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IVF 成功定义—基于 Delphi 法的中国专家意见

IVF 成功定义专家组

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【摘要】 目的 旨在采用 Delphi 法对体外受精 (*in vitro* fertilization, IVF) 成功的定义提出专家意见, 为临床实践提供参考依据。方法 采用 Delphi 法对衡量 IVF 成功定义进行专家调查, 由 8 名专家基于相关文献制定陈述框架, 并通过会议讨论细化陈述内容, 形成陈述初始内容。通过发放调研问卷, 就陈述内容征询 23 名生殖专家意见。据专家反馈意见对陈述进行修改, 并再次发放问卷, 直至达成共识。结果 共进行 2 轮问卷调查, 专家参与的积极程度分别为 100% (23/23) 和 73.9% (17/23), 专家权威系数为 0.895。就 IVF 成功定义相关的 19 条陈述达成共识, 主要包括: ①IVF 治疗的目标 (1 条陈述), 即安全地尽快获得单胎健康活产。②IVF 成功的定义 (13 条陈述), 包括 IVF 治疗的有效性、安全性和效率的评估, 单个卵巢刺激周期 2 年内的累积活产率是衡量 IVF 治疗成功的绩效指标。衡量 IVF 成功应从以患者为中心角度出发, 结合患者的负担和满意度进行评价。③IVF 成功的保障 (3 条陈述)。IVF 治疗应遵循循证医学证据, 尽量避免在诊疗过程中实施未经证实的、患者获益不明确的治疗方案。辅助生殖机构应通过建立关键技术指标的监测并完善质控体系来优化治疗质量。④IVF 成功的挑战 (2 条陈述)。取卵前取消周期和治疗周期失败后放弃继续治疗是 IVF 成功不可忽视的挑战。结论 基于 Delphi 法, 结合生殖专家组的临床观点, 就 IVF 成功的定义形成了专家意见, 可作为临床指南的补充, 用于指导临床实践, 助力改善治疗结局。

【关键词】 受精, 体外; 成功率; 累积活产率

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Definition of IVF success: Chinese expert opinion based on Delphi method

Expert Suggestions Group on the Definition of IVF Success

Corresponding author: Li Rong, Department of Obstetrics and Gynecology, Peking University Third Hospital, Beijing 100191, China, Email: roseli001@sina.com

【Abstract】 Objective To formulate expert opinion on definition of *in vitro* fertilization (IVF) success by a Delphi consensus, to provide a reference basis for clinical practice. **Methods** Chinese experts in assisted reproduction technology (ART) were surveyed using the Delphi method. Based on the literature related to IVF success, 8 experts developed a framework of statements and items. A questionnaire was then distributed to 23 experts to canvas their opinions on these statements. If consensus was not achieved, the statement was revised and re-voted upon until a consensus was reached. **Results** In the two rounds of questionnaire survey, the positive degree of expert participation was 100% (23/23) and 73.9% (17/23) respectively, and the coefficient of expert authority was 0.895. Consensus was reached for 19 statements related to the definition of IVF success, the most relevant of which are summarized as follows: 1) Goal of IVF treatment (1 statement), attain a health live birth in the shortest possible time and with the lowest possible risks. 2) Definition of IVF success (13 statements). Effectiveness, safety and efficiency of IVF treatment should be included in the definition of success, with the cumulative live birth rate per ovarian stimulation cycle in 2 years being a performance indicator of success, and IVF success should be measured from a patient-centered perspective, including the patient's burden and satisfaction. 3) Assurance of IVF success (3 statements). IVF treatment should follow evidence-based guidelines and avoid implementing unverified treatment plans with unclear patient benefits during the diagnosis and treatment process. Assisted reproductive institutions should optimize treatment quality by establishing monitoring of key technical indicators and improving quality control systems. 4) Hurdles of IVF success (2 statements). Cycle cancellation before oocyte pick-up and treatment discontinuation after failed cycles are hurdles of success with IVF. **Conclusion** The opinions on the definition of IVF success was based on the joint input of reproductive expert panel members which could complement guidelines and may help improve treatment outcomes.

【Key words】 Fertilization *in vitro*; Success rate; Cumulative live birth rate
Fund program: National Key R&D Program of China (2022YFC2702500, 2022YFC2705305)

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临床研究

促性腺激素使用时长对促性腺激素释放激素激动剂长方案体外受精-胚胎移植妊娠结局的影响

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【摘要】 目的 探讨黄体期促性腺激素释放激素激动剂(gonadotrophin-releasing hormone agonist, GnRH-a)长方案中促性腺激素(gonadotrophin, Gn)使用时长对体外受精/卵胞质内单精子注射(*in vitro* fertilization/intracytoplasmic sperm injection, IVF/ICSI)新鲜周期及解冻周期妊娠结局的影响。方法 回顾性队列研究分析2017年1月至2021年12月期间在北京大学第三医院妇产科生殖医学中心采用长方案行IVF/ICSI助孕患者的临床资料,根据控制性促排卵过程中Gn使用时长分为两组(Gn使用时长>15 d组, 1 198例; Gn使用时长≤15 d组, 4 792例),比较两组一般资料及在新鲜周期及解冻周期妊娠结局情况。采用多因素二分类logistic回归控制混杂因素,分析Gn使用时长与活产之间的关系。结果 新鲜周期中, Gn使用时长>15 d组无可移植胚胎率[16.4% (195/1 187)]显著高于Gn使用时长≤15 d组[7.1% (338/4 757), $P<0.001$], 两组临床妊娠率、新鲜周期活产率、胚胎着床率和早期自然流产率相比差异均无统计学意义(均 $P>0.05$)。在解冻周期中, 两组临床妊娠率、活产率、胚胎着床率及早期流产率相比差异均无统计学意义(均 $P>0.05$)。多因素二分类logistic回归分析排除混杂因素后, 无论新鲜周期还是解冻周期中Gn使用时长与活产均无显著相关性($P=0.432$ 和 $P=0.856$)。结论 在黄体期长方案控制性促排卵过程中, 与Gn使用时长≤15 d组相比, Gn使用时长>15 d组无可移植胚胎周期率增加, 但一旦有可移植胚胎, 新鲜周期和解冻周期妊娠结局相似, 未发现通过影响子宫内膜容受性而影响新鲜周期妊娠结局。

【关键词】 促性腺激素; 生殖技术, 辅助; 受精, 体外; 黄体期长方案; 妊娠结局

基金项目: 国家重点研发计划项目(2022YFC2703800)

Effect of the duration of gonadotropin stimulation on pregnancy outcome of *in vitro* fertilization and embryo transfer with GnRH-a long protocol

Zhang Hongxia, Yang Shuo, Tian Tian, Zhen Xiumei

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【 Abstract 】 Objective To explore the effect of gonadotropin (Gn) stimulation duration on the pregnancy outcome in both fresh and frozen embryo transfer cycles in patients underwent *in vitro* fertilization (IVF) with gonadotrophin-releasing hormone agonist (GnRH-a) long protocol. **Methods** A retrospective cohort study was used to analyze the clinical data of patients who underwent IVF/intracytoplasmic sperm injection (ICSI) with GnRH-a long protocol in Reproductive Medicine Center, Department of Obstetrics and Gynecology of Peking University Third Hospital from January 2017 to December 2021. According to the duration of Gn used in controlled ovarian stimulation, they were divided into two groups (Gn stimulation duration>15 d group, 1 198 cases; Gn stimulation duration≤15 d group, 4 792 cases), the general information and pregnancy outcome between the two groups were compared, and multiple factors binary logistic regression was used to control confounding factors and analyze the relationship between Gn stimulation duration and live birth. **Results** In the fresh cycles, the rate of non-transplantable embryos in the group of Gn stimulation duration>15 d [16.4% (195/1 187)] was significantly higher than that in the group of Gn stimulation duration≤15 d group [7.1% (338/4 757), $P<0.001$], but there were no statistical differences in clinical pregnancy rate, live birth rate, implantation rate and early spontaneous abortion rate between the two groups (all $P>0.05$). In the frozen cycles, there were no statistical differences in clinical pregnancy rate, live birth rate, embryo implantation rate and early abortion rate between the two groups (all $P>0.05$). Multiple factors binary logistic analysis showed that there was no significant correlation between Gn stimulation duration and live birth in both fresh and frozen cycles ($P=0.432$, $P=0.856$). **Conclusion** Compared with the group of Gn stimulation duration≤15 d in patients with GnRH-a protocol, there was an increase in the rate of non-transplantable embryos in the fresh cycles in the group of Gn stimulation duration>15 d. However, once transferable embryos were available, pregnancy outcomes were similar in fresh and thawed cycles, and no effect on pregnancy outcomes in fresh cycles by affecting endometrial tolerance was observed.

