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紧急避孕临床应用专家共识 (2024 年)

中国妇幼保健研究会安全避孕专委会

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【摘要】 紧急避孕是指在无保护性生活或发现避孕失败后数天内为避免或减少非意愿妊娠而采用的补救避孕措施, 可以有效降低母婴患病和死亡风险。中国妇幼保健研究会安全避孕专委会组织国内计划生育临床、流行病学和药物不良反应等方面专家, 从紧急避孕的种类、机制、有效性、临床应用策略等方面进行了探讨。推荐紧急避孕在无保护性生活后越早使用避孕效果越好。左炔诺孕酮、米非司酮和醋酸乌利司他尽可能在无保护性生活后 72 h 内使用; 含铜宫内节育器在无保护性生活后 120 h 内放置具有较好的紧急避孕作用, 不取出即可作为长效避孕措施; 任何育龄期女性都适合按需使用紧急避孕方法; 紧急避孕药的使用没有绝对的医疗禁忌证; 应避免反复多次使用紧急避孕药; 紧急避孕后应及时转换使用常规避孕方法。本共识可为从事避孕节育服务的临床工作者提供决策依据。

【关键词】 紧急避孕; 临床应用; 专家共识

Consensus on clinical practice of emergency contraception (2024)

The Safe Contraception Committee of the Chinese Maternal and Child Health Research Association

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【Abstract】 Emergency contraception is a therapeutic intervention used to prevent pregnancy within 3 to 5 d after unprotected or suboptimally protected sexual intercourse. The Safe Contraception Committee of the Chinese Maternal and Child Health Research Association convened a meeting of family planning experts to discuss the various aspects of emergency contraception, including its types, mechanisms of action, efficacy, and clinical applications. The expert consensus suggests that emergency contraception should be administered as early as possible after unprotected intercourse to optimize contraceptive efficacy. Emergency contraceptive pills (ECP), which encompass levonorgestrel, mifepristone, and ulipristal acetate formulations, should be taken within 72 h after unprotected intercourse. The copper intrauterine device is efficacious for emergency contraception when inserted within 120 h of unprotected intercourse and offers the additional benefit of long-term contraception without the need for removal. Emergency contraception methods are deemed appropriate for all women of reproductive age on an as-needed basis. It is important to note that there are no absolute medical contraindications to the use of ECP. However, the repeated use of ECP should be discouraged as a regular contraceptive strategy. Instead, individuals are advised to transition to a consistent contraceptive method following the use of emergency contraception. This consensus document offers valuable guidance for healthcare providers in the realm of family planning services.

【Key words】 Emergency contraception; Clinical practice; Expert consensus

标准与讨论

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《不孕不育人群肥胖/超重诊疗指南 (2025 年版)》制定计划书

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黄佳和江琳琳对本文有同等贡献

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【摘要】 肥胖通过多种机制导致患者低生育力、不孕和不良母婴结局。肥胖症患者在生育治疗和妊娠后均面临多种障碍, 造成患者身心、社会经济等负担增加。近年来伴随研究的深入及治疗手段的丰富, 亟须通过多学科方法, 优化对肥胖合并不孕不育症患者的诊治。为进一步提升我国肥胖/超重不孕不育人群诊治水平, 由中国医师协会生殖医学专委会发起, 多学科、多中心专家参与, 依照循证证据拟制定中国肥胖/超重在不孕不育人群中诊疗指南。该指南将遵循已有的国际、国内指南制定与报告规范, 为临床实践提供推荐意见。本文将阐述指南制定的背景及目的, 制定方法, 包括制定流程, 拟采用的证据检索、质量评价方法, 指南发表、推广及更新等计划。

【关键词】 肥胖; 不孕症; 指南; 计划书

Protocol for the guidelines for the diagnosis and treatment of obesity/overweight in infertile populations (2025)

Huang Jia¹, Jiang Linlin², Chen Hui¹, Bai Shiyu¹, Tang Jing¹, Wang Zheng³, Li Rong³, Yang Dongzi¹

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Huang Jia and Jiang Linlin contributed equally to the article

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【Abstract】 Obesity contributes to reduced fertility, infertility and adverse maternal and infant outcomes through multiple mechanisms. Individuals with obesity encounter numerous impediments during fertility treatments and subsequent pregnancy, leading to intensified physical, psychological, and socio-economic burdens. Given the recent progress in research and the expansion of treatment modalities, there is an imperative need to refine the diagnostic and therapeutic frameworks for obese patients with infertility through a multidisciplinary approach. The Reproductive Medicine Specialized Committee of the Chinese Medical Doctor Association (CMDA) has established a multidisciplinary

team of experts to develop an evidence-based guideline. This guideline's development will adhere to both national and international standards for guideline development and reporting. This proposal mainly describes the significance and purpose of guideline development, the method of evidence retrieval and quality assessment, the process of guideline development, and the plan for publication, implementation and dissemination of the guideline.

【Key words】 Obesity; Infertility; Guideline; Protocol

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临床研究

波塞冬标准年轻预期低预后患者卵泡期长效长方案不同促性腺激素启动剂量的临床及围产结局比较

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【摘要】 目的 探讨符合波塞冬诊断标准年轻预期低预后患者卵泡期长效长方案不同促性腺激素 (gonadotropin, Gn) 启动剂量的临床结局及围产结局是否存在差异。方法 本研究为回顾性队列研究, 分析了2016年1月1日至2022年6月30日于郑州大学第一附属医院生殖医学中心首次行新鲜周期体外受精/卵胞质内单精子注射 (*in vitro* fertilization/intracytoplasmic sperm injection, IVF/ICSI)-胚胎移植 (embryo transfer, ET) 患者的临床资料, 筛选促排卵方案为卵泡期长效长方案且符合年轻预期低预后患者诊断标准的首个周期纳入研究。按照卵巢刺激周期的 Gn 启动剂量将患者分为低剂量组 ($Gn < 225$ U)、中剂量组 ($225 \text{ U} \leq Gn < 300$ U) 和高剂量组 ($Gn = 300$ U), 分别比较各组间患者的临床及围产结局。结果 本研究共纳入 1 659 个周期, 包括 Gn 启动低剂量组 316 个周期, 中剂量组 536 个周期, 高剂量组 807 个周期。高剂量组获卵总数 [6.00 (4.00, 9.00) 个] 小于中剂量组 [8.00 (6.00, 11.00) 个] 和低剂量组 [11.00 (7.00, 13.00) 个],

