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不同黄体支持方案对 ≤ 35 岁助孕患者行改良自然周期冻融胚胎移植的孕产结局影响

张文 吴余玲 任炳楠 嘉若琳 张文娟 王碧君 杜晓芳 管一

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【摘要】 目的 探讨不同黄体支持方案对 ≤ 35 岁助孕患者行改良自然周期冻融胚胎移植(modified natural cycle frozen-thawed embryo transfer, mNC-FET)的孕产结局影响。方法 采用回顾性队列研究, 分析2018年1月至2020年12月期间在郑州大学第三附属医院生殖健康医院接受mNC-FET的年龄 ≤ 35 岁助孕患者, 共2 086个周期, 根据不同黄体支持方案分为3组。A组为黄体酮软胶囊联合地屈孕酮片组(446个周期), B组为地屈孕酮片组(439个周期), C组为黄体酮阴道缓释凝胶联合地屈孕酮片组(1 201个周期)。使用倾向性评分匹配(propensity score matching, PSM)法按1:1的比例进行匹配基线数据后, 分别比较A组与B组、C组与B组的助孕结局。通过单因素及多因素广义估计方程调整影响活产率的混杂因素后, 分析不同黄体支持方案对活产率的影响。结果 PSM后, A组与B组、C组与B组的血人绒毛膜促性腺激素阳性率、临床妊娠率、异位妊娠率、移植周期活产率、低出生体质量儿及巨大儿发生率、早产率、妊娠期并发症发生率及出生缺陷发生率等方面组间比较差异均无统计学意义(均 $P>0.05$)。广义估计方程调整混杂因素后显示, 不同黄体支持方案并不是移植周期活产率的独立影响因素。结论 在mNC-FET周期, ≤ 35 岁助孕患者单独选择地屈孕酮片作为黄体支持药物, 与黄体酮软胶囊或黄体酮阴道缓释凝胶联合地屈孕酮片的活产率和围产期结局没有差异, 但仍需大样本前瞻性研究证实。

【关键词】 冻融胚胎移植； 妊娠结局； 黄体支持； 改良自然周期； 围产期结局

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Impact of different luteal phase support protocols on pregnancy outcomes in patients aged ≤ 35 years undergoing modified natural cycle frozen-thawed embryo transfer

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【Abstract】 Objective To investigate the impact of different luteal phase support protocols on pregnancy outcomes in patients aged ≤ 35 years undergoing modified natural cycle frozen-thawed embryo transfer (mNC-FET). **Methods** A retrospective cohort study was conducted to analyze 2 086 cycles of patients aged ≤ 35 years who received mNC-FET cycles in Reproductive Health Hospital of the Third Affiliated Hospital of Zhengzhou University from January 2018 to December 2020. The cycles were divided into three groups based on luteal phase support protocols used. The patients received a combination of progesterone soft capsule and dydrogesterone in the group A (446 cycles), the patients received dydrogesterone in the group B (439 cycles), and the patients received a combination of progesterone vaginal sustained-release gel and dydrogesterone in the group C (1 201 cycles). The pregnancy and perinatal outcomes were compared between groups A and B, groups C and B after matching the baseline data in a ratio of 1 : 1 using the propensity score matching (PSM). The effect of different luteal phase support on live birth rate was analyzed after adjusting for confounding factors affected by univariate and multivariate generalized estimating equation (GEE). **Results** After PSM, there were no significant differences between groups A and B, groups C and B in human chorionic gonadotropin positive rate, clinical pregnancy rate, ectopic pregnancy rate, live birth rate in transplant cycle, incidence of low weight, macrosomia, premature delivery rate, pregnancy complication rate and incidence of birth defects (all $P>0.05$). GEE analysis showed that three different luteal phase support regimens were not associated with live birth rate. **Conclusion** In the mNC-FET cycle, patients aged ≤ 35 years who chose dydrogesterone alone as luteal phase support drug, had no difference in live birth rate and perinatal outcome between progesterone soft capsules or progesterone vaginal sustained-release gel combined with dydrogesterone, but the outcome still needs to be confirmed by large sample prospective studies.

【Key words】 Frozen-thawed embryo transfer; Pregnancy outcome; Luteal phase support; Modified natural cycle frozen-thawed embryo transfer; Perinatal outcome

Fund program: Joint Project of Medical Disciplines of Henan Province (LHGJ20200435); National Key R&D Program of China (2021YFC2700602); Henan Young and Middle-aged Health Science and Technology Innovation Leading Talent Training Project (YXKC2021020)

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既往巨细胞病毒、风疹病毒和单纯疱疹病毒感染对 IVF/ICSI-ET 妊娠结局的影响

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【摘要】 目的 探讨既往巨细胞病毒 (cytomegalovirus, CMV)、单纯疱疹病毒 (herpes simplex virus, HSV) 和风疹病毒 (rubella virus, RV) 感染对不孕女性首次行体外受精/卵胞质内单精子注射-胚胎移植 (*in vitro* fertilization/intracytoplasmic sperm injection and embryo transfer, IVF/ICSI-ET) 助孕妊娠结局的影响。方法 采用回顾性队列研究, 分析 2017 年 12 月至 2022 年 12 月期间在郑州大学第一附属医院生殖医学中心首次行 IVF/ICSI-ET 助孕女性的临床资料。将患者分为 CMV-IgG (+) 组 ($n=154$)、RV-IgG (+) 组 ($n=86$)、HSV-IgG (+) 组 ($n=93$) 和 IgG 全阴性组 ($n=172$), 分别比较病毒单独感染组和全阴性组患者的妊娠结局。既往同时感染 CMV 和 HSV 的患者为 CMV+HSV-IgG (+) 组

($n=344$), 进一步比较两种病毒同时感染和单独感染的妊娠结局。结果 CMV-IgG (+) 组的双原核 (two pronuclei, 2PN) 受精率 [63.90% (1 195/1 870)]、临床妊娠率 [51.30% (79/154)]、活产率 [45.45% (70/154)] 显著低于 IgG 全阴性组 [68.68% (1 469/2 139), $P=0.001$; 68.60% (118/172), $P=0.001$; 61.05% (105/172), $P=0.005$]。HSV-IgG (+) 组的 2PN 受精率 [61.62% (729/1 183)]、临床妊娠率 [50.54% (47/93)]、活产率 [43.01% (40/93)] 显著低于 IgG 全阴性组 [68.68% (1 469/2 139), $P=0.001$; 68.60% (118/172), $P=0.004$; 61.05% (105/172), $P=0.005$]。RV-IgG (+) 组的 2PN 受精率、临床妊娠率、活产率与 IgG 全阴性组相比差异均无统计学意义 (均 $P>0.05$)。CMV-IgG (+) 组、RV-IgG (+) 组、HSV-IgG (+) 组的妊娠期糖尿病、妊娠期高血压病等并发症的发生风险及新生儿结局与 IgG 全阴性组相比差异均无统计学意义 (均 $P>0.05$)。多因素 logistic 回归分析显示, CMV-IgG (+) ($OR=0.453$, 95% CI : 0.280~0.734, $P=0.001$; $OR=0.515$, 95% CI : 0.321~0.825, $P=0.006$)、HSV-IgG (+) ($OR=0.425$, 95% CI : 0.245~0.738, $P=0.002$; $OR=0.447$, 95% CI : 0.259~0.771, $P=0.004$)、CMV+HSV-IgG (+) ($OR=0.491$, 95% CI : 0.329~0.733, $P=0.001$; $OR=0.528$, 95% CI : 0.357~0.780, $P=0.001$) 均是患者临床妊娠和活产的独立影响因素。既往同时感染 CMV 和 HSV 组的临床结局与单独感染组相比差异均无统计学意义 (均 $P>0.05$)。结论 既往单独感染 CMV 或 HSV 降低了患者 IVF/ICSI-ET 的受精率、临床妊娠率和活产率, 但对妊娠期并发症和新生儿结局无明显影响。既往同时感染 CMV 及 HSV 与单独感染患者的妊娠结局相似。