【 Key words 】 Gonadotropin; Reproductive technology, assisted; Fertilization *in vitro*; Luteal phase long protocol; Pregnancy outcome

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临床研究

既往孕产史对首次新鲜周期移植妊娠及围产结局的影响

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张琳琳和黄钰对本文有同等贡献

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【摘要】 目的 探讨既往孕产史是否影响首次体外受精/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) 后的妊娠及围产结局。方法 本研究是一项以 2018 年 1 月至 2022 年 12 月期间在北京大学第三医院生殖医学中心首次接受 IVF/ICSI 新鲜周期移植女性为研究对象的回顾性队列研究。根据既往孕产史分为 5 组: 未妊娠组 ($n=14\ 239$)、终止妊娠组 ($n=4\ 076$)、妊娠丢失组 ($n=1\ 773$)、异位妊娠组 ($n=1\ 169$) 和活产组 ($n=857$)。通过个案控制匹配女方年龄和移植胚胎数量等关键变量, 采用逻辑回归分析校正混杂因素, 分析匹配前后既往不同孕产史类型对 IVF/ICSI-ET 后妊娠与围产结局的影响。结果 最终分析共包括 22 114 例女性。未进行匹配时, 以未妊娠组为参照组, 校正混杂因素后, 有异位妊娠史的患者发生异位妊娠的风险更高 ($OR=2.134$, 95% CI : 1.262~3.606, $P=0.005$), 本次单胎分娩小于孕龄儿的概率更高 ($OR=2.005$, 95% CI : 1.248~3.712, $P=0.008$)。有活产史的患者更易临床妊娠 ($OR=1.323$, 95% CI : 1.084~1.616, $P=0.006$) 和活产分娩 ($OR=1.312$, 95% CI : 1.061~1.623, $P=0.012$), 本次双胎分娩的患者更不易发生早产 ($OR=0.483$, 95% CI : 0.299~0.847, $P=0.023$)。妊娠丢失组本次单胎分娩小于孕龄儿 ($OR=2.289$, 95% CI : 1.497~3.491, $P=0.002$)、双胎分娩早产 ($OR=1.569$, 95% CI : 1.193~1.916, $P=0.006$) 的风险更高。其他主要妊娠结局和围产结局指标差异均无统计学意义 (均 $P>0.05$)。结论 既往孕产史与首次新鲜周期移植的妊娠与围产结局有一定相关性。既往曾异位妊娠的女性再次发生异位妊娠的风险更高,

本次单胎分娩的女性分娩小于孕龄儿的风险更高。既往曾活产分娩的女性临床妊娠率及活产率更高，本次双胎分娩的女性更不易早产。既往曾有过妊娠丢失的女性本次单胎妊娠时分娩小于孕龄儿的风险更高，双胎妊娠时早产的风险更高。

【关键词】 受精，体外； 胚胎移植； 孕产史； 活产率； 围产结局

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Effect of women's reproductive history on live birth rate and perinatal outcome after first IVF-ET

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【Abstract】 Objective To investigate the effect of women's reproductive history on pregnancy and perinatal outcome after first *in vitro* fertilization/intracytoplasmic sperm injection and embryo transfer (IVF/ICSI-ET). **Methods** This was a retrospective cohort study of women who had undergone their first IVF/ICSI and fresh cycle embryo transfer between January 2018 and December 2022 at Reproductive Medical Center, Peking University Third Hospital. The women were categorized into five groups based on their reproductive history: no pregnancy group ($n=14\ 239$), termination of pregnancy group ($n=4\ 076$), pregnancy loss group ($n=1\ 773$), ectopic pregnancy group ($n=1\ 169$), and live birth group ($n=857$). The women with no previous pregnancy were considered as the reference group. The primary outcome was the live birth rate and secondary endpoints included rates of positive pregnancy test, clinical pregnancy, pregnancy loss and ectopic pregnancy as well as perinatal outcomes such as birth weight and preterm birth. Logistic regression analyses were used to control for a number of potential confounders before and after case control matching for female age and number of embryos transferred. **Results** In total, 22 114 women were included in the final analysis. When case control matching was not performed, after correcting for several potential confounders, the risk of ectopic pregnancy ($OR=2.134$, 95% CI : 1.262–3.606, $P=0.005$) and the risk of small-for-gestational age in patients with singleton births ($OR=2.005$, 95% CI : 1.248–3.712, $P=0.008$) after ET was elevated among women with a previous ectopic pregnancy. Previous was more likely to clinical pregnancy ($OR=1.323$, 95% CI : 1.084–1.616, $P=0.006$) and live birth ($OR=1.312$, 95% CI : 1.061–1.623, $P=0.012$), and patients with twin births were less likely to preterm birth ($OR=0.483$, 95% CI : 0.299–0.847, $P=0.023$). The risk of small-for-gestational age after embryo transfer in patients with singleton births ($OR=2.289$, 95% CI : 1.497–3.491, $P=0.002$) and the risk of preterm birth in patients with twins births ($OR=1.569$, 95% CI : 1.193–1.916, $P=0.006$) was elevated among women with a previous pregnancy loss when compared with the group of women with no previous pregnancy. There was no increased risk of other reproductive

outcomes and adverse perinatal outcomes associated with reproductive history compared with the reference group. Results after case control matching for age and number of embryos transferred were consistent with results before matching.

Conclusion Previous reproductive history has a significant effect on pregnancy outcomes and perinatal outcomes in women who had undergone their first IVF/ICSI-ET. The risk of ectopic pregnancy and small-for-gestational age in patients with singleton births was elevated among women with a previous ectopic pregnancy. Previous live birth was more likely to clinical pregnancy and live birth, and patients with twin births are less likely to preterm birth. The risk of small-for-gestational age after embryo transfer in patients with singleton births and preterm birth in patients with twins births was elevated among women with a previous pregnancy loss when compared with the group of women with no previous pregnancy.