中剂量组小于低剂量组, 差异均有统计学意义 (均 $P < 0.017$)。3 组间卵子成熟率、IVF/ICSI 正常受精率及优质胚胎率差异均无统计学意义 (均 $P > 0.05$) , 囊胚形成率在低剂量组 [20.33% (425/2 090)] 、中剂量组 [17.28% (510/2 951)] 、高剂量组 [14.62% (518/3 542)] 依次降低, 组间两两比较差异均有统计学意义 (均 $P < 0.017$)。不同 Gn 启动剂量分组患者之间的临床妊娠率、生化妊娠率、异位妊娠率、流产率、流产组织绒毛染色体异常率及早产率差异均无统计学意义 (均 $P > 0.05$) , 高剂量组活产率 [47.83% (386/807)] 显著低于低剂量组 [57.28% (181/316)] , $P = 0.004$ 。多因素 logistic 回归调整混杂因素后, 高剂量的 Gn 启动剂量是活产率下降的独立危险因素 ($aOR = 0.659$, 95% CI : 0.462~0.941, $P = 0.022$)。无论是否调整混杂因素, 各组间围产结局差异均无统计学意义 (均 $P > 0.05$)。结论 对于行首次卵泡期长效方案促排卵的年轻预期低预后患者, 增加 Gn 启动剂量不能增加获卵数且与囊胚形成率降低有关, 高剂量 Gn 启动会降低活产率, 但不会增加围产期不良结局的风险。

【关键词】 促性腺激素; 卵巢低反应; 波塞冬标准; 卵泡期长效方案; 围产结局

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Comparison of clinical and perinatal outcomes of different gonadotropin starting dosages in the early-follicular phase long-acting GnRH agonist long protocol in young patients with expected poor prognosis according to POSEIDON criteria

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【Abstract】 **Objective** To investigate whether there are differences in clinical outcomes and perinatal outcomes associated with different initial dosages of gonadotropin (Gn) in expected poor prognosis young patients, diagnosed according to the POSEIDON criteria, undergoing the early-follicular phase long-acting gonadotropin-releasing hormone agonist (GnRH-a) long protocol. **Methods** This retrospective cohort study analyzed clinical data from patients who underwent their first *in vitro* fertilization/intracytoplasmic sperm injection (IVF/ICSI)-fresh embryo transfer (ET) cycle at the Reproductive Medicine Center of the First Affiliated Hospital of Zhengzhou University between January 1, 2016, and June 30, 2022. Patients included in the study were those who underwent ovarian stimulation with the early-follicular phase long-acting GnRH-a long protocol and young expected poor prognosis. Patients were divided into three groups based on the starting Gn dosage: low-dose group ($Gn < 225$ U), medium-dose group ($225 \text{ U} \leq Gn < 300$ U), and high-dose group ($Gn = 300$ U). Clinical and perinatal outcomes were compared among the three groups. **Results** A total of 1 659 cycles were included in the study, with 316 cycles in the low-dose group, 536 cycles in the medium-dose group, and 807 cycles in the high-dose group. The number of oocytes retrieved in the high-dose group [6.00 (4.00,9.00)] was less than that in the

medium-dose group [8.00 (6.00,11.00)] and the low-dose group [11.00 (7.00,13.00)], which in the medium-dose group was less than that in the low-dose group, and the differences were statistically significant (all $P<0.017$). There were no significant statistical differences in oocyte maturation rate, normal fertilization rate of IVF/ICSI, or high-quality embryo rate among the three groups (all $P>0.05$). The blastocyst formation rates decreased sequentially in the low-dose group [20.33% (425/2 090)], medium-dose group [17.28% (510/2 951)], and high-dose group [14.62% (518/3 542)], with significant differences between each pair of groups (all $P<0.017$). There were no significant differences in clinical pregnancy rate, biochemical pregnancy rate, ectopic pregnancy rate, miscarriage rate, chromosomal abnormalities in miscarriage tissues, or preterm birth rate among the three groups (all $P>0.05$). However, the live birth rate was significantly lower in the high-dose group [47.83% (386/807)] than in the low-dose group [57.28% (181/316), $P=0.004$]. After adjusting for confounding factors using multivariate logistic regression, the high starting Gn dosage was found to be an independent risk factor for decreased live birth rate (aOR=0.659, 95% CI: 0.462–0.941, $P=0.022$). There were no significant differences in perinatal outcomes among the groups, regardless of whether confounding factors were adjusted for (all $P>0.05$).

Conclusion In young patients with expected poor prognosis undergoing their first ovarian stimulation with the long-acting follicular phase protocol, increasing the starting Gn dosage does not increase the number of oocytes retrieved and is associated with a lower blastocyst formation rate and a reduced live birth rate, but does not increase the risk of adverse perinatal outcomes.

【Key words】 Gonadotropin; Poor ovarian response; POSEIDON criteria; Early-follicular phase long-acting GnRH agonist long protocol; Perinatal outcomes

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临床研究

经 IVF/ICSI 助孕首次单胎活产后患者二孩生育意愿影响因素分析

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【摘要】 目的 探讨通过体外受精/卵胞质内单精子注射 (*in vitro* fertilization/intracytoplasmic sperm injection, IVF/ICSI) 获得首次单胎活产后二孩生育意愿的影响因素。**方法** 本研究是一项回顾性队列研究, 分析 2016 年 7 月至 2021 年 7 月于郑州大学第三附属医院生殖健康医院经 IVF/ICSI 实现首次单胎活产的患者资料, 截止至 2023 年 7 月, 根据患者是否为生育二孩再次返回接受辅助生殖治疗分为回诊组 ($n=1\ 809$) 与未回诊组 ($n=5\ 824$), 比较两组人群的临床资料, 分析影响患者二孩生育意愿的因素。**结果** 比较两组患者特征, 纳入单因素分析后有统计学意义的变量构建多因素 logistic 回归方程, 结果显示女方年龄 ($OR=0.93$, 95% CI : $0.91\sim0.94$, $P<0.001$)、不孕年限 ($OR=0.96$, 95% CI : $0.93\sim0.98$, $P=0.002$)、不孕因素中的混合因素 ($OR=0.82$, 95% CI : $0.70\sim0.97$, $P=0.023$)、既往生育史 ($OR=0.33$, 95% CI : $0.27\sim0.42$, $P<0.001$)、助孕方式 ($OR=1.31$, 95% CI : $1.11\sim1.55$, $P=0.001$)、移植方案 ($OR=0.83$, 95% CI : $0.74\sim0.93$, $P=0.002$)、分娩方式 ($OR=0.63$, 95% CI : $0.55\sim0.71$, $P<0.001$)、妊娠合并症 ($OR=0.70$, 95% CI : $0.60\sim0.82$, $P<0.001$)、有无剩余胚胎 ($OR=2.67$, 95% CI : $2.24\sim3.19$, $P<0.001$)、活产儿性别 ($OR=0.40$, 95% CI : $0.36\sim0.45$, $P<0.001$)、文化程度 ($OR=0.74$, 95% CI : $0.64\sim0.85$, $P<0.001$)、户籍类型 ($OR=0.74$, 95% CI : $0.65\sim0.84$, $P<0.001$) 是患者经 IVF/ICSI 获得首次单胎活产后二孩生育意愿的影响因素。**结论** 女方年龄、不孕年限、不孕因素、既往生育史、冷冻周期移植、剖宫产、患有妊娠期合并症、活产儿性别为男孩、高中及以上学历、城市户籍与患者回诊呈负相关, ICSI 助孕、有剩余胚胎与患者回诊呈正相关。