【关键词】 病毒; 受精, 体外; 胚胎移植; 妊娠结局; 既往感染
基金项目: 国家自然科学基金面上项目 (82071649)

Effects of previous cytomegalovirus, rubella virus, and herpes simplex virus infections on IVF/ICSI-ET pregnancy outcomes

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【 Abstract 】 **Objective** To explore the impact of previous cytomegalovirus (CMV), herpes simplex virus (HSV), and rubella virus (RV) infection on pregnancy outcomes in infertile women undergoing the first *in vitro* fertilization/intracytoplasmic sperm injection and embryo transfer (IVF/ICSI-ET) treatment. **Methods** A retrospective cohort study was conducted to analyze the clinical data of women who underwent IVF/ICSI-ET for the first time at the Reproductive Medicine Center, the First Affiliated Hospital of Zhengzhou University from December 2017 to December 2022. The patients were divided into CMV-IgG (+) group ($n=154$), RV-IgG (+) group ($n=86$), HSV-IgG (+) group ($n=93$) and IgG all-negative group ($n=172$). The pregnancy outcomes of the patients in the virus-only infection group and the IgG all-negative group were compared. Patients

who were previously co-infected with CMV and HSV were classified as the CMV+HSV-IgG (+) group ($n=344$), and the pregnancy outcomes of patients with previous CMV and HSV co-infection and those with infection alone were further compared. **Results** The two pronuclei (2PN) fertilization rate [63.90% (1 195/1 870)], the clinical pregnancy rate [51.30% (79/154)], and the live birth rate [45.45% (70/154)] of the CMV-IgG (+) group were significantly lower than those of the IgG completely negative group [68.68% (1 469/2 139), $P=0.001$; 68.60% (118/172), $P=0.001$; 61.05% (105/172), $P=0.005$]. The 2PN fertilization rate [61.62% (729/1 183)], the clinical pregnancy rate [50.54% (47/93)], and the live birth rate [43.01% (40/93)] of the HSV-IgG (+) group were significantly lower than those of the IgG completely negative group [68.68% (1 469/2 139), $P=0.001$; 68.60% (118/172), $P=0.004$; 61.05% (105/172), $P=0.005$]. There were no statistical differences in the 2PN fertilization rate, the clinical pregnancy rate, and the live birth rate between the RV-IgG (+) group and the IgG completely negative group (all $P>0.05$). Compared with the IgG completely negative group, there were no significant differences in the risk of complications such as gestational diabetes, hypertensive disorders of pregnancy and neonatal outcomes in the CMV-IgG (+) group, RV-IgG (+) group, and HSV-IgG (+) group (all $P>0.05$). Multivariate logistic regression analysis showed that CMV-IgG (+) ($OR=0.453$, 95% CI : 0.280–0.734, $P=0.001$; $OR=0.515$, 95% CI : 0.321–0.825, $P=0.006$), HSV-IgG (+) ($OR=0.425$, 95% CI : 0.245–0.738, $P=0.002$; $OR=0.447$, 95% CI : 0.259–0.771, $P=0.004$) and CMV+HSV-IgG (+) ($OR=0.491$, 95% CI : 0.329–0.733, $P=0.001$; $OR=0.528$, 95% CI : 0.357–0.780, $P=0.001$) were all independent influencing factors of patients' clinical pregnancy and live birth. There were no statistical differences in the clinical outcomes between the previous CMV and HSV co-infection group and the single infection group ($P>0.05$). **Conclusion** Previous CMV or HSV infection alone reduced the fertilization rate, the clinical pregnancy rate and the live birth rate of patients undergoing IVF/ICSI-ET treatment, but had no significant impact on pregnancy complications and neonatal outcomes. Pregnancy outcomes of patients with previous CMV and HSV co-infection were similar to those with infection alone.

【 Key words 】 Virus; Fertilization *in vitro*; Embryo transfer; Pregnancy outcomes; Previous infection

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IVF/ICSI 助孕患者单卵双胎妊娠风险因素分析及其对围产期结局的影响

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【摘要】 目的 分析体外受精/卵胞质内单精子注射-胚胎移植 (*in vitro* fertilization/ intracytoplasmic sperm injection and embryo transfer, IVF/ICSI-ET) 患者发生单卵双胎 (monozygotic twins, MZT) 妊娠的影响因素及围产期结局。 **方法** 本研究为回顾性队列研究, 收集 2015 年 1 月至 2023 年 9 月期间于郑州大学第三附属医院生殖健康医院行 IVF/ICSI 选择性单胚胎移植 (elective single embryo transfer, eSET) 后实现妊娠的 12 079 例患者的临床资料, 根据患者移植后 30 d 超声胎心数分为单胎妊娠组和 MZT 妊娠组。最终纳入 MZT 妊娠 300 例, 根据辅助生殖技术助孕时间按照 1:5 进行随机抽样匹配单胎妊娠 1 500 例。比较两组患者一般资料、胚胎相关指标及围产期结局, 采用多因素 logistic 回归模型分析 MZT 的危险因素。 **结果** 单胚胎移植后双胎妊娠发生率为 2.48% (300/12 079), 高于自然受孕 MZT 妊娠。两组患者一般资料比较差异均无统计学意义 (均 $P>0.05$); MZT 妊娠组的囊胚移植率 [93.3% (280/300)] 比单胎妊娠组更高 [88.8% (1 332/1 500), $P=0.022$]。多因素 logistic 回归分析结果也表明囊胚移植会增加 MZT 发生风险 ($OR=0.552$, $P=0.016$, 95% CI : 0.341~0.894); 对囊胚周期进行分析, 结果显示移植优质囊胚时发生 MZT 风险较高 [MZT 妊娠组为 79.6% (223/280), 单胎妊娠组为 67.8% (903/1 332), $P<0.001$], 而滋养层细胞 (trophectoderm, TE) 分级为 C 时, MZT 发生风险较低 [MZT 妊娠组为 20.4% (57/280), 单胎妊娠组为 32.2% (429/1 332), $P<0.001$]。多因素 logistic 回归校正相关混杂因素后显示移植内细胞团 (inner cell mass, ICM) 分级为 B ($OR=0.601$, $P=0.001$, 95% CI : 0.442~0.819)、TE 分级为 A/B (A 级: $OR=2.951$, $P<0.001$, 95% CI : 1.980~4.399; B 级: $OR=1.840$, $P<0.001$, 95% CI : 1.315~2.576) 囊胚, MZT 发生风险增加。MZT 妊娠组的妊娠期并发症 [47.7% (143/300)]、早产 [55.1% (140/254)]、死胎发生风险 [3.7% (11/300)] 比单胎妊娠组 [19.3% (289/1 500), $P<0.001$; 7.4% (101/1 368), $P<0.001$; 1.5% (22/1 500), $P=0.016$] 均显著增高。 **结论** 辅

助生殖技术增加了 MZT 发生风险。移植囊胚，尤其是移植 ICM 排列松散、TE 排列致密的囊胚，患者发生 MZT 风险增加。

【关键词】 体外受精； 胚胎移植； 单卵双胞胎妊娠； 囊胚分级； 内细胞团； 滋养层细胞

Risk factor analysis of monozygotic twin pregnancy in IVF/ICSI and its impact on perinatal outcomes