【Key words】 Fertilization *in vitro*; Embryo transfer; Reproductive history; Live birth rate; Perinatal outcome

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·临床研究·

坤泰胶囊联合 PPOS 方案在 IVF/ICSI 预期卵巢低反应患者中的 应用疗效: 一项回顾性队列研究

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【摘要】 目的 评估坤泰胶囊联合高孕激素促排卵 (progestin-primed ovarian stimulation, PPOS) 方案对预期卵巢低反应 (poor ovarian response, POR) 患者体外受精/卵胞质内单精子注射 (*in vitro* fertilization/intracytoplasmic sperm injection, IVF/ICSI) 周期中卵巢反应、胚胎实验室和移植妊娠结局的影响。**方法** 回顾性队列研究分析2020年6月至2023年7月期间于江西省妇幼保健院生殖医学中心行IVF/ICSI助孕的1733例预期POR患者临床资料,按照1:1倾向性评分匹配分为单一PPOS方案组(对照组)和坤泰胶囊联合PPOS方案组(试验组),每组各423例。分析两组的促排卵和实验室结局,并比较所获胚胎首次冻融移植周期的妊娠结局。主要观察指标为获卵数。结果匹配后组间基线资料差异均无统计学意义(均 $P>0.05$)。与对照组相比,试验组的获卵数差异无统计学意义($P=0.295$)。扳机日试验组的黄体生成素(luteinizing hormone, LH)水平[3.3 (2.2, 5.0) U/L]、可利用囊胚形成数[1 (0, 1)个]和可利用囊胚形成率[46.2% (85/184)]均显著高于对照组[2.9 (1.9, 4.5) U/L, $P=0.004$; 0 (0, 1)个, $P=0.034$; 30.0% (48/160), $P=0.002$]。两组促性腺激素使用时间和使用总量、扳机日孕酮和雌二醇水平、早发LH峰比例、正常受精数/率、正常卵裂数/率、优质胚胎数/率和无可利用胚胎率等差异均无统计学意义(均 $P>0.05$)。试验组和对照组相比,首次冻融胚胎移植后的种植率、临床妊娠率、早期流产率、持续妊娠率和活产率组间比较差异均无统计学意义(均 $P>0.05$)。结论 相较于单一PPOS方案组,坤泰胶囊联合PPOS促排卵未显著增加预期POR患者的获卵数,但可增加可利用囊胚形成数和可利用囊胚形成率。

【关键词】 受精, 体外; 坤泰胶囊; 高孕激素促排卵; 卵巢低反应

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Application efficacy of Kuntai capsules combined with PPOS regimen for expected poor ovarian response patients undergoing IVF/ICSI cycles: a retrospective cohort study

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【 Abstract 】 Objective To evaluate the effect of Kuntai capsules combined with progestin-primed ovarian stimulation (PPOS) protocol on the ovarian response, laboratory parameters and embryo transfer outcomes of expected poor ovarian response (POR) patients undergoing *in vitro* fertilization/intracytoplasmic sperm injection (IVF/ICSI) cycles. **Methods** A retrospective cohort study was performed at Center for Reproductive Medicine,

Jiangxi Maternal and Child Health Hospital from June 2020 to July 2023. A total of 1 733 expected POR patients were enrolled and divided into the PPOS only group (control group) and the Kuntai capsules combined with PPOS regimen group (trial group). After a 1 : 1 propensity score matching, 423 cases were included in each group. Further analyses and comparisons were made between the two groups, concerning the ovarian stimulation outcomes, embryo laboratory parameters and pregnancy rates after the first frozen-thawed embryo transfer cycles. The primary outcome measure was the number of oocytes retrieved. **Results** No statistically significant difference was found in baseline characteristics after matching between the two groups (all $P>0.05$). Compared with control group, the number of oocytes retrieved did not differ significantly in the trial group ($P=0.295$). The level of luteinizing hormone (LH) on the trigger day [3.3 (2.2, 5.0) U/L], the number of available blastocysts formed [1 (0, 1)] and the available blastocyst formation rate [46.2% (85/184)] in the trial group were significantly higher than those in control group [2.9 (1.9, 4.5) U/L, $P=0.004$; 0 (0, 1), $P=0.034$; 30.0% (48/160), $P=0.002$]. However, there were no significant differences in the duration and dosage of gonadotropin used, progesterone and estradiol levels on the trigger day, incidence of premature LH surge, number/rate of fertilized oocytes, number/rate of cleaved embryos, number/rate of high-quality embryos, as well as rate of unavailable embryos (all $P>0.05$). Compared with control group, the trial group demonstrated comparable implantation rate, clinical pregnancy rate, early miscarriage rate, ongoing pregnancy rate and live birth rate after the first frozen-thawed embryo transfer cycles (all $P>0.05$). **Conclusion** Compared with the PPOS only regimen, the combination of Kuntai capsules and PPOS did not increase the number of oocytes retrieved but could increase the number and rate of available blastocysts formed in expected POR patients.

【 Key words 】 Fertilization *in vitro*; Kuntai capsules; Progestin-primed ovarian stimulation; Poor ovarian response

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·临床研究·

PCOS 患者卵泡液中血管紧张素 II-1 型受体自身抗体与卵泡发育的关系研究

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【摘要】 目的 探讨多囊卵巢综合征 (polycystic ovary syndrome, PCOS) 不孕患者卵泡液中血管紧张素 II-1 型受体自身抗体 (angiotensin II type 1 receptor autoantibodies, AT1-AA) 水平与卵泡发育的相关性。**方法** 选取 2021 年 6 月至 2022 年 10 月期间太原市中心医院辅助生殖中心行体外受精/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) 助孕的不孕患者 182 例进行病例对照研究, 其中因输卵管因素所致不孕患者 80 例, 记为输卵管因素组, PCOS 患者 102 例, 记为 PCOS 组。分别比较两组患者的一般资料、促排卵指标及胚胎实验室指标; 采用酶联免疫吸附方法 (enzyme-linked immunosorbent assay, ELISA) 检测取卵日卵泡液中 AT1-AA 的水平, Pearson 或 Spearman 分析 AT1-AA 水平和卵泡发育指标之间的相关性, 应用多元线性回归调整干扰因素后分析 AT1-AA 与胚胎实验室指标的相关性。**结果** PCOS 组体质质量指数 [body mass index, BMI, (25.29±3.25) kg/m²]、窦卵泡计数 [antral follicle count, AFC, 24.00 (17.00, 24.00)]、基础血清睾酮 [0.50 (0.36, 0.79) μg/L]、抗苗勒管激素 [anti-Müllerian hormone, AMH, 4.92 (2.57, 8.28) μg/L] 水平均显著高于输卵管因素组 [(23.01±2.92) kg/m², $P<0.001$; 15.00 (10.25, 19.00), $P<0.001$; 0.38 (0.20, 0.59) μg/L, $P=0.019$; 3.06 (2.19, 4.89) μg/L, $P=0.006$]; 并且 PCOS 组卵泡液中 AT1-AA P/N 值 [4.24 (2.07, 8.89)] 显著高于输卵管因素组 [2.96 (1.86, 4.84), $P=0.027$]。另外, PCOS 组初潮年龄 [13.00 (12.00, 14.00) 岁] 早于输卵管因素组 [14.00 (13.00, 15.00) 岁, $P=0.007$], 催乳素水平 [12.09 (9.65, 16.64) μg/L] 低于输卵管因素组 [16.27 (12.86, 20.94) μg/L, $P=0.002$], 两组其余指标差异均无统计学意义 (均 $P>0.05$)。相关性分析结果显示 PCOS 患者卵泡液中 AT1-AA 水平与获卵率呈负相关 ($r=-0.159$, $P=0.019$)。多

元线性回归分析结果显示,在调整混杂因素后,卵泡液中 AT1-AA 水平与获卵率及正常受精率呈负相关 ($\beta=-0.598$, $P=0.028$; $\beta=-0.527$, $P=0.022$)。结论 PCOS 患者卵泡液 AT1-AA 水平较输卵管因素不孕患者明显升高,且与获卵率及正常受精率呈负相关。

【关键词】 多囊卵巢综合征; 卵泡液; 血管紧张素 II-1 型受体自身抗体; 卵泡发育

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Relationship between angiotensin II type 1 receptor autoantibody levels in follicular fluid and follicular development in patients with PCOS

