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·述评·

加强人类精子冻干保存的研究

朱伟杰

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【摘要】 人类精子冻干保存,核心是精子核完整性的保存。冻干保存利用真空冷冻干燥,使精子处于失水干燥状态,导致精子的生化、代谢活动完全中止。冻干保存能够避免液氮冷冻保存的诸多不足,已取得的研究进展显示了精子冻干保存雄性生育力是可行的,将会是未来人类精子的一种保存形式。当前应加强人类精子冻干保存的各方面研究,重点解决冻干精子的高生殖安全性、冻干方法的高保存效率、精子冻干损伤的机制、冻干精子的评价指标和长期储存风险等关键问题,使人类精子冻干保存早日成为男性生育力保存的安全、高效、实用方法。

【关键词】人类精子; 冻干; 生育力; 安全性 基金项目: 广东省科技计划项目 (2014A020213007)

·述评·

Strengthening investigations on freeze-drying preservation of human sperm Zhu Weijie

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【Abstract】 Freeze-drying is a method in which frozen material is dried by sublimation of ice, which can induce spermatozoa to completely remove water and result in stop of physiological and biochemical activities. Freeze-drying avoids problems related to cryopreservation in liquid nitrogen on economy, practice and safety, and has been proposed as an alternative method to preserve human sperm in the future. Further investigations should be focused on reproductive safety of freeze-dried sperm, improvement of freeze-drying efficacy, understanding of injuring mechanism, selection of testing markers, and risk of long-term preservation.

Key words Human sperm; Freeze-drying or lyophilization; Fertility; Safety

Fund program: Science and Technology Planning Project of Guangdong Province, China (2014A020213007)

多囊卵巢综合征患者颗粒细胞自噬的发生及影响因素

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【摘要】目的 探讨多囊卵巢综合征 (polycystic ovary syndrome, PCOS) 患者颗粒细胞自噬的发生及影响因素。方法 取卵日收集行体外受精 / 卵胞质内单精子显微注射 (IVF/ICSI) 的 PCOS 患者和非 PCOS 患者的卵泡液和颗粒细胞,检测患者卵泡液性激素以及颗粒细胞自噬相关基因的表达,进一步将患者的颗粒细胞自噬相关基因与卵泡液性激素和临床结局等指标进行相关性分析。结果 PCOS 患者颗粒细胞自噬相关基因 $BECN1(2.13\pm0.94)$ 和 $ATG7(1.38\pm0.45)$ mRNA 水平显著高于非 PCOS 组患者颗粒细胞(1.46±0.52,P=0.002; 1.16 ± 0.29 ,P=0.026) mRNA 水平; PCOS 患者卵泡液黄体生成素 (LH)[(5.32 ±4.14) IU/L]、雌二醇 (E2)[(990.36±390.53) mg/L] 和 睪酮 (T)[(53.18±28.36) nmol/L] 水平显著高于非 PCOS 组患者卵泡液[(2.38±1.34) IU/L,P=0.001; (715.61±325.18) mg/L,P=0.007; (24.44±15.12) nmol/L,P=0.000], PCOS 患者卵泡液 P4[(12.81±6.78) mg/L] 水平显著低于非 PCOS 组患者 [(17.77±9.60) mg/L,P=0.036]。相关性分析显示,颗粒细胞中 BECN1 mRNA 水平与血清基础T水平 (P=0.490, P=0.000)、卵泡液T水平 (P=0.329, P=0.031)、血清抗苗勒管激素 (AMH)(P=0.337, P=0.018) 均呈显著正相关。结论 PCOS 患者颗粒细胞自噬可能存在异常激活,可能为 PCOS 发生的重要机制。

【关键词】 自噬; 抗苗勒管激素 (AMH); 雄激素; 多囊卵巢综合征 (PCOS)

基金项目: 国家自然科学基金面上项目 (81771648, 81571499); 科技部重点专项子课题 (2017YFC1001403); 国家 973 子课题 (2014CB943300); 上海市卫生系统优秀人才培养计划 (2017BR015); 上海市教育委员会高峰高原学科建设计划 (20161413)

Autophagy of ovarian granulosa cells in polycystic ovary syndrome Li Xiaoxue, Wang Guiquan, Zhu Qinling, He Yaqiong, Wang Yuan, Qi Jia, Wu Hasiximuke, Sun Yun

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[Abstract] Objective To investigate autophagy in granulosa cells and its related factors in patients with polycystic ovary syndrome (PCOS). Methods Follicular fluid (FF) and ovarian granulosa cells from PCOS and non-PCOS patients who underwent in vitro fertilization/intracytoplasmic sperm injection (IVF/ICSI) were collected, and sex hormones in FF and the expression of autophagy-related genes in granulosa cells were detected. Then, correlations between the expression of autophagy-related genes in granulosa cells with sex hormones and clinical outcomes were analyzed. **Results** The mRNA levels of autophagy-related genes BECN1 (2.13 \pm 0.94) and ATG7 (1.38 \pm 0.45) in granulosa cells of PCOS patients were significantly higher than that in non-PCOS patients $(1.46\pm0.52, P=0.002; 1.16\pm0.29, P=0.026)$. Concentrations of luteinizing hormone (LH) [$(5.32\pm0.002, P=0.002; 1.16\pm0.29, P=0.026)$] 4.14) IU/L], estradiol (E₂) [(990.36 \pm 390.53) mg/L], testosterone (T) [(53.18 \pm 28.36) nmol/L] in FF of PCOS patients were also higher than those of non-PCOS patients [(2.38±1.34) IU/L, P=0.001; (715.61±325.18) mg/L, P=0.007; (24.44 ± 15.12) nmol/L, P=0.000]. Concentration of progesterone (P4) [(12.81 ± 6.78) mg/L] in FF of PCOS patients was lower than that of non-PCOS patients [(17.77 ± 9.60) mg/L, P=0.036]. BECN1 mRNA abundance in granulosa cells and testosterone levels in serum (r=0.490, P=0.000) and FF (r=0.329, P=0.031), serum anti-Müllerian hormone (AMH) (r=0.337, P=0.018) showed significantly positive correlations. Conclusion activation of autophagy in granulosa cells in PCOS patients may be an important mechanism for the development of PCOS.

【Key words】 Autophagy; Anti-Müllerian hormone (AMH); Androgen; Polycystic ovary syndrome (PCOS) Fund program: National Natural Science Foundation of China (81771648, 81571499); National Key R&D Program of China (2017YFC1001403); Chinese National Key Basic Research Projects (2014CB943300); Program of Shanghai Academic Research Leader in Shanghai Municipal Commission of Health and Family Planning (2017BR015); Shanghai Municipal Education Commission-Gaofeng Clinical Medicine Grant Support (20161413)