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【 Abstract 】 **Objective** To investigate the influencing factors and perinatal outcomes associated with monozygotic twins (MZT) following elective single embryo transfer (eSET) via *in vitro* fertilization or intracytoplasmic sperm injection and embryo transfer (IVF/ICSI-ET). **Methods** A retrospective cohort study was conducted on 12 079 patients who achieved pregnancy after undergoing IVF/ICSI-eSET at Reproductive Health Hospital of the Third Affiliated Hospital of Zhengzhou University between January 2015 and September 2023. Patients were stratified into two groups based on ultrasound findings 30 d post-transfer: singleton pregnancy group and MZT pregnancy group. Finally, 300 MZT and 1 500 single pregnancies, which were randomly matched according to 1 : 5 were included by study period. General patients' characteristics, embryo-related factors, and perinatal outcomes were compared between the two groups. A multivariate logistic regression model was employed to identify risk factors for MZT after single embryo transfer, adjusting for potential confounding variables. **Results** The incidence of twin pregnancy following single embryo transfer was 2.48% (300/12 079), which was higher than that of naturally conceived monozygotic twin pregnancy. No significant difference was found in baseline characteristics between the two groups (all $P>0.05$). The blastocyst transfer rate was higher in the MZT pregnancy group [93.3% (280/300)] than in the singleton pregnancy group [88.8% (1 332/1 500), $P=0.022$]. Multivariate logistic regression analysis also showed that blastocyst transfer was associated with an increased risk of MZT ($OR=0.552$, $P=0.016$, 95% CI : 0.341–0.894). Analysis of blastocyst cycles showed that the risk of MZT was higher when transferring high-quality blastocysts [79.6% (223/280) vs. 67.8% (903/1 332), $P<0.001$], where as a trophoctoderm (TE) grading of C [20.4% (57/280) vs. 32.2% (429/1 332), $P<0.001$] had a lower risk of MZT. After adjusting for confounding factors, the risk of MZT was found to increase with the transfer of blastocysts with a B-grade inner cell mass (ICM) ($OR=0.601$, $P=0.001$, 95% CI : 0.442–0.819) and A/B grade TE (grade A: $OR=2.951$, $P<0.001$, 95% CI : 1.980–4.399; grade B: $OR=1.840$, $P<0.001$, 95% CI : 1.315–2.576). The risk of complications during pregnancy [47.7% (143/300) vs. 19.3% (289/1 500), $P<0.001$], preterm

labor [55.1% (140/254) vs. 7.4% (101/1 368), $P<0.001$], and the risk of stillbirth [3.7% (11/300) vs. 1.5% (22/1 500), $P=0.016$] were significantly higher in the MZT pregnancy group than in the singleton pregnancy group. **Conclusion** Assisted reproductive technology may contribute to the risk of MZT. Transfer of blastocysts, particularly those with loose ICM arrangement and dense TE arrangement, appears to increase the risk of MZT in patients undergoing eSET.

【Key words】 Fertilization *in vitro*; Embryo transfer; Monozygotic twin pregnancy; Blastocyst grading; Inner cell mass; Trophoblast cells

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滋肾育胎丸在反复种植失败患者冻融胚胎移植中的临床疗效观察

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【摘要】 目的 探讨滋肾育胎丸在反复种植失败 (repeated implantation failure, RIF) 患者冻融胚胎移植 (frozen-thawed embryo transfer, FET) 周期中的临床应用效果。方法 采用回顾性病例对照研究, 选取 2017 年 10 月至 2023 年 4 月期间于山东大学附属生殖医院女性生殖科就诊的 RIF 患者共 744 个周期, 根据黄体支持是否加用滋肾育胎丸分为试验组 (加用滋肾育胎丸, $n=279$) 和对照组 (不加用滋肾育胎丸, $n=465$), 比较两组患者的妊娠结局。根据 FET 周期子宫内膜准备方案的不同, 分为降调节方案 ($n=271$) 和非降调节方案 ($n=473$), 比较每个方案中两组患者的妊娠结局。结果 试验组和对照组患者的生化妊娠率、临床妊

娠率、胚胎种植率、早期流产率、晚期流产率及活产率, 差异均无统计学意义 (均 $P>0.05$)。降调节方案中试验组的生化妊娠率 [69.0% (58/84)]、临床妊娠率 [59.5% (50/84)]、胚胎种植率 [59.4% (57/96)] 明显高于对照组 [56.1% (105/187), $P=0.045$; 46.5% (87/187), $P=0.048$; 44.9% (92/205), $P=0.019$], 差异均有统计学意义。在非降调节方案中, 两组患者的妊娠结局差异均无统计学意义 (均 $P>0.05$)。结论 在 FET 降调节方案中, 滋肾育胎丸可显著提高 RIF 患者的临床妊娠率及胚胎种植率, 改善妊娠结局。

【关键词】 妊娠结局; 滋肾育胎丸; 冻融胚胎移植; 反复种植失败

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Observation on the clinical efficacy of Zishen Yutai Pill in frozen-thawed embryo transfer after repeated embryo implantation failures

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【Abstract】 **Objective** To investigate the clinical application effect of Zishen Yutai Pill in patients with repeated implantation failure (RIF) undergoing frozen-thawed embryo transfer (FET) cycles. **Methods** A retrospective case-control study was conducted, selecting 744 cycles of patients with RIF at the Department of Female Reproductive Medicine, State Key Laboratory of Reproductive Medicine and Offspring Health, Center for Reproductive Medicine, Institute of Women, Children and Reproductive Health, Shandong University from October 2017 to April 2023. The patients were divided into experimental group (treated with Zishen Yutai Pill, $n=279$) and control group (treated without Zishen Yutai Pill, $n=465$) based on whether Zishen Yutai Pill was added to luteal support. The pregnancy outcomes between the two groups were compared. Based on the different endometrial preparation protocols in the FET cycles, the patients were used down-regulation protocol ($n=271$) or non-down-regulation protocol ($n=473$). The pregnancy outcomes of the two groups in each protocol were compared. **Results** There were no statistically significant differences between the two groups in terms of biochemical pregnancy rate, clinical pregnancy rate, embryo implantation rate, early miscarriage rate, late miscarriage rate, and live birth rate (all $P>0.05$). However, the biochemical pregnancy rate [69.0% (58/84)], clinical pregnancy rate [59.5% (50/84)], and embryo implantation rate [59.4% (57/96)] in the experimental group of the down-regulated protocol were significantly higher than those in control group [56.1% (105/187), $P=0.045$; 46.5% (87/187), $P=0.048$; 44.9% (92/205), $P=0.019$], with statistically significant differences. In the non-down-regulated protocol, there were no statistically significant differences in

pregnancy outcomes between the two groups (all $P>0.05$). **Conclusion** In the FET down-regulated protocol, Zishen Yutai Pill can significantly improve the clinical pregnancy rate and the embryo implantation rate in patients with RIF, thereby improving pregnancy outcomes.

【 Key words 】 Pregnancy outcome; Zishen Yutai Pill; Frozen-thawed embryo transfer; Repeated implantation failure

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人类胚胎在干式培养箱和湿式培养箱的培养效果比较

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【摘要】 目的 比较人类胚胎在干式培养箱和湿式培养箱的培养效果。方法 本次研究纳入贵阳市妇幼保健院生殖医学中心 2020 年 10 月至 2022 年 4 月期间行体外受精 (*in vitro* fertilization, IVF) 治疗的不孕患者 479 例。本研究分为两个阶段, 第一阶段为同期同卵源自身对照研究, 共 95 例, 分为干式培养箱组和湿式培养组, 比较两组胚胎发育指标; 第二阶段研究分为 6 组, 即湿式培养箱 10 μ L 微滴组、湿式培养箱 20 μ L 微滴组、湿式培养箱 30 μ L 微滴组、干式培养箱 10 μ L 微滴、干式培养箱 20 μ L 微滴组、干式培养箱 30 μ L 微滴组, 每组 64 例患者。比较各组间患者一般临床资料、胚胎发育指标及妊娠结局, 检测并比较各组 24 h、48 h、72 h 渗透压及 pH 值。结果 同一患者胚胎在干式和湿式培养箱培养后, 干式培养箱的囊胚形成率 [62.3% (162/260)] 及优质囊胚率 [24.6% (64/260)] 低于湿式培养箱 [71.6% (252/352), $P=0.015$; 32.1% (113/352), $P=0.043$]。与其他各微滴组比较, 干式培养箱 10 μ L 组 48 h、72 h 卵裂培养液的渗透压及囊