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【Abstract】 Objective To investigate the presence of angiotensin II type 1 receptor autoantibodies (AT1-AA) in follicular fluid, and to investigate the correlation between AT1-AA levels and follicular development in follicular fluid of infertile patients with polycystic ovary syndrome (PCOS). **Methods** A case-control study was conducted on 182 infertile patients who underwent *in vitro* fertilization/intracytoplasmic sperm injection and embryo transfer (IVF/ICSI-ET) at the Center for Reproductive Medicine of Taiyuan Central Hospital from June 2021 to October 2022. There were 80 cases in the fallopian tube factor group (tubal factor group) and 102 cases in PCOS infertility group (PCOS group). Univariate analysis was performed for the general data, ovulation induction indexes and embryonic laboratory indexes of the two groups. Enzyme-linked immunosorbent assay (ELISA) was used to detect the level of AT1-AA in follicular fluid on the day of oocyte retrieval. Pearson or Spearman was used to analyze the correlation between AT1-AA level and follicle development indexes, and multiple linear regression was used to adjust for interfering factors to analyze the correlation between AT1-AA level and embryonic laboratory indicators. **Results** Body mass index [BMI, (25.29±3.25) kg/m²], antral follicle count [AFC, 24.00 (17.00, 24.00)], basal serum testosterone [0.50 (0.36, 0.79) µg/L] and anti-Müllerian hormone [AMH, 4.92 (2.57, 8.28) µg/L] in PCOS group were significantly higher than those in tubal factor group [(23.01±2.92) kg/m², $P<0.001$; 15.00 (10.25, 19.00), $P<0.001$; 0.38 (0.20, 0.59) µg/L, $P=0.019$; 3.06 (2.19, 4.89) µg/L, $P=0.006$]. Moreover, the AT1-AA P/N value in follicular fluid in PCOS group [4.24 (2.07, 8.89)] was significantly higher

than that in tubal factor group [2.96 (1.86, 4.84), $P=0.027$]. In addition, the age of menarche in PCOS group [13.00 (12.00, 14.00) years] was earlier than that in tubal factor group [14.00 (13.00, 15.00) years, $P=0.007$]. Prolactin level [12.09 (9.65, 16.64) $\mu\text{g/L}$] was lower than that of tubal factor group [16.27 (12.86, 20.94) $\mu\text{g/L}$, $P=0.002$], and there were no statistical differences in other indexes between the two groups (all $P>0.05$). Correlation analysis showed that the level of AT1-AA in follicular fluid of PCOS patients was negatively correlated with oocyte retrieval rate ($r=-0.159$, $P=0.019$). The results of multiple linear regression analysis showed that AT1-AA level in follicular fluid was negatively correlated with oocyte retrieval rate ($\beta=-0.598$, $P=0.028$) and normal fertilization rate ($\beta=-0.527$, $P=0.022$) after adjusting for confounding factors. **Conclusion** The level of AT1-AA in follicular fluid in PCOS patients is significantly higher than that in patients with tubal infertility, and is negatively correlated with oocyte retrieval rate and normal fertilization rate.

【Key words】 Polycystic ovary syndrome; Follicular fluid; Angiotensin II type 1 receptor autoantibody; Follicular development

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·实验研究·

人脐带间充质干细胞外泌体 miR-21-5p 对颗粒细胞凋亡的影响

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【摘要】 目的 探究人脐带间充质干细胞来源的外泌体 miR-21-5p 对人颗粒细胞凋亡的影响。方法 不同浓度 (0 $\mu\text{mol/L}$ 、30 $\mu\text{mol/L}$ 、60 $\mu\text{mol/L}$ 和 100 $\mu\text{mol/L}$) 磷酸胺氮芥作用 KGN 细胞 48 h 构建颗粒细胞凋亡模型, 采用 qPCR 和 Western blotting 分别检测 *bax*、*bcl2* 的 mRNA 和蛋白水平, 并用流式细胞计数检测凋亡率, 以筛选出磷酸胺氮芥构建凋亡模型的最佳浓度。利用 hsa-miR-21-5p 过表达质粒瞬时转染人脐带间充质干细胞, 通过 qPCR 检测 hsa-miR-21-5p 表达水平; 分离过表达 miR-21-5p 的外泌体, 利用纳米流式和电子显微镜鉴定 miR-21-5p 外泌体。对磷酸胺氮芥构建成功的 KGN 细胞凋亡模型中加入不同浓度 (5 $\mu\text{g/mL}$ 、10 $\mu\text{g/mL}$ 和 15 $\mu\text{g/mL}$) 的过表达 miR-21 外泌体, 采用 qPCR 和 Western blotting 分别检测 *bax*、*bcl2* 的 mRNA 和蛋白水平, 采用 PKH-26 标记外泌体示踪其在颗粒细胞的位置。结果 60 $\mu\text{mol/L}$ 磷酸胺氮芥作用的 KGN 细胞中 *bax* mRNA 和蛋白水平均显著高于 0 $\mu\text{mol/L}$ 磷酸胺氮芥组 (均 $P<0.001$), *bcl2* mRNA 和蛋白水平均显著高于 0 $\mu\text{mol/L}$ 磷酸胺氮芥组 ($P=0.005$, $P<0.001$)。60 $\mu\text{mol/L}$ 磷酸胺氮芥作用后 KGN 细胞的凋亡率为 $(38.10\pm2.90)\%$, 而 30 $\mu\text{mol/L}$ 磷酸胺氮芥干预后 KGN 细胞的凋亡率为 $(16.75\pm2.55)\%$, 均显著高于 0 $\mu\text{mol/L}$ 磷酸胺氮芥组 ($P=0.020$, $P=0.006$)。hsa-miR-21-5p 瞬时转染人脐带血间充质干细胞, qPCR 检测到 has-miR-21-5p 的表达高于未转染的空白对照组 ($P<0.001$)。纳米流式检测外泌体表面蛋白 CD9 阳性率为 14.9%, CD63 阳性率为 16.4%, CD81 阳性率为 31.4%; 透射电子显微镜观察到外泌体呈“茶托型”; PKH-26 标记的外泌体共聚焦显示进入颗粒细胞内并发挥生物学效应。5 $\mu\text{g/mL}$ 、10 $\mu\text{g/mL}$ 和 15 $\mu\text{g/mL}$ 空载质粒外泌体组与 60 $\mu\text{mol/L}$ 磷酸胺氮芥组比较 *bax* mRNA 表达水平差异均无统计学意义 (均 $P>0.05$)。但 5 $\mu\text{g/mL}$ 、10 $\mu\text{g/mL}$ 和 15 $\mu\text{g/mL}$ miR-21-5-p 外泌体组 *bax* mRNA 表达水平低于 60 $\mu\text{mol/L}$ 磷酸胺氮芥组 ($P=0.008$ 、 $P=0.003$ 、 $P<0.001$), 而 *bcl2* mRNA 表达在各组中差异均无统计学意义 (均 $P>0.05$)。与 60 $\mu\text{mol/L}$ 磷酸胺氮芥组比, 5 $\mu\text{g/mL}$ 、10 $\mu\text{g/mL}$ 和 15 $\mu\text{g/mL}$ 空载外泌体组 BAX 蛋白表达差异均无统计学意义 (均 $P>0.05$), 而 5 $\mu\text{g/mL}$ 、10 $\mu\text{g/mL}$ 和 15 $\mu\text{g/mL}$ miR-21-5-p 外泌体组与 60 $\mu\text{mol/L}$ 磷酸胺氮芥组比较 BAX 蛋白表达量降低, 差异均具有统计学意义 (均 $P<0.001$)。而 BCL2 蛋白在各个干预组表达差异均无统计学意义 (均 $P>0.05$)。结论 通过脐带间充质干细胞过表达 miR-21 分泌的外泌体, 可以对人颗粒细胞有效地发挥抗凋亡的作用。

【关键词】 人脐带间充质干细胞; 外泌体; 颗粒细胞; 凋亡

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Effects of miR-21-5p exosomes from human umbilical cord mesenchymal stem cells on apoptosis of granular cells

