating the synchronization together with many unknown questions. This review summarizes the present research status of exploring implantation pathways. To elucidate the mechanisms involving embryo implantation not only helps illuminate the unknown infertility in women but also may improve the implantation rate and even pregnancy rate.

[Key words] Embryo implantation; Endometrial receptivity; Blastocyst activation; Window of implantation

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延时摄像技术的研究现状

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【摘要】延时摄像 (time-lapse) 技术被越来越多的胚胎学家运用于人类辅助生殖领域,可通过该技术动态观察胚胎发育的全过程,获取有效信息,进行胚胎形态学评估及动力学参数的研究。一些实验表明胚胎动力学参数与胚胎发育潜能密切相关,这能够指导优质胚胎的选择,提高妊娠结局。已有国内外生殖中心根据动力学参数建立各自妊娠结局预测模型,但未有统一有效的标准。此外,该技术的有效性及安全性仍缺乏有力证据的支持。

【关键词】胚胎发育; 延时摄像; 动力学; 时间参数

Reseach progress of time-lapse monitoring system Zhang Can, Geng Menghui, Xing Aying, Wang Dalin, Hu Yanqiu

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[Abstract] Time-lapse monitoring technology has been widely used in human assisted reproductive technology (ART), which allows for dynamic observation of embryo development, acquisition of useful information and assists research on morphology evaluation and morphological parameters. Some experiments indicated that morphokinetic parameters can help to select high-quality embryos and improve pregnant outcomes for the reason that they were closely related with development potential. A number of clinics have reported validated implantation prediction algorithms according to dynamic parameters while without a unified and valid standard. Moreover, the effectiveness and security of time-lapse system requires definitive evidence to support. The research progress of time-lapse system was summarized in this review.

Key words Embryo development; Time-lapse; Morphokinetics; Time parameters