胚培养液的渗透压明显升高, 组间比较差异均有统计学意义(卵裂培养液, 均 $P < 0.001$; 囊胚培养液: $P = 0.006$, $P = 0.008$)。同一时间点不同微滴体积组 pH 值比较, 差异均无统计学意义(均 $P > 0.05$)。不同体积微滴组比较, 各组患者的一般资料差异均无统计学意义(均 $P > 0.05$)。与其他各微滴组比较, 干式培养箱 10 μL 微滴组可移植胚胎率和优质胚胎率显著降低, 组间比较差异均有统计学意义(均 $P < 0.001$)。与干式培养箱和湿式培养箱的 20 μL 微滴组、30 μL 微滴组比较, 干式培养箱 10 μL 微滴组第 5 天囊胚形成率、总囊胚形成率及优质囊胚形成率均降低, 组间比较差异均有统计学意义(均 $P < 0.05$)。不同体积微滴组移植胚胎数量、移植胚胎中卵裂期胚胎和优质胚胎比例差异均无统计学意义(均 $P > 0.05$); 与其他体积微滴组比较, 干式培养箱中的 10 μL 微滴组临床妊娠率、胚胎着床率、新鲜移植胚胎活产率以及累计妊娠率均有所降低, 流产率有所增加, 但差异均无统计学意义(均 $P > 0.05$)。结论 与湿式培养箱比较, 干式培养箱培养微滴体积在 20 μL 及以上胚胎发育及妊娠结局差异不明显, 但干式培养箱 10 μL 微滴培养不利于胚胎的发育, 而这可能与微滴渗透压升高有关。

【关键词】 妊娠结局; 渗透压; 干式培养箱; 湿式培养箱; 胚胎培养

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Comparison of the effect of culturing human embryos between dry and humid incubators

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【Abstract】 **Objective** To compare the the cultivation effects of human embryos in dry and humid incubators. **Methods** A total of 479 infertile patients who underwent *in vitro* fertilization (IVF) treatment at Reproductive Center of Guiyang Maternal and Child Health Care Hospital from October 2020 to April 2022. The study was divided into two stages. The first stage of the study was a self-comparative research with 95 cases from the same period and source. The embryos were divided into dry and humid incubator groups to compare the embryo development indicators. In the second stage of the study, the patients were divided into six groups, including 10 μL humid incubator group ($n=64$), 20 μL humid incubator group ($n=64$), 30 μL humid incubator group ($n=64$), 10 μL dry incubator group ($n=64$), 20 μL dry incubator group ($n=64$), and 30 μL dry incubator group ($n=64$). The general clinical data, embryo development indicators, pregnancy outcomes, and the osmotic pressure and pH values of each group at 24 h, 48 h and 72 h were detected and compared. **Results** After cultivation of the same patient's embryos in dry and humid incubator, the total blastocyst formation rate [62.3% (162/260)] and high-quality blastocyst rate [24.6% (64/260)] in dry incubator were lower than those in the humid incubator [71.6% (252/352), $P=0.015$; 32.1% (113/352), $P=0.043$]. Compared with the other microdroplet groups, the osmotic pressure of cleavage culture medium in 10 μL group of dry

incubator at 48 h and 72 h and blastocyst culture medium were significantly increased, the differences among the groups were significant (cleavage culture medium, all $P<0.001$; blastocyst culture medium, $P=0.006$, $P=0.008$). There was no significant difference in pH value among different microdroplet volume groups at the same period (all $P>0.05$). There were no significant differences in general data among the different microdroplet groups (all $P>0.05$). Compared with the other microdroplet groups, 10 μL dry incubator group exhibited significantly lower transferable embryo rate (all $P<0.001$). When compared with 20 μL and 30 μL groups in both dry and humid incubators, 10 μL dry incubator group showed a lower day 5 blastocyst formation rate, lower total blastocyst formation rate, and lower high-quality blastocyst formation rate, the differences among the groups were significant (all $P<0.05$). There were no significant differences in the number of transferred embryos, the ratio of cleavage-stage embryos and the ratio of high-quality embryos among different groups (all $P>0.05$). Compared with the other microdroplet groups, the clinical pregnancy rate, the embryo implantation rate, the live birth rate of fresh transplanted embryos and the cumulative pregnancy rate in 10 μL group in the dry incubator decreased, and the miscarriage rate increased, but all were not significant (all $P>0.05$). **Conclusion** Compared with humid incubators, there are no significant differences in embryo development and pregnancy outcomes for droplet volumes of 20 μL or above in dry incubators. However, the 10 μL microdroplet culture in the dry incubator is not conducive to embryonic development, which may be related to the increased osmotic pressure of the microdroplet.

【Key words】 Pregnancy outcome; Osmotic pressure; Dry incubator; Humid incubator; Embryo culture

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实验研究

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皂公二藤汤治疗子宫内膜炎和对 TLR4 介导信号通路的影响

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【摘要】 目的 探讨皂公二藤汤 (Zaogong Erteng decoction, ZGETD) 治疗子宫内膜炎的可能作用机制。**方法** 利用子宫角注射 2.5 mg/mL 脂多糖诱导建立子宫内膜炎模型, 给予低剂量 ZGETD、高剂量 ZGETD 和阿莫西林治疗 7 d。7 d 后观察小鼠子宫的外观和子宫组织的病理变化, 计算小鼠的子宫指数; 酶联免疫吸附试验法检测小鼠子宫组织中肿瘤坏死因子- α (tumor necrosis factor- α , TNF- α)、白细胞介素 (interleukin, IL) 1 β 和 IL-6 的表达; 氧化还原反应测定小鼠子宫组织中髓过氧化物酶 (myeloperoxidase, MPO) 活性; 网络药理学分析 ZGETD 的活性成分和治疗子宫内膜炎的作用靶点和信号通路; Western blotting 和 qRT-PCR 分别检测小鼠子宫中 Toll 样受体 4 (Toll-like receptor 4, TLR4)、P65、p-P65、干扰素调节因子 3 (interferon regulatory factor 3, IRF3) 和 p-IRF3 蛋白以及趋化因子 *CXCL5* 和 *CXCL8* 的表达; 脱氧核糖核苷酸末端转移酶介导的缺口末端标记法检测子宫内膜细胞凋亡, 并测定子宫内膜厚度; 将治疗后的雌鼠与雄鼠交配, 统计交配率、妊娠率和妊娠第 8 天注射侧子宫角的着床点数。**结果** ZGETD 和阿莫西林对子宫内膜炎均有治疗效果, 但高剂量 ZGETD 较低剂量 ZGETD 和阿莫西林, 更明显地缓解了子宫组织的水肿和充血, 显著降低了子宫指数 (均 $P=0.001$), 使得治疗后的子宫腔上皮平滑、完整, 子宫腺体结构正常, 未见出血区域和炎性细胞聚集现象; 高剂量 ZGETD 较阿莫西林显著降低了炎性因子 (TNF- α 、IL-1 β 和 IL-6) 的表达和 MPO 活性 (均 $P<0.001$), 且治疗后趋化因子 (*CXCL5* 和 *CXCL8*) 的表达也显著降低 (均 $P<0.05$); 网络药理学筛选出 ZGETD 治疗子宫内膜炎的相关信号通路 TLR4、核因子 κ B (nuclear factor kappa-B, NF- κ B) 和 TNF- α , 并对其作用靶点 (TLR4、NF- κ B 和 IRF3) 进行了验证, 发现槲皮素、漆黄素和木犀草素是作用这些靶点最多的活性成分; 高剂量 ZGETD 显著抑制了 TLR4/NF- κ B 和 TLR4/IRF3 信号通路的激活 ($P<0.05$), 降低了子宫内膜细胞凋亡 ($P<0.05$), 提高了治疗后子宫内膜厚度 ($P<0.001$)、交配率 ($P<0.001$)、妊娠率 ($P<0.001$) 和 LPS 注射侧子宫角的着床点数 ($P=0.001$)。**结论** 高剂量 ZGETD 对子宫内膜炎具有显著的治疗效果, 这与下调 TLR4 信号通路密切相关。