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【Abstract】 Objective To explore the effects of miR-21-5p exosomes derived from human umbilical cord mesenchymal stem cells on apoptosis of human granular cells. **Methods** A granular cell apoptosis model was constructed by treating KGN cells with different concentrations (0 $\mu\text{mol/L}$, 30 $\mu\text{mol/L}$, 60 $\mu\text{mol/L}$, and 100 $\mu\text{mol/L}$) of phosphoramidite nitrogen mustard for 48 h. The mRNA and protein levels of *bax* and *bcl2* were detected using qPCR and Western blotting, respectively. The apoptosis rate was measured using flow cytometry to screen for the optimal concentration of phosphoramidite nitrogen mustard for constructing an apoptosis model. Hsa-miR-21-5p overexpression plasmid was used for instantaneously transfecting human umbilical cord mesenchymal stem cells, and the expression level of hsa-miR-21-5p was detected by qPCR. The miR-21-5p exosomes were separated and identified by flow cytometry and electron microscope. Different concentrations (5 $\mu\text{g/mL}$, 10 $\mu\text{g/mL}$ and 15 $\mu\text{g/mL}$) of miR-21 exosomes were added into successful KGN cell apoptosis model to overexpress miR-21. The mRNA and protein levels of *bax* and *bcl2* were detected using qPCR and Western blotting, respectively. PKH-26 was used to trace the position of human granular cells. **Results** The levels of *bax* mRNA and protein in KGN cells treated with 60 $\mu\text{mol/L}$ phosphoramidite nitrogen mustard were significantly higher than those in the 0 $\mu\text{mol/L}$ phosphoramidite nitrogen mustard group (all $P<0.001$), while the levels of *bcl2* mRNA and protein were significantly higher than those in the 0 $\mu\text{mol/L}$ phosphoramidite nitrogen mustard group ($P=0.005$, $P<0.001$). The apoptosis rate of KGN cells after 60 $\mu\text{mol/L}$ phosphoramidite nitrogen mustard intervention was $(38.10\pm2.90)\%$, while the apoptosis rate of KGN cells after 30 $\mu\text{mol/L}$ phosphoramidite nitrogen mustard intervention was $(16.75\pm2.55)\%$, they were all significantly higher than that of the 0 $\mu\text{mol/L}$ phosphoramidite nitrogen mustard intervention group ($P=0.020$, $P=0.006$). Hsa-miR-21-5p was transiently transfected into human umbilical cord blood mesenchymal stem cells, and the expression of has-miR-21-5p was higher than that in control group detected by qPCR ($P<0.001$). The positive rate of surface protein CD9, CD63 and CD81 was 14.9%, 16.4% and 31.4%. The exosome was observed as "tea tray" or "concave hemisphere" by electron microscope. The exosome labeled by PKH-26 entered the granular cells and exerted biological effects. There was no statistically significant difference in *bax* mRNA expression levels between the 5

μg/mL, 10 μg/mL, and 15 μg/mL empty plasmid exosomes groups and the 60 μmol/L phosphoramidate nitrogen mustard group (all $P>0.05$). However, the expression levels of *bax* mRNA in the 5 μg/mL, 10 μg/mL, and 15 μg/mL miR-21-5-p exosomes groups were lower than those in the 60 μmol/L phosphoramidate nitrogen mustard group ($P=0.008$, $P=0.003$, $P<0.001$). However, there was no statistically significant difference in the expression of *bcl2* mRNA among the groups (all $P>0.05$). From the perspective of protein levels, there was no statistically significant difference in BAX protein expression between the 5 μg/mL, 10 μg/mL, and 15 μg/mL empty exosomes groups and 60 μmol/L phosphoramidate nitrogen mustard group (all $P>0.05$), while the 5 μg/mL, 10 μg/mL, and 15 μg/mL miR-21-5-p exosomes groups showed a decrease in BAX protein expression compared with the 60 μmol/L phosphoramidate nitrogen mustard group, and the differences were statistically significant (all $P<0.001$). However, there was no statistically significant difference in the expression of BCL2 protein among the intervention groups (all $P>0.05$). **Conclusion** Hsa-miR-21-5p exosomes derived from human umbilical cord blood mesenchymal stem cells can effectively exert the anti-apoptotic effect.

【Key words】 Human umbilical cord mesenchymal stem cells; Exosomes; Granular cells; Apoptosis

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循证医学

产后2年内女性避孕体验质性研究的meta整合

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【摘要】 目的 系统整合产后2年内女性避孕体验的质性研究,明确其需求,为后续构建符合产后女性需求的个性化干预提供更加直接、准确的证据。方法 检索 PubMed、The Cochrane Library、Embase、Web of Science、PscINFO、Scopus、CHIAHL 7个英文数据库及中国知网、中国生物医学文献数据库、万方数据库、维普数据库4个中文数据库,收集关于产后女性避孕体验的质性研究。检索时限均为建库到2023年4月30日。采用澳大利亚JBI循证卫生保健中心质性研究质量评价标准进行质量评价,采用汇集性整合方法对结果进行整合。结果 共检索到1488篇相关文献,根据纳入和排除标准,纳入17篇文献,共计产后女性1251名。提炼出41个研究结果,归纳成11个类别,合并为4个整合结果:女性对妊娠间隔内避孕的认知存在差异性、女性避孕信息需求多样性、避孕决策的影响因素多元化、获取产后避孕支持的实践困境。结论 产后2年内女性避孕需求存在多样化特点,医护人员应充分评估其需求以提供个性化的避孕服务,同时促进男性的积极参与,联合家庭、医院、社会等多层面资源提供多维度、持续性支持,以提升生殖健康水平,保障妇幼健康。

【关键词】 避孕; 产后避孕; 质性研究; Meta整合

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Contraceptive experiences of women within two years postpartum: a meta-synthesis of qualitative studies

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【Abstract】 Objective To systematically integrate qualitative research on contraceptive experiences of women within two years postpartum to clarify their needs and provide an evidence for developing subsequent support programs for reproductive planning. **Methods** We searched 7 English databases, including PubMed, the Cochrane Library, Embase, Web of Science, PsycINFO, Scopus, CHIAHL, and four Chinese databases, including China National Knowledge Infrastructure, China Biology Medicine disc, Wanfang Data, and VIP Database. Qualitative research studies on postpartum women's contraceptive experiences were collected. The search was conducted up to April 30, 2023. The Australian JBI (Joanna Briggs Institute) qualitative research quality assessment criteria was used for quality evaluation, and the convergent synthesis method was employed for result integration. **Results** According to the inclusion and exclusion criteria, a total of 17 studies were included from 1488 relevant literatures retrieved, with 1251 postpartum women. Totally 41 findings were categorized into 11 themes and further consolidated into four integrated results: variations in women's awareness of contraceptive during the interpregnancy interval, diversity in women's

contraceptive information needs, multifactorial influences on contraceptive decision-making, and practical challenges in accessing postpartum contraceptive support. **Conclusion** Women's contraceptive needs within 2 years postpartum exhibit diverse characteristics. Healthcare professionals should thoroughly assess their needs to provide personalized contraceptive services. Simultaneously, encouraging active male involvement and leveraging multi-dimensional, sustained support from family, hospitals, and the community is essential to enhance reproductive health and ensure the well-being of women and children.