【关键词】 生殖技术, 辅助; 受精, 体外; 生育意愿; 二孩

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Analysis of factors influencing the willingness of patients to have a second child after obtaining the first singleton live birth via IVF/ICSI-assisted conception

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【Abstract】 Objective To investigate the factors influencing patients' willingness to have a second child after obtaining their first singleton live birth by *in vitro* fertilization/intracytoplasmic sperm injection (IVF/ICSI). **Methods** The data of patients who achieved their first single live birth via IVF/ICSI at the Reproductive Health Hospital of the Third Affiliated Hospital of Zhengzhou University were collected between July 2016 and July 2021 in a retrospective cohort study. Until July 2023, the patients were divided into the returning group ($n=1\ 809$) and the non-returning group ($n=5\ 824$) according to whether they

returned again to receive assisted reproduction treatment for the birth of a second child. The clinical data of the two groups were compared, and the factors affecting patients' willingness to have a second child were analyzed. **Results** The characteristics of the two groups of patients were compared. Variables that were statistically significant after being included in the univariate analysis were employed to construct a multivariate logistic regression equation. The results indicated that the age of the female ($OR=0.93$, 95% CI : 0.91–0.94, $P<0.001$), the duration of infertility ($OR=0.96$, 95% CI : 0.93–0.98, $P=0.002$), male+female factors of infertility factor ($OR=0.82$, 95% CI : 0.70–0.97, $P=0.023$) the previous reproductive history ($OR=0.33$, 95% CI : 0.27–0.42, $P<0.001$), the method of assisted pregnancy ($OR=1.31$, 95% CI : 1.11–1.55, $P=0.001$), the transplantation plan ($OR=0.83$, 95% CI : 0.74–0.93, $P=0.002$), the mode of delivery ($OR=0.63$, 95% CI : 0.55–0.71, $P<0.001$), pregnancy complications ($OR=0.70$, 95% CI : 0.60–0.82, $P<0.001$), the presence or absence of remaining embryos ($OR=2.67$, 95% CI : 2.24–3.19, $P<0.001$), the gender of the first live birth ($OR=0.40$, 95% CI : 0.36–0.45, $P<0.001$), the degree of education ($OR=0.74$, 95% CI : 0.64–0.85, $P<0.001$), and the type of household registration ($OR=0.74$, 95% CI : 0.65–0.84, $P<0.001$) were the influencing factors of the second-child fertility intention of patients after obtaining the first singleton live birth through IVF/ICSI. **Conclusion** The age of the female, the duration of infertility, the factors of infertility, the previous reproductive history, frozen-thawed embryo transfer, cesarean section, having pregnancy complications, the gender of the first live birth being a boy, having a high school education or above, and urban household registration are negatively correlated with the patients' return visits. ICSI-assisted pregnancy and having remaining embryos are positively correlated with the patients' return visits.

【Key words】 Reproductive techniques, assisted; Fertilization, *in vitro*; Fertility intention; Second child

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·临床研究·

体外受精/卵胞质内单精子注射单 胚胎移植活产周期的性别相关生长 差异研究

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【摘要】 目的 研究单胚胎移植 (single embryo transfer, SET) 单胎活产周期胚胎形态学参数及早期血清 β -人绒毛膜促性腺激素 (human chorionic gonadotropin, hCG) 水平的性别相关生长差异 (sex-related growth difference, SRGD)。**方法** 采用回顾性队列研究, 分析烟台市烟台山医院生殖医学中心 2020 年 1 月至 2022 年 12 月新鲜和冷冻的非供体、SET、单胎活产周期患者的临床资料 ($n=311$), 以新生儿性别分组, 男婴组为 154 例, 女婴组为 157 例, 并根据移植胚胎期 (卵裂期 93 例、囊胚 218 例) 及胚胎质量 (优质胚胎组 250 例、非优质胚胎组 61 例) 行亚组分层分析, 采用单因素和二元 logistic/逐步回归分析是否在胚胎发育阶段和妊娠早期存在胚胎形态学参数及早期 β -hCG 水平的 SRGD。**结果** 单因素分析显示, 父母年龄、母亲体质量指数、移植胚胎期、胚胎质量、授精方式、周期类型等一般资料匹配均具有可比性 (均 $P>0.05$)。性别相关的形态学参数单因素分析显示, 男婴组的第 2 天 (day 2, D2) 胚胎细胞数 [(4.25 \pm 0.94) 枚] 大于女婴组 [(3.98 \pm 0.84) 枚, $P=0.007$], 二元 logistic 回归分析显示 D2 胚胎细胞数与活产男婴呈正相关 ($OR=1.428$, 95% CI : 1.052~1.938, $P=0.022$); 囊胚亚组分析显示, D2 细胞数 ($OR=1.522$, $P=0.021$)、囊胚扩张度 ($OR=2.969$, $P=0.029$) 与活产男婴呈正相关。逐步回归分析显示, 早期 β -hCG 水平男婴组 [776.40 (521.95, 1 127.25) U/L] 高于女婴组 [634.60 (425.80, 973.05) U/L, $P=0.003$], 并与移植胚胎期 ($\beta=0.139$, $P=0.012$)、胚胎质量 ($\beta=0.136$, $P=0.014$) 相关; 不同胚胎期、胚胎质量亚组分层分析中, 卵裂期、囊胚期和优质胚胎中男婴组的 β -hCG 水平 [677.20 (462.63, 1 028.50) U/L, 838.30 (557.50, 1 191.00) U/L, 816.00 (563.95, 1 199.75) U/L] 均高于女婴组 [538.40 (344.80, 804.80) U/L, 724.95 (446.83, 1 016.75) U/L, 651.40 (431.30, 985.73) U/L], 差异均有统计学意义 ($P=0.041$ 、 $P=0.044$ 、 $P=0.001$)。囊胚亚组回归分析显示, β -hCG 水平与较高的囊胚扩张度 ($\beta=0.162$, $P=0.010$)、高滋养外胚层等级 ($\beta=0.344$, $P<0.001$) 呈正相关。**结论** SET 单胎活产周期中, 男婴的 D2 胚胎细胞数、早期 β -hCG 水平高于女婴, 囊胚扩张度与性别相关, 存在 SRGD。