宫腔镜在治疗多囊卵巢综合征合并子宫内膜不典型增生或早期子宫内膜样腺癌后对其生育功能保留的作用及评估

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【摘要】目的 探讨宫腔镜在治疗年轻的多囊卵巢综合征 (PCOS) 合并子宫内膜不典型增生 (EAH) 或早期子宫内膜样腺癌 (EEC) 患者的临床疗效及安全性。方法 本研究为回顾性研究,患者分为 2 组,早期 12 例患者 (9 例 EAH, 3 例 EEC) 采用单纯药物治疗 (单纯药物组): 达英 -35 联合二甲双胍,每 3 个月采用诊断性刮宫 + 病理检查,了解子宫内膜病变转化情况;后期 32 例患者 (21 例 EAH, 11 例 EEC) 采用宫腔镜治疗 (宫腔镜治疗组): 达英 -35 联合二甲双胍,每 3 个月行宫腔镜直视下病灶完全切除 + 全面诊断性刮宫 + 病理检查了解子宫内膜病变转化情况。结果 所有患者经病理证实子宫内膜病变均成功转化,单纯药物组 EAH 成功转化时间为 (6.6±3.1) 个月;宫腔镜治疗组 (4.1±1.3) 个月,组间比较差异有统计学意义 (P=0.025);单纯药物组早期 EEC 成功转化时间为 (6.3±2.8) 个月;宫腔镜治疗组为 (4.7±1.7) 个月,组间比较差异有统计学意义 (P=0.020)。单纯药物组 2 例 EAH 已足月分娩获活婴,此 2 例为自然受孕;宫腔镜治疗组 9 例 (5 例 EEC, 4 例 EAH) 已足月分娩均获活婴,另外有 8 例 EEC 转化成功者目前仍在妊娠中。结论 达英 -35 联合二甲双胍药物治疗能使 PCOS 合并胰岛素抵抗 (IR) 的子宫内膜癌前病变及 EEC 完全转化,宫腔镜能准确、彻底切除子宫内膜病灶,能最大可能达到"无瘤"的治疗要求,所以能明显缩短药物的转化时间 (P<0.05),并能增加子宫内膜病灶对药物保守治疗的反应性,从而保留了此类患者的生育能力。

【关键词】宫腔镜:子宫内膜癌前病变:早期子宫内膜样腺癌(EEC):达英-35;二甲双胍

Effect and evaluation of hysteroscopy on fertility-preserving treatment of endometrial atypical hyperplasia early endometrial adenocarcinoma in polycystic ovary syndrome patients Su Chunlin, Li Xin, Huang Rufei, Lu Huijuan. Lin Jinfang

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[Abstract] Objective To explore the clinical efficacy and safety of hysteroscopy in the treatment of endometrial atypical hyperplasia (EAH) or early endometrioid adenocarcinoma (EEC) in young patients with polycystic ovary syndrome (PCOS). **Methods** This was a retrospective study. The patients were divided into 2 groups, 1) drug treatment group: a total of 12 cases (9 cases of EAH, 3 cases of EEC) were treated with Diane-35 (1 tablet per day, for 21 d per month) combined with metformin (1 000 mg, qd) in the treatment, every 3 months by curettage + pathological evaluation; 2) hysteroscopic treatment group: a total of 32 cases (21 cases of EAH, 11 cases of EEC) were treated with Diane-35 combined with metformin, every 3 months by hysteroscopic surgery under the lesion excision and curettage+pathological evaluation. Results All patients were pathologically confirmed that endometrial lesions were successfully reversed, atypical endometrial hyperplasia of the patients in drug treatment group was successfully reversed in (6.6±3.1) months; atypical endometrial hyperplasia of the patients in hysteroscopy treatment group were successfully reversed in (4.1 ± 1.3) months, the difference was statistically significant (P=0.025); early endometrial adenocarcinoma of the patients in group of drug treatment successfully reversed in (6.3 ± 2.8) months; EEC of the patients in hysteroscopy treatment group was successfully reversed in (4.7 ± 1.7) months, the difference was statistically significant (P=0.020). In drug treatment group, 2 cases with natural conception and full-term delivery in EAH; in hysteroscopy treatment group, 9 cases (5 cases of EEC, 4 cases of EAH) of full-term delivery, another 8 cases in pregnancy. Conclusion The drug treatment of Diane-35 combined with metformin can completely reverse endometrial precancerous lesion and EEC of PCOS with insulin resistance (IR), hysteroscopy, which could radically resect endometrial lesions, can achieve th goal of "Disease-free", so it can significantly shorten the therapeutic time of drugs.

[Key words] Hysteroscopy; Endometrial precancerous lesions; Early endometrial carcinoma (EEC); Diane-35; Metformin

宫、腹腔镜联合手术对子宫内膜异位症合并子宫内膜息肉不孕患者妊娠结局的影响

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【摘要】目的 探讨宫、腹腔镜联合手术对子宫内膜异位症 (EMS) 合并子宫内膜息肉 (EP) 不孕症患者的生殖预后及其相关影响因素。方法 回顾性分析 2014 年 1 月—2014 年 12 月期间接受宫、腹腔镜联合治疗的 301 例 EMS 合并不孕患者作为研究对象,按是否合并 EP 分为 EP 组和非 EP 组,EP 组术后随访治疗效果,并与同期妊娠的 96 例正常孕产妇 (对照组)的妊娠经过和围产结局进行比较,分析其可能相关影响因素。结果 301 例 EMS 合并不孕患者的 EP 发生率为 42.86%(129/301)。III~IV期 EMS 患者 EP 发生率高于 I~II 期 EMS 患者 (P=0.018)。EP 在深部侵润型 EMS 的发生率 (53.13%) 明显高于卵巢型 (36.36%)(P=0.014) 和腹膜型 (42.54%)(P=0.003)。EP 组的胚胎停育率 (4.65%)高于非 EP 组 (2.91%),差异有统计学意义 (P=0.028);而自然妊娠率、临床妊娠率与非 EP 组相比差异无统计学意义。I~II 期患者术后的自然妊娠率 (48.15%)、临床妊娠率 (43.21%) 均高于III~IV 期患者 (31.25%,27.08%),差异有统计学意义 (P=0.002,P=0.017)。EMS 合并 EP 组宫、腹腔镜术后,孕期并发症发生率及围产儿死亡率与对照组比较,差异无统计学意义 (P>0.05),但剖宫产率显著高于对照组,差异有统计学意义 (P=0.012)。结论 EP 在 EMS 合并不孕患者中的发生率明显升高。EMS 合并 EP 不孕症患者应尽早接受宫、腹腔镜手术治疗,以提高术后自然妊娠率。宫、腹腔镜联合手术可明显改善 EMS 合并 EP 不孕患者的生殖预后,不增加孕期并发症,不影响围产儿结局。

【关键词】子宫内膜异位症 (EMS);子宫内膜息肉 (EP);不孕;手术;妊娠基金项目:福建省自然基金 (2017J01236)

Effect of laparoscopy and hysteroscopy in infertility patients with endometriosis and endometrial polyps

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[Abstract] Objective To investigate the reproductive prognosis and its related factors in patients with endometriosis (EMS) complicated with endometrial polyps (EP) infertility treated by laparoscopy and hysteroscopy. Methods A retrospective analysis of 301 cases of EMS complicated with infertility treated by gynecology combined with laparoscopy in Fujian Maternity and Children Health Hospital from January 2014 to December 2014 was retrospectively analyzed. Based on whether the patient suffers from EP, the subjects were divided into EP group (n=129) and non-EP group (n=172). By comparing the efficacy of EP group with control group of 96 normally pregnant women, the effects of the operation were analyzed. Results The rate of contracting EP among patients suffering from EMS and infertility was 42.86% (129/301). In addition, patients with stage III and IV EMS had a higher probability of contracting EP than stage I and II patients (P=0.018). However, such significance disappeared when the comparison was drawn between stage I and stage II patients, as well as between stage III and IV patients. Patients with deep infiltrating EMS were more likely to contract EP (53.13%) than those suffering from ovarian or abdominal EMS (31.25%, P=0.014; 27.08%, P=0.003). The difference between these two types of diseases was not statistically significant. This group also had a higher embryo arrest rate (4.65%) than its negative counterpart (2.91%, P=0.028). Patients with peritoneal EMS combined with EP had a slightly higher probability of natural pregnancy than their ovarian or deep infiltrating counterparts, but the difference failed to achieve any statistical significance. The difference in the rate of pregnancy-induced complications and perinatal mortality between the EMS combined with EP group and control group was not statistically significant, yet the former did have a higher rate in receiving caesarean section, which was statistically significant (P=0.012). Conclusion Infertile patients suffering from EMS are likely to contract EP. Furthermore, infertile patients suffering from both EMS and EP should receive combined laparoscopic and hysteroscopic surgery as soon as possible to increase their chance of natural conception after surgery. The surgery is obviously effective in improving the reproductive prognosis of such patients, while at the same poses no risk of inducing pregnancy-related complications or affecting the neonatal outcomes.