【 Key words 】 Contraception; Postpartum contraception; Qualitative research; Meta-integration

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·临床报道·

反复种植失败患者子宫内膜 MUM1 阳性表达与 子宫内膜血流变化的关系

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【摘要】 目的 探讨反复种植失败 (repeated implantation failure, RIF) 患者子宫内膜中多发性骨髓瘤癌基因 1 (multiple myeloma oncogene 1, MUM1) 阳性表达与子宫内膜血流变化的关系。方法 回顾性队列研究分析选择 2022 年 3

月至2023年5月期间在郑州大学第二附属医院生殖医学中心就诊的62例RIF患者为研究对象。所有患者于围排卵期都接受宫腔镜检查,采集子宫内膜组织,并通过免疫组织化学染色法检测子宫内膜组织MUM1、血管内皮生长因子(vascular endothelial growth factor, VEGF)、微血管密度(microvessel density, MVD)的阳性表达情况,并行三维多普勒超声子宫内膜血流动力学检查,根据MUM1表达的结果分为MUM1阳性组(29例)和MUM1阴性组(33组),比较两组患者子宫内膜厚度、子宫内膜血流血管化指数(vascularization index, VI)、血流指数(blood flow index, FI)、血管化血流指数(vascularized blood flow index, VFI)及双侧子宫动脉血流阻力指数(resistance index, RI)、搏动指数(pulsatility index, PI)、收缩期峰值流速与舒张末期流速比值(peak systolic velocity/peak diastolic velocity, S/D)的参数;比较两组患者中子宫内膜VEGF、MVD的表达水平;采用Pearson相关性分析,探讨两组子宫内膜VEGF、MVD的表达与子宫内膜血流VI、FI、VFI的相关性。结果 在RIF患者中,MUM1阳性组子宫内膜VEGF阳性率[31.03% (9/29)]、MVD的表达(16.97 ± 3.28)及子宫内膜VI(1.45 ± 0.96)、FI(21.13 ± 5.33)、VFI(0.39 ± 0.17)明显低于MUM1阴性组[36.36% (12/33), $P < 0.001$; 33.42 ± 7.97 , $P < 0.001$; 1.91 ± 0.56 , $P = 0.025$; 23.91 ± 5.37 , $P = 0.045$; 0.54 ± 0.14 , $P = 0.004$]。MUM1阳性组双侧子宫动脉血流RI(0.69 ± 0.14)、PI(1.49 ± 0.61)、S/D(2.40 ± 0.62)显著大于MUM1阴性组(0.54 ± 0.15 、 0.92 ± 0.34 、 1.45 ± 0.40 ; 均 $P < 0.001$)。MUM1阳性组子宫内膜MVD的表达水平与子宫内膜血流VI、FI、VFI存在显著正相关($r = 0.931$, $P < 0.001$; $r = 0.968$, $P < 0.001$; $r = 0.914$, $P < 0.001$),子宫内膜VEGF的表达与子宫内膜血流VI、FI、VFI也存在显著正相关($r = 0.965$, $P < 0.001$; $r = 0.954$, $P < 0.001$; $r = 0.935$, $P < 0.001$)。结论 在RIF患者中,MUM1阳性表达影响子宫内膜血流及VEGF、MVD的表达水平,且子宫内膜血流VI、FI、VFI与子宫内膜VEGF、MVD的表达呈显著正相关。

【关键词】 多发性骨髓瘤癌基因1; 反复种植失败; 血管内皮生长因子; 微血管密度; 子宫内膜血流

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Association between positive MUM1 expression and endometrial blood flow changes in patients with repeated implantation failure

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【Abstract】 **Objective** To investigate the relationship between positive expression of multiple myeloma oncogene 1 (MUM1) and changes of endometrial endometrium in patients with repeated implantation failure (RIF). **Methods** A retrospective cohort study of 62 RIF patients who attended the Center for Reproductive Medicine of the Second Affiliated Hospital of Zhengzhou University between March 2022 and May 2023 were selected. All patients were examined by perimetry, endometrial tissue was collected, and the positive expression of MUM1,

vascular endothelial growth factor (VEGF), and microvessel density (MVD) were detected by immunohistochemical staining. The endometrial hemodynamics were examined by three-dimensional Doppler ultrasound, and according to the results of MUM1 expression, the patients were divided into MUM1-positive group (29 cases) and MUM1-negative group (33 cases). The endometrial thickness, endometrial blood flow vascularization index (VI), flow index (FI), vascularized blood flow index (VFI), and bilateral uterine arterial blood flow resistance index (RI), pulsatility index (PI), peak systolic velocity/peak diastolic velocity (S/D) were compared between the two groups. The expression levels of endometrial VEGF and MVD were compared between the two groups. Pearson correlation was used to explore the correlation between the expression of endometrial VEGF, MVD and endometrial blood flow VI, FI, VFI in the two groups. **Results** In RIF patients, the endometrial VEGF positivity rate [31.03% (9/29)], MVD expression (16.97±3.28), and endometrial VI (1.45±0.96), FI (21.13±5.33), and VFI (0.39±0.17) in MUM1-positive group were significantly lower than those in the MUM1-negative group [the VEGF-positive rate: 36.36% (12/33), $P<0.001$; MVD: 33.42±7.97, $P<0.001$; VI: 1.91±0.56, $P=0.025$; FI: 23.91±5.37, $P=0.045$; VFI: 0.54±0.14, $P=0.004$]. Bilateral uterine arterial blood flow RI (0.69±0.14), PI (1.49±0.61), S/D (2.40±0.62) in MUM1-positive group was significantly higher than those in MUM1-negative group (0.54±0.15, 0.92±0.34, 1.45±0.40; all $P<0.001$). There was a significant positive correlation between the endometrial MVD expression level in the MUM1-positive group and endometrial blood flow of VI, FI, and VFI ($r=0.931$, $P<0.001$; $r=0.968$, $P<0.001$; $r=0.914$, $P<0.001$), and there was also a significant positive correlation between endometrial VEGF expression and endometrial blood flow VI, FI, and VFI ($r=0.965$, $P<0.001$; $r=0.954$, $P<0.001$; $r=0.935$, $P<0.001$). **Conclusion** In RIF patients, the positive expression of MUM1 affects endometrial blood flow and the expression levels of VEGF and MVD, and there is a significant positive correlation between endometrial blood flow VI, FI, VFI and the expression of VEGF and MVD in the endometrium.

【Key words】 Multiple myeloma oncogene 1; Repeated implantation failure; Vascular endothelial growth factor; Microvessel density; Endometrial blood flow

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·个案报道·

颅内生殖细胞肿瘤放疗后患者体外受精-胚胎移植助孕成功 1 例

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【摘要】 颅内生殖细胞肿瘤 (intracranial germ cell tumours, iGCTs) 放疗后可能导致女性患者出现低促性腺激素性闭经而不孕。本案例探讨 iGCTs 放疗史患者助孕治疗及助孕方案的选择。对 1 例 iGCTs 放疗史患者使用注射用人尿促性素及注射用重组人促黄体生成素促排卵后, 行新鲜胚胎移植后成功妊娠, 并于孕 39⁺⁵ 周时行剖宫产终止妊娠, 娩一健康女婴。此助孕方案可为相似患者的治疗提供参考, 优化临床决策。

【关键词】 受精, 体外; 胚胎移植; 颅内生殖细胞肿瘤; 放疗

A successful case of *in vitro* fertilization and embryo transfer pregnancy in patients with intracranial germ cell tumors after radiotherapy

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【Abstract】 After radiotherapy of intracranial germ cell tumors (iGCTs), female patients may suffer from hypogonadotropic amenorrhea and infertility. In this case, we investigated the selection of pregnancy assistance treatment and pregnancy assistance program for patients with iGCTs radiotherapy history. This case reported a patient with a history of radiotherapy for iGCTs who underwent fresh embryo transfer and successful pregnancy after ovulation induction with injectable human menopausal gonadotropin and recombinant human luteinizing hormone. The patient underwent cesarean section at 39⁺⁵ weeks of gestation and delivered a healthy female infant. This pregnancy assistance scheme can provide reference for the treatment of similar patients and optimize clinical decision-making.