【关键词】 单胚胎移植; 胚胎发育; 人绒毛膜促性腺激素; 性别因素; 单胎活产; 性别相关生长差异

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Study on sex-related growth difference in the live birth cycle of single embryo transfer by IVF/ICSI

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【Abstract】 Objective To study the sex-related growth difference (SRGD) of embryo morphological parameters and early serum β -human chorionic gonadotropin (β -hCG) level in single embryo transfer (SET) singleton live birth cycles. **Methods** A retrospective cohort study analyzed the clinical data of patients with fresh and frozen non-donor, SET, and singleton live birth cycles from January 2020 to December 2022 in the Reproductive Medicine Center of Yantaishan Hospital ($n=311$), and the neonatal sex group was grouped by gender, with 154 cases in the male infant group and 157 cases in the female infant group. The embryo transfer stage (93 cases in cleavage stage, 218 cases in blastocysts) and embryo quality (250 cases in the good-quality embryo group and 61 cases in the non-good-quality embryo group) were analyzed by subgroup stratification. Univariate and binary logistic/stepwise regression analysis were used to analyze whether there were embryonic morphological parameters and early β -hCG levels in the embryonic development stage and early pregnancy. **Results** Univariate analysis showed that the general data matching of patients, such as parents' age, body mass index, embryo transfer stage, embryo quality, insemination method, and cycle type were comparable (all $P>0.05$). Univariate analysis of sex-related morphological parameters showed that the number of cells on the day 2 (D2) embryo in the male infant group (4.25 ± 0.94) was larger than that in the female infant group (3.98 ± 0.84 , $P=0.007$). Binary logistic regression analysis showed that the number of cells on D2 embryo was positively correlated with the number of live-born males ($OR=1.428$, 95% CI : 1.052–1.938, $P=0.022$). Subgroup analysis of blastocysts showed that the number of cells on D2 embryo ($OR=1.522$, $P=0.021$) and blastocyst expansion ($OR=2.969$, $P=0.029$) were positively correlated with live-born males. The early β -hCG level in the male infant group [776.40 (521.95, 1 127.25) U/L] was higher than that in the female infant group [634.60 (425.80, 973.05) U/L, $P=0.003$], and it was related to the embryo transfer period ($\beta=0.139$, $P=0.012$) and embryo quality ($\beta=0.136$, $P=0.014$). In the stratified analysis of different embryo stages and quality subgroups, β -hCG levels in male infant group during the cleavage stage, blastocyst stage, and high-quality embryos [677.20 (462.63, 1 028.50) U/L, 838.30 (557.50, 1 191.00) U/L, 816.00 (563.95, 1 199.75) U/L] were higher than those in female infant group [538.40 (344.80, 804.80) U/L, 724.95 (446.83, 1 016.75) U/L, 651.40 (431.30, 985.73) U/L], and the differences were statistically significant ($P=0.041$, $P=0.044$, $P=0.001$). Subgroup regression analysis of blastocysts showed that β -hCG level was positively correlated with higher blastocyst expansion ($\beta=0.162$, $P=0.010$) and higher trophoctoderm grade ($\beta=0.344$, $P<0.001$). **Conclusion** In the single live birth cycle of SET, the number of D2 embryo cells and the early β -hCG level of male infants were higher than those

of female infants, and the expansion degree of blastocyst is related to sex, and there is SRGD.

【Key words】 Single embryo transfer; Embryonic development; Human chorionic gonadotropin; Sex factors; Singleton live births; Sex-related growth difference

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·实验研究·

甲基转移酶样蛋白 3 调控 FOXO1 的表达及对子宫内膜基质细胞蜕膜化的影响

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【摘要】 目的 探究甲基转移酶样蛋白 3 (methyltransferase-like 3, METTL3) 对子宫内膜蜕膜化的作用。方法 采用生物信息学分析 26 个 N6-甲基腺嘌呤 (N6-methyladenosine, m6A) 调节因子在反复种植失败 (recurrent implantation failure, RIF)、复发性流产 (recurrent spontaneous abortion, RSA) 及子宫内膜基质细胞蜕膜化中的表达情况; 使用醋酸甲羟孕酮和二丁酰环磷酸腺苷诱导人子宫内膜基质细胞 (human endometrial stromal cells, HESCs) 发生蜕膜化, 检测对照组和蜕膜化组中的总 m6A 水平、METTL3、叉头框蛋白 O1 (Forkhead box protein O1, FOXO1) 及蜕膜化标志物胰岛素样生长因子结合蛋白 1 (insulin-like growth factor binding protein 1, IGFBP1) 和催乳素的表达水平; 通过慢病毒

构建 METTL3 干扰的 HESCs 模型, CCK-8 及 Edu 检测阴性对照组和敲低 METTL3 组的增殖情况。慢病毒转染成功后再诱导蜕膜化, 检测 FOXO1 及蜕膜化标志物的表达变化。结果 生物信息学分析结果显示, METTL3 在 RIF 患者和 RSA 患者子宫内膜中的表达显著下调 ($P=0.014$, $P=0.016$), 而在蜕膜化的子宫内膜中显著上调 ($P=0.029$)。体外诱导 HESCs 蜕膜化, 蜕膜化组中总 m6A、METTL3、FOXO1 蛋白表达量升高 ($P=0.015$, $P=0.016$, $P=0.004$)。敲低 METTL3 后 HESCs 中 FOXO1 蛋白表达量降低 ($P=0.009$); CCK-8 及 Edu 结果显示, 敲低 METTL3 后 HESCs 的增殖被抑制。体外诱导敲低 METTL3 的 HESCs 蜕膜化后, *IGFBP1* mRNA、*PRL* mRNA、FOXO1 蛋白表达量较阴性对照组差异均无统计学意义 (均 $P>0.05$)。结论 在子宫内膜基质细胞中, METTL3 能够调控 FOXO1 的表达, 促进 IGFBP1、催乳素的表达, 影响子宫内膜细胞蜕膜化。

【关键词】 N6-甲基腺嘌呤; 甲基转移酶样蛋白 3; 蜕膜化; 反复种植失败; 复发性流产

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Methyltransferase-like 3 regulates FOXO1 expression and its effect on decidualization of endometrial stromal cells