[Key words] Endometriosis (EMS); Endometrial polyps (EP); Infertility; Surgery; Pregnancy

Fund program: Fujian Province Natural Fund (2017J01236)

第3日胚胎质量对冻融囊胚移植周期临床结局的影响

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【摘要】目的 探讨第 3 日 (D3) 胚胎质量对冻融囊胚移植周期 (frozen-thawed blastocyst transfer, FBT) 临床结局的影响。方法 回顾性分析 2013 年 3 月—2017 年 2 月在本院生殖中心行冻融双囊胚 FBT 的 1 212 个周期的临床资料,按移植囊胚所对应 D3 胚胎的形态学评分将患者分为双优质卵裂胚移植组、单优质卵裂胚组、无优质卵裂胚组;根据移植囊胚所对应 D3 胚胎卵囊球分为双 8-细胞 (8C) 组、单 8C 组及非 8C 组,比较各组 FBT 的临床结局。结果 D3 双优质卵裂胚组的胚胎种植率 (44.7%)、临床妊娠率 (68.3%) 及活产率 (54.9%) 均显著高于 D3 无优卵裂胚组 (34.4%、55.4%、41.1%; P=0.003、P=0.008、P=0.022); D3 中双 8C 组的胚胎种植率 (48.2%)、临床妊娠率 (71.4%) 及活产率 (58.8%) 均显著高于非 8C 组 (40.1%、61.3%、45.2%; P=0.002、P=0.005、P=0.002),但多胎妊娠率 (27.9%) 明显高于 D3 非 8C 组 (19.6%)。结论 FBT 的临床结局与其对应 D3 胚胎质量密切相关,D3 优质卵裂胚尤其 8C 源囊胚临床结局更佳;选择 D3 8C 来源的单囊胚或 D3 非优质卵裂胚来源的双囊胚移植,可在获得高活产率的同时,减少多胎妊娠率。

【关键词】 冻融囊胚移植 (FBT); 妊娠率; 活产率; 多胎率

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Effect of day 3 embryo quality on the clinical outcomes of frozen-thawed blastocyst transfer Shi Sanbao,

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[Abstract] Objective To investigate the relationship between day 3 (D3) embryo quality and the clinical pregnancy outcomes of frozen-thawed blastocyst transfer (FBT). Methods The clinical data of 1 212 frozen blastocysts transfer cycles transferred two good-quality blastocysts in our center from March 2013 to February 2017 were analyzed retrospectively. According to the morphological score of D3 cleavage embryos of transferred blastocysts, all enrolled subjects were divided into two good-quality embryo group, single good-quality group and non good-quality embryo groups, and according to the number of blastomeres on D3, they were also divided into two 8C group, single 8C group, non-8C group. The clinical outcomes of FBT were compared among groups. **Results** The embryo implantation rate (44.7%), the clinical pregnancy rate (68.3%) and the live birth rate (54.9%) in two good-quality embryo group were significantly higher than those in non good-quality embryo groups (34.4%, 55.4%, 41.1%; P=0.003, P=0.008, P=0.022). The embryo implantation rate (48.2%), the clinical pregnancy rate (71.4%) and the live birth rate (58.8%) in two 8C group were significantly higher compared with non-8C group (40.1%, 61.3%, 45.2%; P=0.002, P=0.005, P=0.002). It was also found that the multiple pregnancy rate (27.9%)in two 8C group was obviously higher than non-8C group (19.6%). Conclusion The clinical outcomes of FBT is closely related to the morphological score of D3 cleavage embryo, and the blastocyst derived from good-quality cleavage embryo could achieve a better clinical outcome, especially from 8C of D3. Transferring single blastocyst derived from 8C of D3 or two blastocysts derived from non good-quality cleavage embryo may lead to a higher live rate and lower multiple pregnancy rate.

[Key words] Frozen-thawed bastocyst transfer (FBT); Pregnancy rate; Live birth rate; Multiple pregnancy rate

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钙离子载体 A23817 对卵胞质内单精子显微 注射受精失败者卵母细胞的激活作用

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【摘要】目的 探讨 Ca²⁺ 载体 A23817 对卵胞质内单精子显微注射 (ICSI) 受精失败后卵母细胞的激活效果。方法 回顾性分析 2016 年 1 月—2018 年 1 月期间因第 1 周期 ICSI 受精失败于本中心行第 2 周期 Ca²⁺ 载体 A23817 辅助激活的 53 个 ICSI 周期的患者临床资料。根据男方精液质量分 4 组: A 组,重度少弱精子症或梗阻性无精子症; B 组,圆头精子症; C 组,其他类型严重精子畸形; D 组,其他因素。采用自身前后对照研究,将所有患者第 1 周期行常规 ICSI 的卵母细胞设为对照亚组,将第 2 周期行 Ca²⁺ 辅助激活 ICSI 的卵母细胞设为人工卵母细胞激活 (AOA) 亚组。再分别比较各组间实验室指标、妊娠结局,以及各 AOA 亚组的激活率。结果 ① A、B、C 组各 AOA 亚组的正常受精率 (分别为 36.9%、66.7%、58.2%)均显著高于相应的对照组 (12.7%、0.0%、17.6%; P 均为 0.000),D 组的 AOA 亚组和对照亚组间差异无统计学意义 (P>0.05); ② C 组的 AOA 亚组种植率显著高于对照亚组 (P=0.02),A 组、D 组的 AOA 亚组和对照亚组间种植率差异无统计学意义。B 组研究亚组胚胎移植后部分成功着床并发生临床妊娠,而其对照亚组无胚胎可进行移植; ③各组的 AOA 亚组间激活率差异有统计学意义 (P=0.00),其中以 B 组 (86.7%) 的激活率最高。结论 对于精源性因素导致的 ICSI 受精失败可行 Ca²⁺ 载体 A23817 辅助激活,以改善 ICSI 后的受精情况,并能改善精子畸形患者的周期结局。

【关键词】Ca²⁺ 激活;卵胞质内单精子显微注射(ICSI);受精失败;精子畸形 基金项目:国家自然科学基金(81501331);河南省科技攻关项目(172102310193)

Activation effect of calcium ionophore A23817 on the oocyte after failure of intracytoplasmic sperm injection fertilization Song Wenyan, Liu Minrui, Jin Haixia, Yao Guidong, Shi Senlin