【Key words】 Fertilization *in vitro*; Embryo transfer; Intracranial germ cell tumours; Radiotherapy

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个案报道

PATL2 基因 c.1363C>T 纯合无义突变致卵母细胞成熟阻滞 1 例

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【摘要】 卵母细胞成熟阻滞是一种极其罕见的原发性不孕症, 表现为卵子发育停滞, 卵母细胞完全受精失败, 受精前后卵母细胞凋亡以及早期胚胎发育停滞等。本案例探讨了 1 例经 2 次控制性超促排卵均未获成熟卵母细胞为特征的原发不孕患者的遗传学病因。采集患者外周血进行全外显子组测序, 经生物信息学筛选可疑致病突变, 并对患者及其父母进行 Sanger 测序验证。结果显示, 患者检测到 *PATL2* 基因的纯合无义突变 c.1363C>T (p.Gln455*), Sanger 测序结果显示其父母均为携带该突变的杂合变异, 经 HGMD 数据库查询 c.1363C>T 为目前未见报道的罕见致病变异。本案例显示 *PATL2* 基因突变可引起卵母细胞成熟阻滞, 建议对这类患者尽早进行外显子测序并行遗传咨询, 以选择适宜的助孕措施。

【关键词】 原发不孕; 全外显子组测序; 卵母细胞成熟阻滞; *PATL2* 基因

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A case of oocyte maturation defect caused by homozygous of *PATL2* gene c.1363C>T

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【 Abstract 】 Oocyte maturation defect is an extremely rare primary infertility, which is characterized by ovum development arrest, oocyte complete fertilization failure, oocyte apoptosis before and after fertilization, and early embryonic development arrest. This case explored the genetic etiology of a primary infertility patient, who had no mature oocyte after two cycles of controlled ovarian hyperstimulation. Peripheral blood samples of the patient were collected for whole exome sequencing, the suspected pathogenic variants were screened by bioinformatics and verified by sanger sequencing on the patient and her parents. Results showed that the patient was found to harbor homozygous variant of the *PATL2* gene, namely c.1363C>T (p.Gln455*). Sanger sequencing has verified that the parents are both heterozygous. The mutation of c.1363C>T is a rare pathogenic mutation that had not yet been recorded in HGMD database. In this case, *PATL2* gene mutation can cause oocyte maturation arrest, it is recommended to use whole exome sequencing and genetic counseling as soon as possible for these patients, so as to select appropriate treatment.

【 Key words 】 Primary infertility; Whole exome sequencing; Oocyte maturation defect; *PATL2* gene

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综述

特纳综合征女性的卵巢组织冷冻: 生育力保存的挑战

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【摘要】 特纳综合征 (Turner syndrome, TS) 是一种常见的女性染色体异常疾病, 其主要临床特征为早期卵巢功能衰竭和生育力下降。TS 患者生育力下降的主要原因是 X 染色体异常, 不同染色体核型 TS 患者在卵巢储备功能损伤程度上存在差异。国内外已广泛应用卵巢组织冷冻技术来保存 TS 女性生育力。本文回顾总结了 TS 患者生育力下降机制及卵巢组织冷冻技术在其中的应用现状, 未来需建立标准化卵巢功能评估标准和开展前瞻性研究, 精确选择适合卵巢组织冷冻的 TS 患者, 优化生育力保存的结局。

【关键词】 特纳综合征; 卵巢组织冷冻; 生育力保存

Fertility preservation in Turner syndrome patients: challenges in ovarian tissue cryopreservation

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【Abstract】 Turner syndrome (TS) is a common chromosomal anomaly affecting females, characterized primarily by premature ovarian failure and reduced fertility. The decline in fertility among TS patients is mainly due to abnormalities in the X chromosome, with varying degrees of ovarian reserve damage across different chromosomal karyotypes. Ovarian tissue cryopreservation has been widely used both domestically and internationally to preserve the fertility of women with TS. This article reviews the mechanisms underlying the decline in fertility in TS patients and the current application of ovarian tissue cryopreservation technology. Future efforts should focus on establishing standardized criteria for ovarian function assessment and conducting prospective studies to accurately select TS patients suitable for ovarian tissue cryopreservation, thereby optimizing outcomes for fertility preservation.

【Key words】 Turner syndrome; Ovarian tissue cryopreservation; Fertility preservation

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高孕激素状态下促排卵在多囊卵巢综合征中应用的机制及研究进展

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【摘要】 多囊卵巢综合征 (polycystic ovary syndrome, PCOS) 是女性最常见的妇科内分泌疾病之一,也是无排卵性不孕的首要原因。与正常排卵女性相比,PCOS 患者在辅助生殖治疗中更易面临卵巢过度刺激综合征、卵母细胞质量差和受精失败等问题,因此 PCOS 患者的促排卵问题备受生殖领域的关注。高孕激素状态下促排卵 (progestin-primed ovarian stimulation, PPOS) 方案利用外源性孕激素有效阻断黄体生成素峰,达到理想的获卵数、胚胎质量及妊娠结局。本文就 PPOS 方案对 PCOS 患者的作用机制、临床应用及发展进行综述。

【关键词】 促排卵; 黄体期刺激; 高孕激素状态下促排卵; 受精, 体外; 胚胎移植; 多囊卵巢综合征

Mechanism and progress for progestin-primed ovarian stimulation protocol in the patients with polycystic ovary syndrome

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【Abstract】 Polycystic ovary syndrome (PCOS) is one of the most common gynaecological endocrine diseases in women and the main cause of anovulatory infertility. Compared with women with normal ovulation, PCOS patients are more likely to face ovarian hyperstimulation syndrome, poor-quality of oocyte and fertilization failure in assisted reproduction treatment, so ovulation induction in PCOS patients has attracted much attention in the reproductive field. Progestin-primed ovarian stimulation (PPOS) protocol uses exogenous progesterone effectively to block luteinizing hormone surge to achieve ideal

number of retrieved oocytes, embryo quality and pregnancy outcomes. This article reviews the mechanism, clinical application and development of PPOS protocol in PCOS patients.

【Key words】 Ovarian stimulation; Luteal-phase stimulation; Progestin-primed ovarian stimulation; Fertilization *in vitro*; Embryo transfer; Polycystic ovary syndrome

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综述

线粒体异常在多囊卵巢综合征中的研究进展

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【摘要】 多囊卵巢综合征 (polycystic ovary syndrome, PCOS) 是育龄女性最常见的一种内分泌疾病, 以高雄激素血症、胰岛素抵抗、排卵功能障碍等为主要临床特征, 可能导致糖尿病、心血管疾病等远期并发症危险因素的增加。目前有关 PCOS 的发病机制研究较多, 研究热点包括但不限于线粒体异常、氧化应激、维生素 D 异常、钙稳态失衡, 但具体机制尚未明确。本文综述近 5 年有关线粒体异常与 PCOS 的相关研究进展, 以期为进一步探索其发病机制提供理论依据, 为其治疗方法探索更多思路。

【关键词】 多囊卵巢综合征; 线粒体; 氧化磷酸化; 氧化应激

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Mitochondrial abnormalities in polycystic ovary syndrome: a review

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【Abstract】 Polycystic ovary syndrome (PCOS) is one of the most common endogenous diseases in women of childbearing age. Its main clinical features are hypertrophy, insulin resistance, ovulation dysfunction and so on, which may lead to the increase of long-term complications risk factors such as diabetes mellitus and cardiovascular disease. At present, the pathogenesis of PCOS includes but not limited to mitochondrial abnormalities, oxidative stress, vitamin D metabolism abnormalities, calcium homeostasis imbalance, but the specific mechanism has not been clarified. This article reviews the recent five years related research progress on mitochondrial abnormality and PCOS in order to provide theoretical basis for further exploration of its pathogenesis and explore more ideas for its treatment.