【关键词】 子宫内膜炎; 网络药理学; 胚胎植入; 皂公二藤汤; TLR4 介导信号通路; 炎性因子

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Effect of Zaogong Erteng decoction on endometritis and TLR4-mediated signaling pathways

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【Abstract】 Objective To investigate the possible mechanism of Zaogong Erteng decoction (ZGETD) in the treatment of endometritis. **Methods** Femal mice were injected 2.5 mg/mL lipopolysaccharide into uterine horn to induce endometritis model. After modelling, low-dose ZGETD, high-dose ZGETD or amoxicillin was given once a day for 7 d. The appearance of the uterus and pathological changes of uterine tissue were observed 7 d later, and the uterine index was calculated. The expression of tumor necrosis factor (TNF)- α , interleukin (IL)-1 β and IL-6 in mouse uterine tissue was detected by enzyme-linked immunosorbent assay. The activity of myeloperoxidase (MPO) in mouse uterine tissue was measured by redox reaction. The active ingredients of ZGETD and the target and signal pathway of treatment of endometritis were analyzed by network pharmacology. Western blotting and qRT-PCR were used to detect the expressions of Toll-like receptor 4 (TLR4), P65, p-P65, interferon regulatory factor 3 (IRF3) and p-IRF3 proteins and chemokines *CXCL5* and *CXCL8* in the mouse uterus, respectively. Terminal dUTP nick end labeling detected endometrial cell apoptosis and endometrial thickness was measured. After treatment, the female rats were mated with the male rats, and the mating rate, the pregnancy rate and the number of implantation sits in the injected uterine horn on day 8 of gestation were counted. **Results** Both ZGETD and amoxicillin have atherapeutic effect on endometritis, but compared with low-dose ZGETD and amoxicillin, high-dose ZGETD can significantly alleviate the edema and congestion of uterine tissue and reduce the uterine index (all $P=0.001$). After treatment, the uterine cavity epithelium of mice was smooth and complete, the uterine gland structure was normal, and no bleeding area and inflammatory cell aggregation were observed. Compared with amoxicillin, high-dose ZGETD significantly decreased the expression of inflammatory factors (TNF- α , IL-1 β and IL-6) and MPO activity (all $P<0.001$). The expression of chemokines (*CXCL5* and *CXCL8*) was significantly reduced (all $P<0.05$). The signaling pathways TLR4, nuclear factor kappa-B (NF- κ B) and TNF related to the

treatment of endometritis by ZGETD were screened by network pharmacology, and their action targets (TLR4, NF- κ B and IRF3) were verified. Quercetin, fisetin and luteolin were found to be the most active ingredients acting on these targets. High-dose ZGETD significantly inhibited the activation of TLR4/NF- κ B and TLR4/IRF3 pathways ($P<0.05$), decreased endometrial cell apoptosis ($P<0.05$), and increased endometrial thickness ($P<0.001$), mating rate ($P<0.001$), pregnancy rate ($P<0.001$) and implantation site number of uterine horn on the injection side of LPS after treatment ($P=0.001$). **Conclusion** High-dose ZGETD has a significant therapeutic effect on endometritis, which may be closely related to the down-regulation of TLR4 signaling pathway.

【Key words】 Endometritis; Network pharmacology; Embryo implantation; Zaogong Erteng decoction; TLR4-mediated signaling pathways; Inflammatory factor

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流行病学研究

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江西省辅助生殖技术出生缺陷流行现状及相关因素分析

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【摘要】 目的 调研 2014—2023 年江西省辅助生殖技术 (assisted reproductive technology, ART) 出生缺陷流行病学特征及发展趋势, 探讨出生缺陷发生的相关因素。方法 回顾性收集 2014 年 1 月至 2023 年 12 月期间江西省 18 家生殖中心的 ART 分娩周期治疗数据及随访结果。分析出生缺陷的流行趋势与疾病类型顺位关系, 采用精确概率法估计出生缺陷发生率的 95% 置信区间 (confidence interval, CI), 通过 Poisson 回归分析独立相关因素。结果 本研究共纳入 65 003 例 ART 子代, 包括 2 025 例宫腔内人工授精 (intrauterine insemination, IUI) 子代和 62 978 例体外受精-胚胎移植 (*in vitro* fertilization and embryo transfer, IVF-ET) 子代, 总的出生缺陷发生率为 13.46‰ (95% CI: 12.59‰~14.38‰); 其中 IUI 为 9.38‰ (95% CI: 5.66‰~14.61‰), IVF-ET 为 13.59‰ (95% CI: 12.70‰~14.53‰)。2014—2023 年出生缺陷发生率呈下降趋势 (17.11‰至 11.47‰, $P_{\text{trend}}=0.003$)。前 3 位出生缺陷类型分别为循环系统畸形 (3.71‰, 95% CI: 3.25‰~4.21‰)、肌肉骨骼系统畸形 (2.37‰, 95% CI: 2.01‰~2.77‰) 和面、耳、眼、颈部畸形 (1.23‰, 95% CI: 0.98‰~1.53‰)。单因素分析显示, ART 男婴出生缺陷发生率 (14.72‰) 高于女婴 (12.31‰, $P=0.009$), 此外, 出生孕周、出生体质量、胎儿数、不孕原因以及分娩年份与出生缺陷发生率显著相关 ($P<0.001$ 、 $P<0.001$ 、 $P<0.001$ 、 $P=0.025$ 、 $P=0.037$)。多因素分析结果显示, 单胎中, 男婴、出生孕周 32~36 周、出生体质量 $<1\ 500\text{ g}$ 和双方因素不孕是出生缺陷的独立相关因素 ($OR=1.21$, 95% CI: 1.00~1.47, $P=0.046$; $OR=1.90$, 95% CI: 1.41~2.56, $P<0.001$; $OR=3.37$, 95% CI: 1.33~8.51, $P=0.010$; $OR=1.38$, 95% CI: 1.12~1.69, $P=0.003$); 而多胎中, 男婴、出生孕周 <32 周、出生孕周 32~36 周、出生体质量 $<1\ 500\text{ g}$ 、出生体质量 $1\ 500\sim2\ 499\text{ g}$ 、母亲年龄 25~29 岁以及母亲年龄 30~34 岁是出生缺陷的独立相关因素 ($OR=1.25$, 95% CI: 1.03~1.52, $P=0.023$; $OR=2.06$, 95% CI: 1.35~3.15, $P=0.001$; $OR=1.32$, 95% CI: 1.05~1.66, $P=0.016$; $OR=1.98$, 95% CI: 1.19~3.28, $P=0.009$; $OR=2.06$, 95% CI: 1.64~2.60, $P<0.001$; $OR=2.00$, 95% CI: 1.31~3.06, $P=0.001$; $OR=1.90$, 95% CI: 1.24~2.92, $P=0.003$)。结论 2014—2023 年江西省 ART 出生缺陷发生率呈逐年下降趋势, 其中循环系统畸形最常见。IVF-ET 出生缺陷的发生主要与母婴特征有关, 如胎儿数、性别、出生孕周、出生体质量、不孕原因以及母亲年龄, 与 ART 治疗因素无关。