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[Abstract] Objective To explore the effect of calcium (Ca²⁺) ionophore A23817 on the oocyte after intracytoplasmic sperm injection (ICSI) fertilization failure. Methods A total of 53 cycles conducted oocyte activation with Ca²⁺ ionophore A23817 in the second ICSI treatment, due to low fertilization and total fertilization failure in the first ICSI cycles, from January 2016 to January 2018 in reproductive center of the First Affiliated Hospital of Zhengzhou University, were included in this retrospective research. According to the sperm quality, patients were divided into four groups, including group A (severe oligoasthenospermia and obstructive azoospermia), group B (globozoospermia), group C (other types of sperm deformity), group D (other factors). According to self-control study, oocytes in the second oocyte activation cycles were set as assisted oocyte activation (AOA) subgroup, and the oocytes in their first cycles conducted normal ICSI treatment were set as control subgorup. Laboratory indexes and pregnancy outcomes were compared between AOA subgroup and control subgroup, and the activation rate in AOA subgroup was compared among different experimental groups. Results 1) The 2 pronucleurs (PN) rate in AOA subgroup of groups A, B and C (36.9%, 66.7%, 58.2%) was statistical significantly higher than control subgroup in groups of A, B and C (12.7%, 0.0%, 17.6%; all P was 0.00), which was not significantly different in group D (P>0.05). 2) The implantation rate in AOA subgroup (56.5%) was statistically higher than that in control group (0.0%) in group C (P=0.02), which was not significantly different in groups A and D. In AOA subgroup of group B, some embryos were successfully implanted after transfer, whereas no embryos can be transferred in control subgroup. 3) There were significant differences of activation rate among groups A, B and C, and that of group B (86.7%) was the highest among them. Conclusion the patients with repeated fertilization failure due to severe sperm factors, Ca2+ activation can significantly improve the fertilization of ICSI, besides, Ca2+ activation can also significantly improve the pregnancy outcomes of ICSI for the patients with sperm deformity.

Key words Activation by calcium ionophore; Intracytoplasmic sperm injection (ICSI); Fertilization failure; Sperm deformity

Fund program: National Natural Science Foundation of China (81501331); Scientific and Technological Project of Henan Province (172102310193)

·实验研究 ·

雌二醇、G蛋白耦联雌激素受体激动剂和抑制剂对去势大鼠5-羟色胺水平的影响

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【摘要】目的 探索雌激素对去势大鼠血清 5- 羟色胺 (HT) 水平的影响,以及 G 蛋白耦联雌激素受体 (GPER) 在其中发挥的作用。方法 健康 12 周龄性成熟雌性大鼠 50 只,随机分为 10 组,每组 5 只。其中 30 只通过卵巢去势手术建立绝经大鼠模型,20 只行假手术作为对照组。去势大鼠再分为 6 组,分别注射 1 周的雌二醇 (E2) 组、E2+GPER 特异性激动剂 (G1) 组、G1 组、抑制剂 (G15) 组、E2+G15 组、油剂组;假手术大鼠分别注射 1 周的 G1 组、G15 组、空白组、油剂。于手术前及用药前后分别进行心脏采血,采用酶联免疫吸附法 (ELISA) 检测血清中 5-HT 的水平。结果 大鼠卵巢去势手术后 5-HT 水平显著降低 (P=0.031),假手术后 5-HT 水平无显著变化 (P=0.380)。卵巢去势的大鼠在连续注射 1 周 E2 后,5-HT 水平显著升高 (P=0.007)。单独注射 G1 或 G15 及 E2+G1 或 E2+G15 1 周后,5-HT 水平变化均无统计学意义。结论 大鼠卵巢去势后血清 5-HT 水平显著降低,而使用雌激素治疗使 5-HT 水平升高,G1 和 G15 治疗 1 周对大鼠 5-HT 水平没有显著影响。

【关键词】 G 蛋白耦联雌激素受体 (GPER); 去势大鼠; 雌二醇 (E_2); 5- 羟色胺 (5-HT) 基金项目: 上海市科学技术委员会 (15411950202)

·实验研究 ·

Effects of estrogen, G-protein coupled estrogen receptor agonists and inhibitors on 5-hydroxytryptamine levels in ovariectomized rats *Hu Jiangshan, Yang Ruwei, Tao Minfang*

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[Abstract] Objective To explore the effect of estrogen on 5-hydroxytryptamine (5-HT) levels in ovariectomized rats and the role of the G protein-coupled estrogen receptor (GPER) in it. **Methods** Fifty 12-week-old female mice were randomly divided into two groups in which 30 rats were ovariectomized to establish the model of menopause, the other 20 rats were sham-operated. Ovariectomized rats were subdivided into 6 groups, including injection with estradiol (E_2), E_2 +GPER specific agonist (G1), G1, inhibitor (G15), E_2 +G15, oil for one week; sham operation rats were injected with G1, G15, blank and oil for 1 week. Blood samples were taken from the heart before operation, and before and after treatment. Serum 5-HT levels were measured by enzyme-linked immunosorbent assay (ELISA). **Results** After ovariectomy, the level of 5-HT was significantly decreased (P=0.031) in rats and the level of 5-HT did not change significantly after sham operation (P=0.380). Serum levels of 5-HT were significantly elevated in ovariectomized rats after one week of continuous injection of E_2 (P=0.007). There was no significant change in 5-HT levels were significantly decreased after ovarian castration, whereas estrogen treatment resulted in elevated 5-HT levels. No significant effect of G1 and G15 on serotonin levels in rats was found. However, the mechanisms by which estrogen regulates mood disorders and 5-HT, and the role that GPER plays in them still need to be further explored and studied.

[Key words] G protein-coupled estrogen receptor (GPER); Ovariectomized rats; Estradiol (E₂); 5-hydroxytryptamine (5-HT)

Fund program: The Science and Technology Commission of Shanghai Municipality (15411950202)

·实验研究 ·

重组人生长分化因子 -9 蛋白对小鼠促排卵作用的研究

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【摘要】目的 探讨重组蛋白生长分化因子 -9(GDF-9) 对小鼠卵泡发育的作用。方法 选取 30 只性成熟雌性昆明小鼠随机分为 3 组,每组 10 只。对照组小鼠腹腔注射 0.5 mL 生理盐水;尿促性腺激素 (hMG) 组注射 hMG 10 IU;联合组注射 hMG 10 IU 联合重组蛋白 GDF-9 10 μ g;48 h 后所有小鼠腹腔注射人绒毛膜促性腺激素 (hCG)10 IU。注射 hCG 后 16~20 h 处死小鼠,比较各组小鼠卵巢指数 (卵巢相对重量 / 相对体质量) 及获卵数,酶联免疫吸附法 (ELISA) 法检测小鼠血清雌二醇 (E2) 含量,并对卵母细胞进行体外受精,观察各组受精情况。 结果 hMG 组、联合组获卵数 (28.9±10.2、36.5±13.0)、卵巢指数 [(32.26±6.33) mg/100 g、(38.80±8.90) mg/100 g】、血清 E2 含量 [(45.64±14.19) ng/L、(52.02±16.08) ng/L] 均高于对照组 [11.4±5.4、(26.11±7.16) mg/100 g、(25.03±13.62) ng/L],差异有统计学意义 (P=0.001、P=0.034、P=0.029;P=0.000、P=0.028、P=0.014);尤以联合组获卵数最多、卵巢指数最大、E2 含量最高,与 hMG 组相比差异亦有统计学意义 (P=0.025、P=0.031、P=0.043);对照组、hMG 组、联合组组间小鼠卵母细胞体外受精率相近,差异无统计学意义 (P>0.05)。结论 重组蛋白 GDF-9 可以辅助促性腺激素 (Gn)有效增加小鼠促排卵获卵数,且对卵母细胞的正常受精能力无影响。