【Key words】 Polycystic ovary syndrome; Mitochondria; Oxidative phosphorylation; Oxidative stress

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综述

细胞外囊泡及长链非编码 RNAs 在多囊卵巢综合征中的研究进展

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【摘要】 多囊卵巢综合征 (polycystic ovary syndrome, PCOS) 是一种以高雄激素血症、无排卵或稀发排卵和卵巢多囊样改变为主要特征的生殖内分泌紊乱性疾病。PCOS 的发生、发展与多种因素有关, 表观遗传因素可能在其中起着重要作用。细胞外囊泡 (extracellular vesicles, EVs) 是包载 DNA、RNA、脂质和蛋

白质的脂质双分子层纳米颗粒，在细胞之间通信过程中发挥重要作用。研究显示，PCOS 的发病机制与细胞外囊泡密切相关。长链非编码 RNA (long non-coding RNA, lncRNA) 是由超过 200 个核苷酸组成的 RNA 分子，在颗粒细胞的增殖与凋亡、卵泡发育及内分泌代谢等多个环节发挥重要作用。本文对细胞外囊泡及 lncRNA 在 PCOS 发病机制的研究进行综述，为 PCOS 的诊断和治疗提供新的研究方向。

【关键词】 多囊卵巢综合征； 细胞外囊泡； 长链非编码 RNA

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Extracellular vesicles and long non-coding RNAs in polycystic ovary syndrome

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【Abstract】 Polycystic ovary syndrome (PCOS) is a reproductive endocrine disorder characterized by hyperandrogenemia, anovulation or sporadic ovulation, and polycystic ovarian changes. The development of PCOS is associated with a variety of factors, and epigenetic factors may play an important role. Extracellular vesicles (EVs) are lipid bilayer nanoparticles that contain DNA, RNA, lipids, and proteins, and play an important role in intercellular communication. Studies have shown that the pathogenesis of PCOS is closely related to extracellular vesicles. Long non-coding RNA (lncRNA) is an RNA molecule consisting of more than 200 nucleotides, which plays an important role in various aspects of granulosa cell proliferation and apoptosis, follicular development and endocrine metabolism. In this paper, we review the studies of extracellular vesicles and lncRNA in the pathogenesis of PCOS, which provide new research directions for the diagnosis and treatment of PCOS.

【Key words】 Polycystic ovary syndrome; Extracellular vesicles; Long non-coding RNAs

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综述

生物支架应用于改善卵巢衰老的研究进展

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【摘要】 随着社会生育率下降, 卵巢衰老引发的不孕问题逐渐凸显。再生医学结合组织工程技术是目前改善卵巢衰老的研究焦点, 主要是利用细胞、生物支架以及生长因子达到修复或再生器官的目的。其中制备支架材料是非常关键的环节之一, 大量研究表明进行干细胞移植或体外组织培养, 运用合适的生物支架可以极大地提高细胞或组织的存活率及功能维持时间。本文综述了现阶段应用于改善卵巢衰老的生物支架的相关研究, 为此类患者不孕症的治疗提供一个策略。

【关键词】 再生医学; 不孕症; 卵巢衰老; 生物支架; 组织工程技术

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Application of biological scaffolds to improve ovarian aging

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【Abstract】 With the decline of fertility rate in society, infertility caused by ovarian aging has become increasingly prominent. At present, a combination of regenerative medicine and tissue engineering technology is the focus of research on improving ovarian aging, which primarily utilizes the cells, the biological scaffolds, and the growth factors to repair or regenerate organs. The preparation of scaffold materials plays a crucial role in this process. A large number of studies have demonstrated that stem cell transplantation or tissue culture *in vitro*, along with the use of appropriate biological scaffolds, can significantly enhance the survival rates and the functional maintenance time of cells or tissues. This article provides a comprehensive review of the current research on biological scaffolds used for improving ovarian aging, and offers a novel strategy for the treatment of infertility in such patients.

【Key words】 Regenerative medicine; Infertility; Ovarian aging; Biological scaffolds; Tissue engineering technology

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综述

子宫内膜免疫炎症微环境调控胚胎种植的机制研究进展

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【摘要】 子宫内膜免疫细胞与细胞因子共同组成的子宫内膜免疫炎症微环境, 在胚胎种植窗期具有急性、低度、短暂的促炎特征, 此期间通过调节囊胚激活以获得植入能力, 促进子宫内膜建立容受状态, 介导胚胎的定位、黏附及侵袭。子宫内膜免疫细胞数量及比例异常与胚胎种植失败相关, 免疫炎症微环境特征改变导致胚胎种植失败。现就子宫内膜免疫炎症微环境调控胚胎种植的机制研究进展进行综述。

【关键词】 胚胎种植; 囊胚激活; 子宫内膜容受性; 免疫炎症微环境
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Research progress on the mechanism of endometrial immune inflammation microenvironment regulating embryo implantation

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【Abstract】 The endometrial immune inflammatory microenvironment, composed of immune cells and cytokines, exhibits acute, low-grade, and transient pro-inflammatory characteristics during the embryo implantation window period. During this period, implantation capability is achieved by regulating blastocyst activation, promoting the endometrium to establish a receptive state, and mediating the positioning, adhesion, and invasion of the embryo. Abnormalities in the number and proportion of endometrial immune cells were associated with

embryo implantation failure and altered characteristics of the immunoinflammatory microenvironment led to embryo implantation failure. The research progress on the mechanism of endometrial immunoinflammatory microenvironment regulating embryo implantation is now reviewed.

【Key words】 Embryo implantation; Blastocyst activation; Endometrial receptivity; Immune-inflammatory microenvironment

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综述

铁死亡与睾丸功能障碍的研究进展

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【摘要】 铁稳态对人体正常生理代谢至关重要, 铁代谢紊乱与多种疾病的发生、发展相关。铁死亡主要表现为细胞内铁和脂质过氧化物的积累, 抗氧化系统为其主要的防御机制。研究证明铁死亡与氧化应激、男性不育密切相关, 抑制铁和脂质过氧化物的积累可能是治疗铁死亡相关男性生殖疾病的一种潜在策略。近年来, 铁死亡这种新型细胞死亡方式与男性生殖障碍的相关研究引起学者们的广泛关注和不断探索。故本文结合最新的研究进展, 主要从铁死亡机制、铁死亡在睾丸功能中的作用、与男性不育的关系和相关男性生殖疾病的潜在治疗策略等方面阐述铁死亡对睾丸生精功能的影响, 为防治男性生殖疾病拓展思路。

【关键词】 氧化应激; 睾丸; 铁死亡; 男性生殖功能障碍

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Advances in the study of ferroptosis and testicular dysfunction

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【 Abstract 】 Iron homeostasis is essential for normal physiological metabolism in the human body, and disorders of iron metabolism are associated with the development of several diseases. Ferroptosis is mainly manifested by the accumulation of intracellular iron and lipid peroxides, with the antioxidant system as its main defense mechanism. Current studies have demonstrated that ferroptosis is closely related to oxidative stress and male infertility, and inhibiting the accumulation of iron and lipid peroxides may be a potential strategy for the treatment of ferroptosis-associated male reproductive diseases. Recently, the study of ferroptosis, a novel cell death mode, and male reproductive disorders has attracted extensive attention and continuous exploration by scholars. Therefore, this article combines the latest research progress, mainly elaborates on the effect of ferroptosis on testicular spermatogenesis, from the mechanism of iron death, the role of ferroptosis in testicular function, the relationship with male infertility, and the potential therapeutic strategies for related male reproductive diseases, to expand the ideas for the prevention and treatment of male reproductive diseases.

【 Key words 】 Oxidative stress; Testis; Ferroptosis; Male reproductive disorders

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