【关键词】 生殖技术, 辅助; 出生缺陷; 发生率; 江西省; 相关因素

Monitoring of birth defects and analysis of correlation factors in assisted reproductive technology in Jiangxi Province

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【Abstract】 **Objective** To investigate the epidemiological characteristics and trends of birth defects related to assisted reproductive technology (ART) in Jiangxi Province from 2014 to 2023, and to explore the correlation factors of birth

defect occurrence. **Methods** A retrospective collection of ART treatment data and follow-up results from January 2014 to December 2023 across 18 reproductive centers in Jiangxi Province was conducted. The trend of birth defects and the rank order of defect types were analyzed. Exact probability methods were used to estimate the 95% confidence intervals (CI) of the incidence rates, and Poisson regression was applied to identify independent correlation factors. **Results** A total of 65 003 ART offspring were included in this study, comprising 2 025 offspring from intrauterine insemination (IUI) and 62 978 from *in vitro* fertilization and embryo transfer (IVF-ET). The overall incidence of birth defects was 13.46‰ (95% CI: 12.59‰–14.38‰), with 9.38‰ (95% CI: 5.66‰–14.61‰) for IUI and 13.59‰ (95% CI: 12.70‰–14.53‰) for IVF-ET. The incidence of birth defects showed a decreasing trend from 2014 to 2023 (17.11‰ to 11.47‰, $P_{\text{trend}}=0.003$). The top three birth defect types were circulatory system defects (3.71‰, 95% CI: 3.25‰–4.21‰), musculoskeletal system defects (2.37‰, 95% CI: 2.01‰–2.77‰), and congenital malformations of the face, ears, eyes, and neck (1.23‰, 95% CI: 0.98‰–1.53‰). Univariate analysis indicated that male offspring from IVF-ET had a higher incidence of birth defects than that in female offspring (14.72‰ vs. 12.31‰, $P=0.009$). Additionally, gestational age, birth weight, fetal number, cause of infertility, and year of delivery were significantly associated with birth defect incidence in IVF-ET offspring ($P<0.001$, $P<0.001$, $P<0.001$, $P=0.025$, $P=0.037$). Multivariate analysis showed that in singleton pregnancies, male offspring, gestational age 32–36 weeks birth weight <1 500 g, and infertility with bilateral factors were independent risk factors for birth defects ($OR=1.21$, 95% CI: 1.00–1.47, $P=0.046$; $OR=1.90$, 95% CI: 1.41–2.56, $P<0.001$; $OR=3.37$, 95% CI: 1.33–8.51, $P=0.010$; $OR=1.38$, 95% CI: 1.12–1.69, $P=0.003$), while in multiple pregnancies, male offspring, gestational age <32 weeks, gestational age 32–36 weeks, birth weight <1 500 g, birth weight 1 500–2 499 g, maternal age 25–29 years and maternal age 30–34 years were independent risk factors ($OR=1.25$, 95% CI: 1.03–1.52, $P=0.023$; $OR=2.06$, 95% CI: 1.35–3.15, $P=0.001$; $OR=1.32$, 95% CI: 1.05–1.66, $P=0.016$; $OR=1.98$, 95% CI: 1.19–3.28, $P=0.009$; $OR=2.06$, 95% CI: 1.64–2.60, $P<0.001$; $OR=2.00$, 95% CI: 1.31–3.06, $P=0.001$; $OR=1.90$, 95% CI: 1.24–2.92, $P=0.003$). **Conclusion** Over the past 10 years, the incidence of birth defects in ART offspring in Jiangxi Province has shown a decreasing trend annually, with circulatory system malformations being the most common. The occurrence of birth defects in IVF offspring is primarily associated with maternal and infant characteristics, such as gender, gestational age, birth weight, number of fetuses, and cause of infertility, independent of ART treatment factors.

【Key words】 Reproductive technology, assisted; Birth defects; Incidence; Jiangxi Province; Correlation factors

·现场调查·

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全球204个国家和地区1990—2019年不孕不育疾病负担分析及预测

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孙雅宁和许宁对本文有同等贡献

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【摘要】 目的 分析1990—2019年全球不孕不育疾病负担变化趋势,并对2020—2029年男女不育不孕的年龄标准化患病率(age-standardized prevalence rate, ASPR)与年龄标准化伤残调整寿命年(disability-adjusted life-year, DALY)率进行预测,从而为不孕不育疾病防治提供一定的参考依据。方法 基于2019版全球疾病负担数据库,采用患病率、ASPR、DALY率和年龄标准化DALY率综合评估全球不孕不育疾病负担。采用估计年度变化百分比来描述全球21个区域不孕不育疾病负担变化趋势。使用贝叶斯年龄-时期-队列模型预测2020—2029年全球204个国家和地区男女不育不孕的ASPR与年龄标准化DALY率,并通过自回归移动平均模型进行敏感性分析。结果 全球男性不育的患病率、DALY率、ASPR和年龄标准化DALY率分别从1990年的319.52/10万、1.82/10万、2 856.53/10万和16.19/10万上升至2019年的565.30/10万、3.22/10万、3 398.53/10万和19.36/10万。全球女性不孕的患病率、DALY率、ASPR和年龄标准化DALY率分别从1990年

的 656.67/10 万、3.53/10 万、6 036.36/10 万和 32.27/10 万上升至 2019 年的 1 223.78/10 万、6.59/10 万、7 483.12/10 万和 40.33/10 万。30~34 岁男女不育不孕疾病负担最高, 2019 年男女的 ASPR 分别为 4 407.47/10 万、10 270.55/10 万, 年龄标准化 DALY 率分别为 25.08/10 万、55.65/10 万。仅在 45~49 岁, 2019 年女性不孕的患病率(11.31/10 万)和 DALY 率(0.06/10 万)低于男性(患病率为 15.68/10 万, DALY 率为 0.08/10 万)。高社会人口学指数地区不孕不育的疾病负担最低。喀麦隆国家男性不育的 ASPR (7 652.40/10 万) 和年龄标准化 DALY 率 (43.94/10 万)最高, 中国女性不孕的 ASPR(20 402.30/10 万)和年龄标准化 DALY 率(106.16/10 万) 最高。预测结果显示 2020—2029 年全球 204 个国家和地区男女不育不孕疾病负担均呈现上升趋势。结论 1990—2019 年全球 204 个国家和地区男女不育不孕疾病负担均呈上升趋势, 预测在 2020—2029 年全球不育不孕疾病负担仍呈上升趋势。应尽早开展不孕不育的初步筛查, 加强健康教育并制定有效的防治策略。

【关键词】 患病率; 不孕不育; 贝叶斯年龄-时期-队列模型; 自回归移动平均模型; 估计年度变化百分比; 伤残调整寿命年

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Global analysis and forecast of the burden of infertility in 204 countries and territories from 1990 to 2019