【关键词】促排卵;生长分化因子-9(GDF-9);促性腺激素;卵巢反应基金项目:天津市卫生局科技基金(2013KY40)

•实验研究•

In vivo effects of recombinant human growth differentiation factor-9 protein on ovulation induction in mice

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[Abstract] Objective To explore the effect of recombinant protein growth differentiation factor-9 (GDF-9) on follicular development in mice. **Methods** Thirty eugamic KM mice were divided into three groups, which received human menopausal gonadotropin (hMG) 10 IU, hMG 10 IU with recombinant protein GDF-9 10 μg (combination group) and normal saline (0.5 mL) i.p. (control group), respectively; 48 h later, human chorionic gonadotropin (hCG) 10 IU was injected into each mouse, 16-20 h later 30 mice were killed, their ovary weight and the number of follicles were compared. Enzyme linked immunosorbent assay (ELISA) was used to examine the level of serum estrogen (E2), their oocytes were fertilized in vitro, and fertilization information was observed. Results The number of follicles $(28.9 \pm 10.2, 36.5 \pm 13.0)$, ovary index $[(32.26 \pm 6.33) \text{ mg/}100 \text{ g}]$ (38.80 ± 8.90) mg/100 g] and the level of serum E₂ [(45.64 ± 14.19) ng/L, (52.02 ± 16.08) ng/L] after ovulation induction in hMG group and combination group were higher than those of control group $[11.4\pm5.4, (26.11\pm$ 7.16) mg/100 g, (25.03 ± 13.62) ng/L], with statistical significances (P=0.001, P=0.034, P=0.029; P=0.000, P=0.028, P=0.014), especially, and they were significantly higher in combination group than in hMG group (P=0.025, P=0.031, P=0.043). There were no significant differences in fertilization rate among different groups (P>0.05). Conclusion Recombinant protein GDF-9 combined with gonadotropin (Gn) could effectively increase oocyte retrieval rate in mice, while had no influence on mouse oocytes fertilizability. Utilizing recombinant protein GDF-9 combined with Gn provide a new clinical idea for improving ovarian response to ovulation stimulation.

[Key words] Ovulation induction; Growth differentiation factor-9 (GDF-9); Gonadotropin (Gn); Ovarian response (OR)

Fund program: Tianjin Health Bureau Technology Fund (2013KY40)

第5日与第6日高质量冻融囊胚移植临床结局的比较研究

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【摘要】目的 比较研究冻融囊胚移植 (frozen-thawed blastocyst transfer,FBT) 周期移植第 5 日 (D5) 与第 6 日 (D6) 高质量囊胚的临床结局差异。方法 回顾性分析 2013 年 1 月—2017 年 8 月期间在本中心接受 FBT 的 365 例共 387 个周期不孕症患者的临床结局,根据形成扩张囊胚的天数及移植胚胎的个数分 4 组,分别为第 5 日双囊胚移植组 (double D5 blastocysts transfer group,DET5 组)88 个周期、第 5 日单囊胚移植组 (single D5 blastocyst transfer group,SET5 组)69 个周期、第 6 日双囊胚移植组 (double D6 blastocysts transfer group,DET6 组)129 个周期及第 6 日单囊胚移植组 (single D6 blastocyst transfer group,SET6 组)101 个周期。结果 四组患者的平均年龄、不孕年限、内膜厚度、基础卵泡刺激素 (FSH) 及冻融胚胎的复苏率比较,组间差异无统计学意义 (P>0.05);SET5 组的临床妊娠率 (62.3%) 和种植率 (62.3%) 显著高于 SET6 组 (46.5%, 46.5%)(P 均为 0.04),与 DET5 组和 DET6 组比较差异无统计学意义 (P>0.05);DET5 组及 DET6 组的多胎率均为 42.6%,分别与 SET5 组及 SET6 组 (均为 0.0%) 比较,差异有统计学意义 (P 均为 0.00)。结论 FBT 周期选择高质量的 D5 囊胚进行单胚胎移植,可以确保临床妊娠率和种植率,并显著降低多胎率。

【关键词】玻璃化冷冻;囊胚;冻融囊胚移植(FBT) 基金项目:广东省清远市科技计划项目(编号 2013B015)

Comparative study of the clinical outcomes of the day 5 and day 6 high-quality frozen-thawed blastocyst transplantation

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[Abstract] Objective To compare the differences of clinical outcomes in frozen-thawed blastocyst transfer (FBT) cycles between high-quality blastocysts on day 5 (D5) and on day 6 (D6). **Methods** Retrospective analysis of clinical outcomes was performed on 365 infertility patients with 387 FET cycles from January 2013 to August 2017. It was divided into four groups according to the days of the expanded blastocyst formation and the numbers of embryo transfer, there were respectively 88 cycles in double D5 blastocysts transfer group (DET5) group, 69 cycles in single D5 blastocyst transfer group (SET5) group, 129 cycles in double D6 blastocysts transfer group (DET6) group and 101 cycles in single D6 blastocyst transfer group (SET6) group. **Results** There was no significant difference in the age of patients, the infertile duration, the endometrium thickness and the proportion of embryos that survived the thawing process (P>0.05). The pregnancy rate (62.3%) and the implantation rate (62.3%) of SET5 group were significantly higher than those of SET6 group (46.5%, 46.5%) (P=0.04, P=0.04), but there was no significant difference with DET5 group and DET6 group (P>0.05). The multiple pregnancy rate of DET5 group (42.6%) and DET6 group (42.6%) was significantly higher than that of SET5 group (0.0%) and SET6 group (0.0%) (P=0.00, P=0.00). **Conclusion** In FBT cycles, selecting D5 high-quality blastocyst for SET can ensure the clinical pregnancy rate and implantation rate, and significantly reduce the multiple pregnancy rate.

[Key words] Vitrification; Blastocyst; Frozen-thawed blastocyst transfer (FBT) **Fund program**: Qingyuan Municipal Science and Technology Project (2013B015)

不孕症患者焦虑抑郁情绪的影响因素及其对体外受精妊娠结局的影响

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【摘要】目的 研究不孕症女性患者焦虑抑郁情绪状态和相关的影响因素,及其对体外受精 (IVF) 妊娠结局的影响。方法 采用焦虑自评量表 (SAS) 与抑郁自评量表 (SDS) 对 IVF 的女性患者进行焦虑抑郁情绪自评调查,分析临床和实验室资料,随访妊娠结局。结果 共纳入 842 例女性患者,统计量表结果显示,29.5% 的患者存在情绪问题,其中 18.4% 有焦虑情绪,21.6% 有抑郁情绪。文化程度是不孕患者出现焦虑抑郁情绪的影响因素,文化程度低的不孕患者比文化程度高者更易出现焦虑或抑郁情绪,差异有统计学意义 (P=0.012; P=0.000)。不孕年限≥ 10 年的患者更容易出现抑郁情绪。妊娠组和非妊娠组的SAS、SDS 标准分、焦虑抑郁程度差异均无统计学意义 (P>0.05)。Logistic 回归分析未提示焦虑抑郁情绪对妊娠结局有不良影响。结论 文化程度高是不孕症女性患者出现情绪问题的保护因素。我们的研究并未提示轻中度焦虑抑郁情绪对 IVF 妊娠结局有明显不良影响,严重焦虑抑郁情绪是否影响妊娠结局尚不清楚。