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【Abstract】 **Objective** To explore the role of methyltransferase-like 3 (METTL3) on endometrial decidualization. **Methods** Bioinformatics was used to analyze the expression of 26 N6-methyladenosine (m6A) regulators in recurrent implantation failure (RIF), recurrent spontaneous abortion (RSA) and the decidualization of endometrial stromal cells. Using Medroxyprogesterone and Dibutyryl-cAMP to induce human endometrial stromal cells (HESCs) decidualization, we examined changes in the expression of total m6A, METTL3, Forkhead framing protein O1 (FOXO1), and decidualization markers insulin-like growth factor binding protein 1 (IGFBP1) and prolactin in the control and decidualization group. Constructing HESC models with METTL3 interference using lentivirus, we used CCK-8 and Edu to detect proliferation in the negative control and knockdown METTL3 group. Lentiviral transfection was successfully followed by induction of decidualization, and we examined changes in the expression of FOXO1 and decidualization markers. **Results** The results of bioinformatics analysis showed that the expression of METTL3 was significantly downregulated in the endometrium of patients with RIF and RSA ($P=0.014$, $P=0.016$), while it was significantly upregulated in the endometrium with decidualization ($P=0.029$). *In vitro*, induction of HESCs decidualization increased in the expression levels of total m6A, METTL3, and FOXO1 proteins in the decidualization group ($P=0.015$, $P=0.016$, $P=0.004$). Knocking down METTL3 resulted in a decrease in FOXO1 protein expression in HESCs ($P=0.009$). The CCK-8

and Edu results showed that the proliferation of HESCs was inhibited after knocking down METTL3. After inducing the knockdown of METTL3 *in vitro*, there was no statistically significant difference in the expression levels of *IGFBP1* mRNA, *PRL* mRNA, and FOXO1 protein in HESCs compared with the negative control group (all $P>0.05$). **Conclusion** In endometrial stromal cells, METTL3 can regulate the expression of FOXO1, promote the expression of IGFBP1 and PRL, and affect the decidualization of endometrial cells.

【 Key words 】 N6-methyladenosine; Methyltransferase-like 3; Decidualization; Recurrent implantation failure; Recurrent spontaneous abortion

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实验研究

基于 HIF-1 α /VEGFA 信号通路探讨育肾养卵方对小鼠卵巢储备功能减退改善

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【摘要】 目的 观察育肾养卵方对卵巢储备功能减退 (diminished ovarian reserve, DOR) 小鼠卵巢储备功能的影响, 并基于低氧诱导因子 (hypoxia-inducible

factor, HIF)-1 α /血管内皮生长因子 A (vascular endothelial growth factor A, VEGFA) 信号通路探讨其作用机制。方法 基于人工智能的网络药理学进行机制分析, 将 50 只 6 周龄 C57BL/6 雌鼠按体质量随机区组法分为对照组、模型组、中药低剂量组、中药中剂量组、中药高剂量组, 每组 10 只。通过苏木精-伊红染色法观察卵巢窦卵泡计数, 酶联免疫吸附法 (enzyme-linked immunosorbent assay, ELISA) 检测血清激素水平, 缺口末端标记法 (TdT-mediated dUTP nick end labeling, TUNEL) 检测卵巢颗粒细胞凋亡; 免疫组织化学法检测卵巢 HIF-1 α 的表达; 蛋白印迹法检测卵巢 HIF-1 α 、VEGFA、B 淋巴细胞瘤-2 (B-cell lymphoma-2, BCL2) 的表达。结果 采用育肾养卵方低、中、高剂量治疗 DOR 模型小鼠后, 中药低、中、高剂量组小鼠卵巢窦卵泡计数均高于模型组 ($P=0.024$ 、 $P<0.001$ 、 $P<0.001$), 卵泡刺激素水平均低于模型组 ($P=0.003$ 、 $P<0.001$ 、 $P<0.001$), 中药中、高剂量组血清抗苗勒管激素水平均高于模型组 ($P=0.001$ 、 $P<0.001$)。网络药理学与分子结合提示育肾养卵方可能通过核心靶点 HIF-1 α 、BCL2、VEGFA 影响 HIF 信号通路。TUNEL 提示中药低、中、高剂量治疗后小鼠卵巢颗粒细胞凋亡率均显著低于模型组 ($P=0.017$ 、 $P=0.003$ 、 $P<0.001$), 免疫组织化学结果显示中药低、中、高剂量治疗后小鼠卵巢颗粒细胞 HIF-1 α 表达较模型组升高 ($P=0.008$ 、 $P<0.001$ 、 $P<0.001$), 蛋白印迹法显示中药中、高剂量组 HIF-1 α 的蛋白表达量均显著高于模型组 ($P=0.004$ 、 $P<0.001$), 低、中、高剂量组的 VEGFA、BCL2 的蛋白表达量均显著高于模型组 ($P=0.003$ 、 $P=0.002$ 、 $P=0.001$; $P=0.029$ 、 $P=0.007$ 、 $P=0.001$)。结论 育肾养卵方可能是通过 HIF-1 α /VEGFA 信号通路抑制卵巢颗粒细胞凋亡达到治疗效果。

【关键词】 卵巢储备功能减退; 育肾养卵方; 人工智能; 网络药理学; HIF-1 α /VEGFA 信号通路

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Exploration of the effects of Yushen Yangluan decoction on improving ovarian reserve function in mice based on the HIF-1 α /VEGFA signaling pathway

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【Abstract】 **Objective** To observe the effect of the Yushen Yangluan decoction on ovarian reserve function in mice with diminished ovarian reserve (DOR) and to explore its mechanism of action based on the hypoxia-inducible factor (HIF)-1 α /vascular endothelial growth factor A (VEGFA) signaling pathway. **Methods** Mechanism analysis was conducted using artificial intelligence-based