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【Abstract】 **Objective** To analyze the trend of infertility disease burden from 1990 to 2019 and predict the age-standardized prevalence rate (ASPR) and age-standardized disability-adjusted life-year (DALY) rate of male and female infertility for 2020—2029, providing a certain reference for the prevention and treatment of infertility diseases. **Methods** Based on the Global Burden of Disease 2019, prevalence, ASPR, DALY rate, and age-standardized DALY rate were used to evaluate the global burden of infertility comprehensively. The estimated annual percentage change was used to describe trends in the disease burden of infertility in 21 regions worldwide. The Bayesian age period cohort model was used to predict the ASPR and age-standardized DALY rate for male and female infertility in 204 countries and regions from 2020 to 2029. Sensitivity analysis was performed using the autoregressive integrated moving average model. **Results** The

prevalence, DALY rate, ASPR and age-standardized DALY rate of global male infertility increased from 319.52 per 100 000, 1.82 per 100 000, 2 856.53 per 100 000, and 16.19 per 100 000 in 1990 to 565.30 per 100 000, 3.22 per 100 000, 3 398.53 per 100 000, and 19.36 per 100 000 in 2019, respectively. The prevalence, DALY rate, ASPR, and age-standardized DALY rate of global female infertility increased from 656.67 per 100 000, 3.53 per 100 000, 6 036.36 per 100 000, and 32.27 per 100 000 in 1990 to 1 223.78 per 100 000, 6.59 per 10 000, 7 483.12 per 100 000, and 40.33 per 100 000 in 2019, respectively. The burden of infertility disease was the highest in men and women aged 30–34 years, and the ASPR and age-standardized DALY rates were 4 407.47 per 100 000, 25.08 per 100 000, 10 270.55 per 100 000 and 55.65 per 100 000, respectively. Only in 45–49 years of age, the prevalence of infertility (11.31 per 100 000) and DALY rate (0.06 per 100 000) in women were lower than those in men (15.68 per 100 000 and 0.08 per 100 000). In addition, the burden of infertility was the lowest in high socio-demographic index regions. Cameroon had the highest ASPR (7 652.40 per 100 000) and age-standardized DALY rate (43.94 per 100 000) for male infertility. Chinese women had the highest ASPR (20 402.30 per 100 000) and age-standardized DALY rate (106.16 per 100 000) of infertility. The forecast results show that the burden of male and female infertility diseases will increase in 204 countries and regions from 2020 to 2029. **Conclusion** The burden of infertility diseases in men and women increased in 204 countries and regions from 1990 to 2019, and it is predicted that the global burden of infertility diseases will continue to rise in 2020 — 2029. Preliminary screening of infertility should be carried out as soon as possible, health education should be strengthened and effective prevention and treatment strategies should be formulated.

【Key words】 Prevalence; Infertility; Bayesian age period cohort model; Autoregressive integrated moving average model; Estimated annual percentage change; Disability-adjusted life-years

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个案报道

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冻融胚胎移植后发生自发性卵巢过度刺激综合征行卵巢囊肿穿刺治疗 1 例

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【摘要】 本文回顾分析和报道 1 例采用人工周期冻融胚胎移植妊娠发生自发性卵巢过度刺激综合征 (spontaneous ovarian hyperstimulation syndrome, sOHSS) 的病例资料和诊治过程。该患者系人工周期冻融单胚胎移植后双胎妊娠, 孕中期发生 sOHSS, 首次行双侧卵巢囊肿穿刺抽吸治疗, 明显改善腹胀症状, 使患者继续妊娠并成功分娩 2 个女婴。sOHSS 疾病罕见发生, 重在早期识别并采用相应治疗措施缓解患者症状, 改善患者预后。

【关键词】 卵巢囊肿; 穿刺术; 抽吸; 自发性卵巢过度刺激综合征; 冻融胚胎移植; 人工周期

A case report of spontaneous ovarian hyperstimulation syndrome after FET with ovarian cyst puncture and aspiration

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【Abstract】 In this article, we reviewed and reported the diagnosis and treatment of a pregnant woman with spontaneous ovarian hyperstimulation syndrome (sOHSS) after artificial cycle frozen-thawed embryo transfer. The patient had twins after artificial cycle frozen-thawed single embryo transfer. In the second trimester pregnancy, the patient had sOHSS and was firstly received ovarian cyst puncture and aspiration to reduce abdominal distension significantly, then she continued the pregnancy and delivered 2 girls successfully. The sOHSS is a rare disease, so the early diagnose and appropriate treatment should be taken to alleviate the symptoms and improve patients prognosis.

【Key words】 Ovarian cyst; Puncture; Aspiration; Spontaneous ovarian hyperstimulation syndrome; Frozen-thawed embryo transfer; Artificial cycle

综述

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支持细胞 FSH 受体介导男性生殖调节及其研究进展

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【摘要】 睾丸内卵泡刺激素受体 (follicle-stimulating hormone receptor, FSHR) 仅支持细胞表达。卵泡刺激素 (follicular-stimulating hormone, FSH) 由 FSHR 介导, 通过 cAMP/PKA 信号通路、mTORC1 信号通路和 AMPK 信号通路诱导未成熟支持细胞增殖、成熟, 同时 FSH 与雄激素以叠加和协同的方式调节精子发生。基于以上生理机制, FSH β 亚基突变常导致无精子症; FSHR 激活突变使精子发生不受 FSH 限制; FSHR 失活突变可致男性生精功能受损; FSHR 基因的单核苷酸多态性与男性不育的关系受基因位点、种族等影响较大, 暂无一致性结论。本文提示 FSHR 调节剂对未来不育症诊治具有深远的意义, 也为男性避孕提供潜在新途径。

【关键词】 卵泡刺激素受体; 支持细胞; 不育, 男(雄)性; 单核苷酸多态性; 精子发生

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Research progress in the male reproduction mediated by FSH receptor of Sertoli cells

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【Abstract】 Follicle-stimulating hormone receptor (FSHR) is exclusively expressed in Sertoli cells within the testis. Mediated by FSHR, follicle-stimulating hormone (FSH) stimulates the proliferation and maturation of immature Sertoli cells via the cAMP/PKA, mTORC1 and AMPK signaling pathways. Simultaneously, FSH and androgen collaboratively regulate spermatogenesis in a synergistic manner. Given these physiological mechanisms, mutations in the FSH β subunit frequently result in azoospermia; activating mutations in FSHR enable spermatogenesis to bypass FSH restrictions; while inactivating mutations in FSHR can impair male spermatogenesis. The association between FSHR single nucleotide polymorphisms and male infertility is influenced by gene locus and ethnicity, leading to inconsistent conclusions. This article highlights the profound

significance of FSHR modulators for future infertility diagnosis and treatment, while also presenting a potential new avenue for male contraception.

【Key words】 Follicle-stimulating hormone receptor; Sertoli cell; Infertility, male; Polymorphism, single nucleotide; Spermatogenesis

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综述

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粒细胞集落刺激因子治疗薄型子宫内膜临床应用及作用机制研究进展

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【摘要】 子宫内膜厚度是评估妊娠成功与否的关键指标, 内膜厚度不足通常与较低的临床妊娠率和活产率相关。现有研究表明, 粒细胞集落刺激因子 (granulocyte colony-stimulating factor, G-CSF) 作为一种具备生长因子和细胞因子活性的糖蛋白, 可能通过促进血管生成、参与胚胎黏附、促进滋养层细胞侵袭等途径, 在内膜容受态建立和胚胎着床过程中发挥积极作用, 进而提高薄型子宫内膜的厚度及临床妊娠率。然而, 学术界对 G-CSF 治疗薄型子宫内膜的疗效仍存在分歧, 部分研究认为其作用有限或无作用。因此, 深入探究薄型子宫内膜发生发展的病理机制及 G-CSF 影响子宫内膜厚度和容受态建立的机制, 对于提升薄型子宫内膜群体的妊娠率及活产率具有重要的临床意义。本文就 G-CSF 治疗薄型子宫内膜的临床研究进展及其作用机制进行综述。

【关键词】 粒细胞集落刺激因子; 子宫内膜厚度; 薄型子宫内膜
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Clinical application and research progress of granulocyte colony-stimulating factor in the treatment of thin endometrium

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【Abstract】 The endometrial thickness is a crucial indicator for pregnancy success. Thin endometrium is typically related to low clinical pregnancy and live birth rate. Current research indicates that granulocyte colony-stimulating factor (G-CSF) is a glycoprotein that recognized as a cytokine and growth factor, which may support the establishment of endometrial receptivity during embryo implantation through promoting angiogenesis, embryo adhesion, and trophoblast invasion, thus increasing the endometrial thickness and clinical pregnancy rate. However, there are still conflicts about the efficacy of G-CSF. Therefore, identifying the pathological mechanism of thin endometrium and how G-CSF promotes endometrial thickness and receptivity has clinical significance. This article will review the progress on clinical research and molecular mechanism of G-CSF in treating thin endometrium.