【关键词】不孕症;焦虑;抑郁;体外受精(IVF)

Evaluation of factors associated with the anxiety and depression of infertility patients and the effect on in vitro fertilization outcomes Dai Kailing, Li Ruiqi, Zheng Lingyan, Li Ying, Li Di, Wang Wenjun Reproductive Medicine Center, Department of Obstetrics and Gynecology, Sun Yat-Sen Memorial Hospital, Sun Yat-Sen University, Guangzhou 510120, China (Dai KL, Li RQ, Zheng LY, Li Y, Li D, Wang WJ) Corresponding author: Wang Wenjun, Tel: +86-20-81332233, Email: wenjungzcn@163.com

[Abstract] Objective To investigate factors related to the anxiety and depression of female infertility patients and to evaluate whether anxiety and depression is related to the outcomes in women undergoing *in vitro* fertilization (IVF). **Methods** The self-rating anxiety scale (SAS) and self-rating depression scale (SDS) were used to evaluate anxiety and depression among the women undergoing IVF. Clinical and laboratory data of patients were analyzed, and pregnancy outcomes were followed up. **Results** A total of 842 patients were enrolled in this study. There were 29.5% of the cases with anxiety or depression, 18.4% of the cases with anxiety, and 21.6% of the cases with depression. The lower educational background was identified as risk factor associated with both depressive and anxiety symptoms (P=0.012; P=0.001). Patients with infertility duration longer than 10 years tended to be more depress. There were no significant differences between the pregnant and non-pregnant women in terms of the SAS scores and SDS scores. The result of logistic regression analysis showed that the anxiety or depression was not related to the outcomes in women undergoing IVF. **Conclusion** Higher education is a protective factor for anxiety and depression of female infertility patients. We found no evidence that anxiety and depression had any influence on the outcome of IVF treatment. It is unclear whether severe anxiety and depression is related to the outcomes in women undergoing IVF.

Key words Infertility; Anxiety; Depression; *In vitro* fertilization (IVF)

从转诊患者看剖宫产瘢痕妊娠的规范化诊断与治疗

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【摘要】目的 探讨剖宫产瘢痕妊娠 (CSP) 的规范化诊断与治疗。方法 对 28 例因"剖宫产术后瘢痕妊娠"治疗后转诊的患者相关资料进行回顾性分析。包括首诊医院的诊断治疗情况及转诊我院后的诊断及治疗情况。结果 18 例在首诊医院误诊为宫内妊娠,直接行清宫术。其中 10 例因术中/术后大出血,8 例因术后阴道出血淋漓不净转诊本院。入院后三维彩色超声联合磁共振成像 (MRI) 确诊为 CSP,后续给予药物保守或手术治疗。10 例在首诊医院诊断为 CSP,均给予子宫动脉介入栓塞术 (UAE) 联合 B 超阴道下清宫术。术后患者因月经量减少、闭经转诊我院。入院后三维彩色超声确诊为宫腔粘连/子宫下段粘连,后续给予宫腔镜手术或扩宫治疗。结论 对多次剖宫产史、怀疑子宫瘢痕处妊娠的患者应联合三维彩色超声明确诊断。处理 CSP 前采用阴道超声必要时联合三维超声明确 CSP 分型,明确 UAE 治疗的适应证,并充分考虑 UAE 对卵巢储备功能以及宫腔粘连的不利影响。

【关键词】剖宫产瘢痕妊娠 (CSP); 三维彩色超声; 子宫动脉介入栓塞术 (UAE); 甲氨蝶呤 (MTX); 宫腔粘连

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Necessity of establishing standardized diagnosis and treatment of cesarean scar pregnancy from referring patients Xiao Zhuoni, Cheng Dan, Chen Jiao, Yang Jing, Xu Wangming

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CAbstract Dobjective To explore the establishment of standardized diagnosis and treatment of cesarean scar pregnancy (CSP). **Methods** Twenty-eight referring patients treated with CSP at first visit hospital were recruited in this retrospective study. The diagnosis and treatment in both first visit hospital and our hospital were evaluated. **Results** Eighteen patients were misdiagnosed as intrauterine pregnancy, and were given medical or artificial abortion directly at first visit hospital. Ten of them urgently visited our hospital because of intraoperative or postoperative heavy bleeding. Eight of them visited our hospital because of persistent vaginal bleeding after suction. All these patients were diagnosed CSP with three-dimensional color ultrasound scan and magnetic resonance imaging (MRI) after hospitalization. The patients were improved after medical or surgical treatment. Ten patients were diagnosed as CSP, and given the combination of uterine artery embolization (UAE) and ultrasound-guided dilatation and curettage (D&G) at first visit hospital. They came to visit us because of the significantly reduced menstruation or amenorrhea. All of them were diagnosed as uterine or lower uterine adhension and were given dilatation or hysteroscopic surgery. **Conclusion** Three-dimensional color ultrasound should be recommended for multiple caesarean section or suspicion of CSP patients. The combination of UAE with surgery should be chosen carefully because of its potential fertility complication.

Key words Cesarean scar pregnancy (CSP); Three-dimensional color ultrasound; Uterine artery embolization (UAE); Methotrexate (MTX); Uterine adhension

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早期官角妊娠的临床转归与治疗

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【摘要】目的 探讨早期宫角妊娠的临床转归及治疗。方法 回顾性分析了近6年在本院行促排卵或宫腔内人工受精/体外受精-胚胎移植(IUI/IVF-ET)助孕的16例孕早期超声诊断为宫角妊娠患者的临床资料。结果 16例无症状型早期宫角妊娠患者均动态超声观察及严密随访,其中5例孕囊转为宫内妊娠;8例孕囊继续向宫角肌层扩展者中7例行手术终止妊娠,1例行经阴道宫角妊娠减胎术;2例孕囊位置无明显改变者行宫角妊娠减胎术;1例胚胎停育者行药物杀胚加清宫术。结论 早期宫角妊娠具有生长方向的双向性,对于无明显临床症状且有强烈生育要求的妇女,超声早期诊断和孕8周内的严密动态监测可作为帮助选择继续期待观察或终止妊娠的重要依据。

【关键词】宫角妊娠;生育需求;超声;诊断;监测;处理

Clinical outcomes and treatment of early stage of corneal heterotopic pregnancy Wang Yaqin, Zhao Qinghong, Xu Wangming, Yang Jing

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[Abstract] Objective To explore the clinical outcomes and treatment of early stage of corneal heterotopic pregnancy for desired fertility women. Methods The clinical data were analyzed in 16 cases with early stage of cornual pregnancy diagnosed by ultrasound who underwent stimulate ovulation, intrauterine insemination (IUI), in vitro fertilization (IVF)-embryo transfer (ET) in our hospital. Results Sixteen cases of asymptomatic patient with early stage of cornual pregnancy opted for expectant treatment by close ultrasound monitoring. Eight cases gestation sac expanded to the horn of uterus, 2 cases remained in original site, 5 cases shifted to cavity and 1 case occurred spontaneous abortion. Seven cases of expanded to horn of uterus were offered with surgery while 3 cases were successfully treated by transvaginal ultrasound guided selective embryo reduction, 1 case of spontaneous abortion was successfully treated by methotrexate and mifepristone with curettage. Conclusion It's possible that cornual pregnancy turns into uterine pregnancy, therefore early ultrasonographic diagnosis and close ultrasonographic and clinical monitoring within 8 weeks of pregnancy maybe provide important principles of treatments of specific measures which include observation and interruption of pregnancy for desired fertility patients with early stage of cornual pregnancy.