network pharmacology. Fifty 6-week-old female C57BL/6 mice were randomly divided into five groups according to body weight, with 10 mice in each group. The groups were as follows: control group, model group, low-dose Traditional Chinese Medicine (TCM) group, medium-dose TCM group, and high-dose TCM group. Hematoxylin-eosin staining was used to observe the number of antral follicles in the ovaries, enzyme-linked immunosorbent assay was employed to detect serum hormone levels, and TdT-mediated dUTP nick end labeling (TUNEL) was used to assess apoptosis in ovarian granulosa cells. Immunohistochemistry (IHC) was performed to detect ovarian expression of HIF-1 α , and Western blotting was used to measure the protein expressional levels of HIF-1 α , VEGFA, and B-cell lymphoma-2 (BCL2) in the ovaries. **Results** After treating DOR model mice with the Yushen Yangluan decoction at low, medium, and high dosages, the ovarian antral follicle count of the mice in the TCM groups was all higher than that in the model group ($P=0.024$, $P<0.001$, $P<0.001$), the follicle-simulating hormone level was lower than that in the model group ($P=0.003$, $P<0.001$, $P<0.001$), and the serum anti-Müllerian hormone level in the medium- and high-dose TCM groups was higher than that in the model group ($P=0.001$, $P<0.001$). Network pharmacology and molecular docking suggested that the formula may influence the HIF signaling pathway through core targets such as HIF-1 α , BCL2 and VEGFA. TUNEL assays indicated that the apoptosis rate of ovarian granulosa cells in the low-, medium-, and high-dose TCM groups was significantly lower than that in the model group ($P=0.017$, $P=0.003$, $P<0.001$). Immunohistochemistry results showed that the expression level of HIF-1 α in the granulosa cells of the follicles in the low-, medium- and high-dose TCM groups was significantly higher than that in the model group ($P=0.008$, $P<0.001$, $P<0.001$). Western blotting analysis indicated that the protein expression level of HIF-1 α in medium-, and high-dose TCM groups was significantly higher than that in the model group ($P=0.004$, $P<0.001$), and the protein expression levels of VEGFA and BCL2 in low-, medium-, and high-dose TCM groups were significantly higher than those in the model group ($P=0.003$, $P=0.002$, $P=0.001$; $P=0.029$, $P=0.007$, $P=0.001$). **Conclusion** The Yushen Yangluan decoction may exert its therapeutic effect by inhibiting apoptosis of ovarian granulosa cells through the HIF-1 α /VEGFA signaling pathway.

【 Key words 】 Diminished ovarian reserve; Yushen Yangluan decoction; Artificial intelligence; Network pharmacology; HIF-1 α /VEGFA signaling pathway

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临床报道

控制性卵巢刺激相关参数与染色体结构异常中新发染色体异常的关系分析

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【摘要】 目的 研究胚胎植入前染色体结构变异遗传学检测 (preimplantation genetic testing for structural rearrangements, PGT-SR) 周期中, 控制性卵巢刺激 (controlled ovarian stimulation, COS) 相关参数对新发染色体异常的影响。方法 采用病例对照研究, 回顾性分析天津医科大学总医院妇产科生殖中心 2023 年 1 月至 2024 年 8 月期间行 PGT-SR 助孕的 70 个周期及行胚胎植入前单基因遗传学检测 (preimplantation genetic testing for monogenic, PGT-M) 的 39 个周期的患者临床资料, 分析 COS 中促排卵方案、不同促性腺激素 (gonadotropin, Gn) 使用时间和总量、人绒毛膜促性腺激素 (human chorionic gonadotropin, hCG) 注射日雌二醇水平和孕酮水平与新发染色体异常的相关性。结果 ①PGT-SR 组的 341 个囊胚和 PGT-M 组的 196 个囊胚进行活检。PGT-SR 组的非整倍体率 [62.1% (205/330)] 和 PGT-M 组 [30.2% (58/192)] 比较, 差异有统计学意义 ($P < 0.001$)。两组的新发染色体异常率比较差异无统计学意义 ($P > 0.05$)。②校正女方年龄、男方年龄、囊胚质量后, 新发染色体异常率在不同促排卵方案之间、不同 Gn 使用时间和总量之间、hCG 注射日不同雌二醇水平和孕酮水平之间差异均无统计学意义 (均 $P > 0.05$)。③新发染色体整条异常、片段异常和复杂异常发生率在不同促排卵方案、不同 Gn 使用时间和总量、hCG 注射日不同雌二醇和孕酮水平间差异均无统计学意义 (均 $P > 0.05$)。结论 不同的促排卵方案、Gn 使用时间、Gn 使用总量、hCG 注射日雌二醇和孕酮水平不影响染色体结构异常患者的总体新发染色体异常率及新发整条、片段和复杂染色体异常率。

【关键词】 控制性卵巢刺激; 胚胎植入前染色体结构变异遗传学检测; 新发染色体异常

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Analysis of the relationship between parameters of controlled ovarian stimulation and *de novo* chromosomal abnormalities in chromosomal structural abnormalities

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【Abstract】 Objective To explore the parameters of controlled ovarian stimulation (COS) on the occurrence of *de novo* chromosomal abnormalities in preimplantation genetic testing for structural rearrangements (PGT-SR) cycles. **Methods** A retrospective analysis control study was performed on 70 PGT-SR cycles and 39 preimplantation genetic testing for monogenic (PGT-M) embryos in the Department of Obstetrics and Gynecology, Reproductive Medicine Center of Tianjin Medical University General Hospital from January 2023 to August 2024. The correlation between *de novo* chromosomal abnormalities and ovarian stimulation protocol, duration and total dosage of gonadotropin (Gn) used, estradiol and progesterone levels on human chorionic gonadotropin (hCG) trigger day in COS were analyzed. **Results** 1) Biopsies were performed on 341 blastocysts in the PGT-SR group and 196 blastocysts in the PGT-M group. There was a significant difference in aneuploid rate of blastocyst between PGT-SR and PGT-M groups [62.1% (205/330) vs. 30.2% (58/192), $P<0.001$]. There was no significant difference in the incidence of *de novo* chromosomal abnormalities, between PGT-SR and PGT-M groups ($P>0.05$). 2) After adjusting for couples' age and blastocyst grade, there were no significant differences in the incidence of *de novo* chromosomal abnormalities among different ovarian stimulation protocols, different duration and total dosage of Gn used, different estradiol and progesterone levels on hCG trigger day (all $P>0.05$). 3) There were no significant differences the incidence of *de novo* whole, fragment and complex chromosomal abnormalities among different ovarian stimulation protocols, different duration and total dosage of Gn used, different estradiol and progesterone levels on hCG trigger day (all $P>0.05$). **Conclusion** Different ovarian stimulation protocols, duration and total dosage of Gn used, estrogen and progesterone levels on hCG trigger day don't affect the whole *de novo* chromosomal abnormalities, *de novo* whole, fragment, complex chromosomal abnormalities in patients with structural chromosomal abnormalities.