【Key words】 Granulocyte colony-stimulating factor; Endometrial thickness; Thin endometrium

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综述

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肿瘤坏死因子- α 对多囊卵巢综合征发病机制影响及治疗的研究进展

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【摘要】 多囊卵巢综合征 (polycystic ovary syndrome, PCOS) 是育龄期女性常见的生殖、内分泌、代谢性疾病, 以排卵功能障碍、卵巢多囊样改变和高雄激素血症为主要特征, 在一定程度上影响着患者的身心健康。近年来很多研究表明 PCOS 的发生发展与体内慢性低度炎症密不可分, 肿瘤坏死因子- α (tumor necrosis factor- α , TNF- α) 作为炎症因子可通过不同途径诱导 PCOS 的发生。基于此, TNF- α 抑制剂也被用于治疗 PCOS, 部分患者也因此受益, 但其属于超说明书用药, 且目前研究较少。TNF- α 抑制剂是否能够改善 PCOS 及其应用是否能够保障母婴安全等仍尚不明确。因此, 本文将对 TNF- α 在 PCOS 发病机制中的作用以及其抑制剂在 PCOS 患者中应用疗效、安全性进行综述, 以期 PCOS 的发病机制的研究提供新线索, 为 PCOS 临床治疗提供新思路。

【关键词】 肿瘤坏死因子- α ; 多囊卵巢综合征; 氧化应激; 胰岛素抵抗; 肥胖; 肠道菌群; 高雄激素血症; 肿瘤坏死因子- α 抑制剂

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Research progress on the effect of tumor necrosis factor- α on the pathogenesis and treatment of polycystic ovary syndrome

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【Abstract】 Polycystic ovary syndrome (PCOS), a common reproductive, endocrine and metabolic disease among women of childbearing age, is mainly characterized by ovulation dysfunction, polycystic ovary changes and hyperandrogenism. To some extent, it impacts patients' physical and mental health. In recent years, numerous researches have indicated that the occurrence and development of PCOS are closely associated with chronic low-level inflammation in the body. Tumor necrosis factor- α (TNF- α), as an inflammatory factor, induces PCOS through different means. Accordingly, TNF- α inhibitors are also used to treat PCOS, and some patients benefit from them. However, they are off-label drugs and there are few studies. Whether TNF- α inhibitors can improve PCOS and ensure the safety of mother and child remains unclear. Therefore, this paper will review the role of TNF- α in the PCOS pathogenesis and the efficacy and safety of its inhibitors in PCOS patients, so as to offer new clues for studying the PCOS pathogenesis and new ideas for its clinical treatment.

【Key words】 Tumor necrosis factor- α ; Polycystic ovary syndrome; Oxidative stress; Insulin resistance; Obesity; Gut flora; Hyperandrogenism; Tumor necrosis factor- α inhibitors

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尿酸对女性生育力及辅助生殖助孕结局的影响

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【摘要】 尿酸是人体内嘌呤物质代谢的最终产物。近年来, 尿酸在女性生育力与辅助生殖技术中的作用引起了研究者的关注。尿酸代谢障碍会导致高尿酸血症(hyperuricemia, HUA)。HUA不仅与代谢综合征、心血管疾病密切相关, 还可能通过影响卵巢功能、胚胎发育等机制对女性的生育力产生不良影响。本文重点探讨了尿酸在女性生育力中的作用, 包括尿酸与女性低生育力、不孕症、不良妊娠结局、代谢综合征等之间的关系, 以及在体外受精-胚胎移植和卵胞质内单精子注射助孕中的潜在影响。未来的研究应进一步明确育龄女性尿酸水平的界值及临床干预价值, 为HUA育龄女性患者的生殖健康咨询及个体化助孕提供依据。

【关键词】 尿酸; 高尿酸血症; 生育力; 生殖技术, 辅助; 体外受精; 妊娠结局

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Impact of uric acid on female fertility and the pregnancy outcomes of assisted reproductive technology

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【Abstract】 Uric acid is the end product of purine metabolism in the human body. In recent years, the role of uric acid in female fertility and assisted reproductive technology (ART) has gained increasing attention. Dysregulation of uric acid metabolism can lead to hyperuricemia (HUA). HUA is not only closely related to metabolic syndrome and cardiovascular diseases but may also adversely affect female fertility by influencing ovarian function and embryos development. In this review, we explored the role of uric acid in female fertility, including its association with female subfertility, infertility, adverse pregnancy outcomes and metabolic syndrome, as well as its potential impact on ART like *in vitro* fertilization-embryo transfer and intracytoplasmic sperm injection. Further studies are needed to clarify the threshold and clinical intervention value of uric acid levels in women of childbearing age, providing a basis for reproductive health counseling and personalized pregnancy assistance for HUA patients of childbearing age.

【Key words】 Uric acid; Hyperuricemia; Fertility; Reproductive techniques, assisted; Fertilization *in vitro*; Pregnancy outcome

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综述

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同型半胱氨酸对女性生殖健康的影响

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【摘要】 关于同型半胱氨酸和不良妊娠结局的关系已有大量文献报道, 研究者们越来越关注同型半胱氨酸对女性生殖健康的影响, 以及降低同型半胱氨酸水平可能对改善生育能力产生的积极作用。本文结合近 15 年的相关研究, 对同型半胱氨酸在女性生殖障碍疾病中的可能作用及以同型半胱氨酸为靶点的治疗前景作一综述。

【关键词】 同型半胱氨酸; 女性; 生殖健康; 治疗前景

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Impacts of homocysteine on female reproductive health

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【Abstract】 Various researches have reported on the relationship between homocysteine levels and adverse pregnancy outcomes. Researchers are increasingly focusing on the impact of homocysteine on female reproductive health and figuring out the potential positive effects of lowering homocysteine levels on women fertility. Our review aims to systematically summarize the possible roles of homocysteine in female reproductive disorders based on relevant studies from the past 15 years and therapeutic prospects targeting homocysteine to improve the reproductive health of women.

【Key words】 Homocysteine; Female; Reproductive health; Therapeutic prospect

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浅析辅助生殖技术的应用与管理

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【摘要】 “十四五”期间中国人口进入负增长阶段, 生育率面临下行压力, 不孕不育率逐渐提升。辅助生殖技术作为治疗不孕不育的有效途径, 为众多患者带来了生育的曙光。然而, 当前辅助生殖技术的推行应用之路仍然障碍重重。对此, 本文聚焦辅助生殖技术在中国发展应用面临的现实挑战, 以问题为导向, 以国外辅助生殖治疗的相关政策为参考, 提出我国辅助生殖技术进一步落地的政策建议: 协调区域辅助生殖资源均衡分布、强化辅助生殖技术的政策保障、增强医学伦理专业协会的机构职能、规范辅助生殖技术治疗的应用。

【关键词】 生殖技术, 辅助; 不孕不育; 伦理规范

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Analyzing the application and management of assisted reproductive technology

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【Abstract】 During the 14th Five-Year Plan period, the population of China has turned into a stage of negative growth, the fertility rate gradually declined, and the infertility rate gradually increased. The most effective treatment for infertility is assisted reproductive technology (ART), which has brought hope for fertility to many patients. However, the current promotion of the utilization of ART is still fraught with many obstacles. In this context, focusing on the realistic challenges of ART on its development in China, we will take a problem-oriented approach, utilize the relevant policies of ART in foreign countries as references, and put forward policy recommendations for the further implementation of ART, such as coordinating the balanced distribution of ART resources in the region, strengthening policy safeguards for ART, enhancing the institutional functioning of professional associations in medical ethics, and standardizing the application of ART treatments.

【Key words】 Reproductive technology, assisted; Infertility; Ethical norms

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