[Key words] Cornual pregnancy; Fertility desire; Ultrasound; Diagnostics; Monitor; Treatment

连续硬膜外麻醉与气管插管静脉全麻下宫内外合并妊娠腹腔镜手术患者的妊娠结局分析

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【摘要】目的 比较罗哌卡因连续硬膜外麻醉与气管插管丙泊酚静脉全麻对宫内外合并妊娠 (HP) 腹腔镜手术患者妊娠结局的影响。方法 回顾性分析 2010 年 12 月—2018 年 1 月期间完成的 70 例宫内外合并妊娠腹腔镜手术的临床资料,根据麻醉方式不同分为气管插管丙泊酚静脉全麻组 (A 组,n=37) 和罗哌卡因连续硬膜外麻醉组 (B 组,n=33)。记录两组患者的术前资料、术中情况、围术期不良事件情况、妊娠结局及新生儿情况。结果全部手术均顺利完成。① A 组 5 例患者 (13.5%) 自然流产,32 例患者 (86.5%)继续妊娠直至分娩;B 组 4 例患者 (12.1%) 自然流产,29 例患者 (87.9%)继续妊娠直至分娩;组间比较差异无统计学意义 (P=1.000)。② A 组 2 例患者早产 (6.3%),B 组 2 例患者早产 (6.9%),组间比较差异无统计学意义 (P=1.000)。③所有新生儿均无窒息,无出生缺陷,其中 A 组低体质量儿 2 名 (6.3%),B 组低体质量儿 2 名 (6.9%),组间比较差异无统计学意义 (P=1.000)。结论 HP 患者在罗哌卡因连续硬膜外麻醉与气管插管丙泊酚静脉全麻两种麻醉方式下腹腔镜手术均可获得良好的妊娠结局。

【关键词】连续硬膜外麻醉:气管插管静脉全麻;宫内外合并妊娠(HP);腹腔镜手术;妊娠结局;新生儿

Analysis of pregnancy outcomes in patients with heterotopic pregnancy combined with laparoscopic surgery under continuous epidural anesthesia and tracheal intubation intravenous anesthesia Rao Jie, Yang Ruimin, Su Gaosheng, Mo Yi

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[Abstract] Objective To compare the effects of continuous epidural anesthesia with ropivacaine and tracheal intubation intravenous anesthesia with propofol on pregnancy outcomes in patients with heterotopic pregnancy undergoing laparoscopic surgery. Methods Seventy patients with heterotopic pregnancy undergoing laparoscopic surgery from December 2010 to January 2018 were selected and divided into two groups according to the different ways of anesthesia. One group had tracheal intubation intravenous anesthesia with propofol (group A, n=37), and the other group received continuous epidural anesthesia with ropivacaine (group B, n=33). The preoperative data, intraoperative conditions, peri-operative adverse events, pregnancy outcomes and newborns status were recorded. **Results** All the operations were completed successfully. In group A, 5 patients (13.5%) had spontaneous abortion and 32 patients (86.5%) continued to be pregnant until childbirth. In group B, 4 patients (12.1%) had spontaneous abortion and 29 patients (87.9%) continued to be pregnant until childbirth. There was no significant difference between the two groups (P=1.000). In group A, 2 patients had premature delivery (6.3%) and 2 patients in group B were premature (6.9%), there was no significant difference between the two groups (P=1.000). No asphyxia or congenital malformation was seen in all the newborns. There were 2 low weight neonates in group A (6.3%) and 2 low weight neonates in group B (6.90%), there was no significant difference between the two groups (P=1.000). Conclusion All patients with heterotopic pregnancy combined with laparoscopic surgery under continuous epidural anesthesia with ropivacaine and tracheal intubation intravenous anesthesia with propofol can achieve good pregnancy outcome.

[Key words] Continuous epidural anesthesia; Tracheal intubation intravenous anesthesia; Heterotopic pregnancy (HP); Laparoscopic surgery; Pregnancy outcomes; Newborn

·个案报道·

冻融胚胎移植术后早期官内妊娠合并输卵管脓肿: 1 例病例报道并文献复习

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【摘要】目的 探讨早期宫内妊娠合并输卵管脓肿的诊断及治疗方案。方法 分析 1 例冻融胚胎移 植术后早期妊娠合并输卵管脓肿的病例并进行文献回顾。结果 患者经手术及抗生素治疗后好转出院,于孕 37^{+2} 周剖宫产 1 名活婴。结论 腹腔镜探查术结合术后抗生素的应用可作为早期妊娠合并输卵管脓肿的首选的治疗方案。

【关键词】早期宫内妊娠;输卵管脓肿;冻融胚胎移植(FET)

· 个案报道 ·

Tubal abscess in early pregnancy after frozen-thawed embryo transfer: a case report and review of literature Liu Fengxia, Jiang Qiu

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[Abstract] Objective To discuss the diagnosis and treatment of the tubal abscess in early pregnancy. **Methods** A case of tubal abscess in early pregnancy after frozen-thawed embryo transfer (FET) was reported and literatures were reviewed. **Results** The patient discharged home after surgery in a stable condition and underwent cesarean section to acquire a live baby at 37^{+2} weeks of gestation. **Conclusion** Laparoscopy combined with antibiotics should be the first-line treatment of early pregnancy complicating tubal abscess.

[Key words] Early intrauterine pregnancy; Tubal abscess; Frozen-thawed embryo transfer (FET)

自然杀伤细胞在反复种植失败中的研究进展

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【摘要】 反复种植失败 (RIF) 是影响体外受精 - 胚胎移植 (IVF-ET) 成功率的重要因素,胚胎种植成功与否与胚胎质量和子宫内膜容受性相关。在月经周期增殖期,子宫内膜细胞功能层有少量自然杀伤 (NK) 细胞,排卵后 NK 细胞显著增加,胚胎着床后 NK 细胞将维持高水平至妊娠早期。蜕膜 NK 细胞是母 - 胎界面含量最多的免疫细胞,对胚胎种植、蜕膜血管重铸、胎盘形成、滋养细胞侵袭和妊娠结局都有非常重要的作用。本文就蜕膜 NK 细胞在胚胎种植过程中发挥作用的研究进展作一综述。

【关键词】 自然杀伤 (NK) 细胞; 反复种植失败 (RIF); 体外受精 - 胚胎移植 (IVF-ET) 基金项目: 广西自然科学基金 (2017GXNSFBA198150); 广西医疗卫生重点科研课题 (2011065)

Progress of nature killer cells and repeated implantation failure *Cai Junying, Huang Dongmei, Zhang Bo Maternal and Child Health Hospital of Guangxi Zhuang Autonomous Region, Nanning 530003, China (Cai JY, Huang DM, Zhang B)*

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[Abstract] Repeated implantation failure (RIF) is one of the important factor to success rate of *in vitro* fertilization-embryo transfer (IVF-ET), the success of embryo implantation is related to the quality of the embryo and the endometrial receptivity. Early in the menstrual cycle, there are a small amount of nature killer (NK) cells in the endometrial cell function layer, they elevate after ovulation, and maintain a high level if the embryo implantated till every pregnancy rate. Decidual NK cells are the most abundant immune cells of maternal-fetal interface, which play an important role in modulating embryo implantation, angiogenesis and vascular remodeling, placentation, trophoblast invasion and pregnancy outcome. Our understanding of this condition is still limited. In this paper, the role of the decidual NK cells and embryo implantation were reviewed.