【 Key words 】 Controlled ovarian stimulation; Preimplantation genetic testing for structural rearrangements; *De novo* chromosomal abnormalities

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·临床报道·

IVF/ICSI 助孕后患者流产组织染色体异常相关因素分析

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【摘要】 目的 探究体外受精/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)助孕后患者流产组织染色体异常相关影响因素, 并建立染色体异常预测模型, 为临床提供更多的治疗依据。方法 收集2022年6月至2023年8月就诊于大连市妇女儿童医疗中心(集团)生殖与遗传实验室的113例IVF/ICSI助孕后患者(106例IVF、7例ICSI)流产组织, 采用拷贝数变异测序(copy number variation sequencing, CNV-seq)技术对样本进行检测, 将结果按照孕妇年龄分为年轻孕妇(<35岁, 45例)和高龄孕妇(≥35岁, 68例)两组。采用回顾性病例对照研究, 分析不同孕妇年龄、男方年龄、不孕年限、既往流产次数、移植胚胎数、胎龄与染色体异常发生的相关性。结果 ①113例IVF/ICSI助孕后患者流产组织中共检出异常染色体72例[63.72% (72/113)], 其中数目异常61例[84.72% (61/72)], 以三体型居多(53例), 结构异常8例[11.11% (8/72)], 其他复杂异常类型3例[4.17% (3/72)]。②年轻孕妇组流产组织染色体异常率[51.11% (23/45)]小于高龄孕妇组[72.06% (49/68)], 差异有统计学意义($P=0.023$)。③高龄孕妇流产组织中, 单因素分析结果显示男方年龄及既往流产次数与染色体异常的发生有关($P=0.004$, $P=0.008$)。④多因素logistic回归分析结果表明, 男方年龄、既往流产次数是导致高龄孕妇(≥35岁)染色体异常的独立危险因素($OR=1.248$, 95% CI : 1.064~1.464, $P=0.006$; $OR=0.493$, 95% CI : 0.287~0.848,

$P=0.011$), 最终确定回归方程为 $\text{logit}(P) = 0.222 \times \text{男方年龄} - 0.707 \times \text{既往流产次数} - 6.042$, 受试者工作特征曲线下面积为 0.789, 95% CI : 0.673~0.905。约登指数最大值为 0.489。结论 孕妇年龄与流产组织染色体异常有关, 同时在年龄 ≥ 35 岁孕妇中, 以女方因素引起的流产率为固定值条件下的男方年龄增加和既往流产次数较少, 均会导致染色体异常发生率的上升。本研究建立的模型对染色体异常的预测价值较好。

【关键词】 染色体异常; 自然流产; 生殖技术, 辅助

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Analysis of factors related to chromosomal abnormalities in abortion tissue of patients after IVF/ICSI assisted conception

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【Abstract】 Objective To explore the related factors of chromosome abnormality in abortion tissue of patients after *in vitro* fertilization/intracytoplasmic sperm injection and embryo transfer (IVF/ICSI-ET) and to establish a predictive model of chromosome abnormality, so as to provide more clinical treatment basis. **Methods** This was a retrospective case-control study. The abortion tissues of 113 cases of IVF/ICSI assisted pregnancy (106 cases of IVF and 7 cases of ICSI) were collected from the Reproduction and Genetics Laboratory of Dalian Women and Children Medical Center (Group) from June 2022 to August 2023. The samples were detected by copy number variation sequencing (CNV-seq). According to the maternal age, the samples were divided into young pregnant women (<35 years old, $n=45$) group and elderly pregnant women (≥ 35 years old, $n=68$) group. The correlations between different maternal age, male age, duration of infertility, times of previous abortion, number of embryos transferred, gestational age and chromosome abnormalities were analyzed. **Results** 1) A total of 72 cases [63.72% (72/113)] of abnormal chromosomes were detected in the abortion tissues of patients with IVF/ICSI-assisted pregnancy, of which 61 cases [84.72% (61/72)] were numerically abnormal, most of them were trisomy (53 cases), structural abnormalities were found in 8 cases [11.11% (8/72)], and other complex abnormalities were found in 3 cases [4.17% (3/72)]. 2) The chromosome abnormality rate of abortion tissue in the young pregnant women [51.11% (23/45)] was lower than that in the elderly pregnant women [72.06% (49/68)], and the difference was statistically significant ($P=0.023$). 3) In the abortion tissue of elderly pregnant women, univariate analysis showed that the age of the man and times of previous abortion were related to the occurrence of chromosome abnormalities ($P=0.004$, $P=0.008$). 4) Multivariate logistic regression analysis showed that the age

of the man and times of previous abortion were the independent risk factors for chromosomal abnormalities in elderly pregnant women ($OR=1.248$, 95% CI : 1.064–1.464, $P=0.006$; $OR=0.493$, 95% CI : 0.287–0.848, $P=0.011$), the regression equation was $\text{logit}(P)=0.222\times\text{male age}-0.707\times\text{times of previous abortion}-6.042$, area under curve was 0.789, 95% CI : 0.673–0.905, and the maximum value of Jordan index was 0.489. **Conclusion** The age of pregnant women was correlated with the occurrence of chromosomal abnormalities in abortion tissues. At the same time, in pregnant women aged 35 years or above, under the condition of fixed abortion rates caused by female factors, an increase in male age and a decrease in previous abortions will lead to an increase in the incidence of chromosomal abnormalities. The model is of good value in predicting chromosome abnormalities.

【 Key words 】 Chromosomal abnormalities; Spontaneous abortion; Reproductive technology, assisted

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·临床报道·

不明原因反复妊娠失败患者的免疫学指标分析

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【摘要】 目的 分析不明原因反复妊娠失败患者的免疫学指标, 探讨其是否与妊娠失败有相关性。方法 采用回顾性研究, 分析了 2022 年 1 月至 2022 年 6 月期间因反复妊娠失败 (包含复发性自然流产及反复种植失败) 于青岛大学附属医院风湿免疫科就诊的 91 例患者, 采用病例对照研究, 从抗核抗体 (antinuclear antibody, ANA) 是否阳性及自然杀伤 (natural killer, NK) 细胞是否升高 2 种不同的角度进行分析, 其中 ANA 阳性组 34 例, ANA 阴性组 57 例; NK 细胞正常组 32 例, NK 细胞升高组 59 例。收集患者的临床资料、不孕持续时间、流产次数、生化妊娠次数、反复种植失败次数等信息, 收集免疫学指标包括 ANA、抗可提取核抗原抗体谱、抗磷脂抗体、外周血淋巴细胞亚群、补体、免疫球蛋白、风湿四项等, 常规化验包含血常规、尿常规、肝肾功能等, 对结果进行统计分析。结果 ANA 阳