[Key words] Nature killer (NK) cell; Recurrent implantation failure (RIF); *In vitro* fertilization-embryo transfer (IVF-ET)

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胰岛素样生长因子 2/H19 印迹基因在辅助生殖中的研究进展

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【摘要】我国不孕不育夫妇呈逐年上升的趋势,而辅助生殖技术 (assisted reproductive technology,ART) 已成为治疗不孕不育的主要方法之一。胰岛素样生长因子 (IGF)2/H19 基因在配子形成、受精过程、胚胎的早期发育中有着至关重要的作用,而 *IGF2/H*19 基因甲基化水平的变化直接影响其基因的表达。ART 过程是否会改变 *IGF2/H*19 基因甲基化水平,这些基因甲基化水平的改变又是否会影响 ART 治疗后的妊娠结局。本文就这些问题结合目前的研究现状进行综述。

【关键词】 胰岛素样生长因子 (IGF)2; H19; 印迹基因; DNA 甲基化; 表观遗传学; 辅助生殖技术 (ART)

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Progress in the study of insulin-like growth factor 2/H19 imprinting genes in assisted reproduction Luo Xi, Wu Ze, Gao Mengying, Deng Lian, Li Yonggang

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【Abstract】 China's infertility couples are increasing year by year, and assisted reproductive technology (ART) has also become one of the main ways to treat infertility couples. Insulin-like growth factor (IGF)2/H19 gene imprinting plays a crucial role in gametogenesis, fertilization, and early development of embryos. Moreover, changes in the methylation level of the *IGF2/H*19 gene directly affect the expression of its gene. Will the ART process change the methylation level of *IGF2/H*19 gene? Futhermore, whether changes in the methylation levels of these genes will affect the pregnancy outcome after ART treatment. This article reviews these issues in conjunction with current research.

Key words Insulin-like growth factor (IGF)2; H19; Imprinting gene; DNA methylation; Epigenetics; Assisted reproductive technology (ART)

Fund program: The Scientific Research Fund Project of the Yunnan Provincial Education Department (2016ZDX021); Yunnan Medical Academic Leader Project (D-201634); Health Science and Technology Plan Fund of Yunnan Province (2016NS212); Yunnan Science and Technology Plan Project (2017HC009)

间充质干细胞与妊娠及妊娠结局关系的研究进展

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【摘要】 间充质干细胞 (mesenchymal stem cells, MSCs) 是一种易得的成体干细胞。近年的研究发现, MSCs 在某些生殖疾病中也发挥作用,并且日益成为生殖领域研究的热点。MSCs 由于其生物学特性,不仅可以作为某些生殖疾病的治疗载体,更可能成为探索疾病发病机制的靶点之一。本文重点回顾并总结了目前 MSCs 在不孕症、自然流产、先兆子痫等疾病中的研究进展,并对未来 MSCs 的应用与研究进行了探讨和思考,希望可为日后研究提供新思路。

【关键词】 间充质干细胞 (MSCs); 生殖; 不孕症; 流产

Mesenchymal stem cells and pregnancy or pregnancy outcomes: advances in studies Chang Zhuo, Feng Xiaoling, Chen Lu

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[Abstract] Mesenchymal stem cells (MSCs) are a kind of common and easily obtainable somatic stem cells. In recent years, it has been found that MSCs also play a role in some reproductive diseases and have become a new hot spot of research in the field of reproductive medicine. Because of the unique biological characteristics of MSCs, it not only may become a carrier for curing some reproductive diseases and is more likely to be an important target for exploring the pathogenesis of diseases. By summarizing the previous research results, this paper focuses on the current research progress of MSCs in infertility, spontaneous abortion, recurrent abortion for unknown reasons and preeclampsia. On the basis of this, to discuss the application of MSCs in the future has been

Key words Mesenchymal stem cells (MSCs); Reproduction; Infertility; Abortion

involved so as to provide new ideas for future researches.

辅酶 Q10 的抗氧化性及其对卵巢功能的影响

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【摘要】氧化应激可能是导致早发性卵巢功能不全的重要原因之一,辅酶 Q10 是一种脂溶性醌类化合物,是存在于线粒体呼吸链中的抗氧化剂。动物实验提示,辅酶 Q10 的缺乏会增加卵母细胞的氧化应激,引起线粒体功能障碍,加快卵母细胞凋亡,最终导致卵巢储备功能下降。辅酶 Q10 的补充可改善卵巢功能,促进排卵,提高卵子质量。本文就辅酶 Q10 的抗氧化性及其对卵巢功能的影响作一综述。

【关键词】 辅酶 Q10;氧化应激;卵巢功能;早发性卵巢功能不全;抗氧化剂基金项目:国家自然科学基金(81703236)

Antioxidant of coenzyme Q10 and its effect on the function of ovary Li Xiaojun, Li Chunming, Ma Linjuan, Zhou Jianhong

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【Abstract】 Oxidative stress is one of the important etiologies of premature ovarian insufficiency (POI). Coenzyme Q10 (CoQ10), as a lipid-soluble benzoquinon, is an antioxidant in the mitochondrial respiratory chain. The deficiency of CoQ10 can increase oxidative stress of oocytes, which induces mitochondrial dysfunction and accelerates granulosa cell apoptosis, diminishing ovarian reserve finally. The supplementation of CoQ10 may preserve ovarian reserve and improve ovulation rates and oocyte quality. This review describes the antioxidant of CoQ10 and its effect on the function of ovary.

[Key words] Coenzyme Q10; Oxidative stress; Ovarian function; Premature ovarian insufficiency; Antioxidant

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Hedgehog 通路对女性生殖系统肿瘤的作用

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【摘要】 Hedgehog(HH)信号通路对女性生殖系统的发育起重要作用,并在多种肿瘤细胞中异常激活,提示其活化可能与肿瘤的发生和进展有关。本文将对近年来 HH 通路在女性生殖系统肿瘤中的研究进展及其抑制剂的临床应用作一综述,旨在为相关肿瘤的靶向治疗提供临床依据。

【关键词】 Hedgehog(HH) 通路; 卵巢癌; 宫颈癌; 子宫内膜癌; 抑制剂

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Effects of Hedgehog signaling pathway in female reproductive system cancer Cao Can, Xie Shuwu, Zhu Yan Key Lab. of Reproduction Regulation of NPFPC, SIPPR, IRD, Fudan University, Shanghai 200032, China (Cao C, Xie SW, Zhu Y)

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[Abstract] Hedgehog (HH) signaling pathway plays an important role in the development of female reproductive system. It is abnormally activated in a variety of tumor cells, which suggests that activation of HH signaling may be related to tumorigenesis and progression. In this review, we summarize the role of HH signaling in the progression and treatment of female reproductive system tumors and the clinical application of its inhibitors in recent years. We aim to provide the clinical evidence for target therapy of related tumors.

[Key words] Hedgehog (HH) pathway; Ovarian cancer; Cervical cancer; Endometrial cancer; Inhibitors **Fund program**: National Key Research & Development Plan Projects during the 13th Five-year Plan Period (2016YFC1000904)