性组和阴性组患者在自然胚胎停育次数、移植后胚胎停育次数、妊娠失败总次数、既往合并妇科及慢性疾病等方面差异均无统计学意义 (均 $P>0.05$)。ANA 阳性组移植后不着床次数为 (3.20 ± 2.04) 次, 明显高于 ANA 阴性组 $[(1.47\pm0.96)$ 次, $P=0.004$] ; ANA 阴性组的 CD19⁺B 细胞比例 $[(12.96\pm4.26)\%]$ 及 CD3⁺HLA-DR⁺活化 B/NK 细胞比例 $[(14.58\pm5.45)\%]$ 均显著高于 ANA 阳性组 $[(10.23\pm3.54)\%, P=0.007; (11.34\pm4.11)\%, P=0.009]$ 。NK 细胞正常组与 NK 细胞升高组在自然胚胎停育次数、移植后胚胎停育次数、妊娠失败总次数等方面差异均无统计学意义 (均 $P>0.05$)。结论 ANA 阳性患者的反复种植失败次数明显升高, 外周血 NK 细胞与妊娠失败的关系尚不明确。

【关键词】 复发性流产; 反复种植失败; 抗核抗体; 淋巴细胞亚群; 自然杀伤细胞

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Analysis of immunological indicators in patients with unexplained recurrent pregnancy failure

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【 Abstract 】 **Objective** To classify and analyze the immunological indicators of patients with unexplained recurrent pregnancy failure, and explore whether the immunological indicators of these patients were related to pregnancy failure. **Methods** We retrospectively studied 91 patients who visited the Rheumatology and Immunology Department of the Affiliated Hospital of Qingdao University from January 2022 to June 2022 due to recurrent pregnancy failures, including recurrent spontaneous abortion and recurrent implantation failures (RIF). We adopted case-control study method. Analysis was conducted from two different perspectives: antinuclear antibody (ANA) positivity and natural killer (NK) cell elevation. Among them, there were 34 ANA positive patients and 57 ANA negative patients; 32 patients had normal NK cells and 59 had elevated NK cell. Clinical data, duration of infertility, number of miscarriages, number of biochemical pregnancies, number of recurrent implant failures, and other information from patients were collected. Immunological indicators included ANA, anti-extractable nuclear antigen antibody, antiphospholipid antibodies, peripheral blood lymphocyte subsets, complement, immunoglobulin, rheumatism, etc. Routine laboratory tests included blood routine, urine routine, liver and kidney function, etc. The results were statistically analyzed. **Results** There were no statistically significant differences between the ANA-positive and negative groups in terms of the number of spontaneous abortion, the number of post-transplantation abortions, the total number of pregnancy failures, and previous gynecological and chronic diseases (all $P>0.05$). The number of no-implanting after transplantation in the ANA-positive group was 3.20 ± 2.04 , which was significantly higher than that in the ANA-negative group $(1.47\pm0.96, P=0.004)$. The proportion of CD19⁺B cells $[(12.96\pm4.26)\%]$ and CD3⁺HLA-DR⁺ activated B/NK cells $[(14.58\pm5.45)\%]$ in the

ANA negative group were significantly higher than those in the ANA positive group [(10.23±3.54)%, $P=0.007$; (11.34±4.11)%, $P=0.009$]. There were no significant differences in the number of spontaneous abortion, the number of fetal abortion after transplantation and the total number of pregnancy failure between the normal NK cell group and the increased NK cell group (all $P>0.05$). **Conclusion** The number of RIF in ANA positive patients is significantly increased. The relationship between NK cells and pregnancy failure is not clear yet.

【 Key words 】 Recurrent miscarriage; Repeated implantation failure; Antinuclear antibodies; Lymphocyte subsets; Natural killer cells

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·现场调查·

我国胚胎植入前遗传学诊断技术配置和服务利用分析

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【摘要】 目的 分析我国胚胎植入前遗传学诊断 (preimplantation genetic diagnosis, PGD) 技术配置特征、服务利用趋势及服务效果。方法 本研究采用纵向研究及 2020 年横断面调查数据分析的方法, 研究 2004—2020 年我国具备 PGD 机构配置数量和服务利用趋势。从不同地域分布、城市定位、机构类别等描述 2020 年技术配置特征和服务效果。应用 PGD 治疗夫妇对数、取卵周期数和诊断周期数初步评价服务规模及特点。结果 2004—2020 年, PGD 机构配置数量从 2004 年仅 4 家 (10.8%) 增至 2020 年的 78 家 (19.0%)。PGD 服务周期数量虽伴随增长, 但总体占比不高, 在 0.3%~4.1% 之间。2020 年报告 PGD 诊断周期总数 21 241 个, 占取卵周期总数的 4.1%。2020 年 PGD 技术配置表现出以省会城市 [82.1% (64/78)]、

公立医院 [94.9% (74/78)]、综合医院 [59.0% (46/78)] 为主的特征。东、中、西部地区机构 PGD 取卵周期数中位数差异显著, 分别为 203.0、177.5 和 79.0。2020 年 PGD 随访临床妊娠率为 60.2% (10 326/17 158), 分娩率为 51.1% (8 767/17 158), 多胎分娩率为 1.9% (163/8 767), 活产婴儿数 8 904。结论 PGD 技术在我国经过 20 余年的快速发展, 地理可及性显著改善。PGD 服务规模较小, 且存在不均衡性。技术配置以东、中部地区省会城市的综合医院为主要特点, 地市级机构和西部地区机构也成为 PGD 技术的重要提供方。

【关键词】 植入前胚胎遗传学诊断; 技术配置; 服务利用
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Configuration and service utilization analysis of preimplantation genetic diagnosis in China

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【Abstract】 **Objective** To analyze the configuration characteristics, service utilization trend and outcome of preimplantation genetic diagnosis (PGD) in China. **Methods** A longitudinal study and a cross-sectional survey in 2020 were used to analyze the number of PGD facilities and the trend of service utilization in China from 2004 to 2020. The characteristics of 2020 technology configuration were described from different geographical distribution, city positioning, and organization categories. The number of couples treated, the number of egg retrieval cycles and the number of diagnostic cycles were used to evaluate the scale of the service. **Results** From 2004 to 2020, the number of PGD institutions increased from only 4 (10.8%) in 2004 to 78 (19.0%) in 2020. Although the number of PGD cycles increased with it, the overall proportion was not high, ranging from 0.3% to 4.1%. A total of 21 241 PGD cycles were reported in 2020, accounting for 4.1% of the total number of egg retrievals. The PGD technology configuration in 2020 was mainly characterized by provincial capitals [82.1% (64/78)], public hospitals [94.9% (74/78)], and comprehensive hospitals [59.0% (46/78)]. There were significant differences in the median of the number of PGD egg retrieval cycles in eastern, central and western institutions, which were 203.0, 177.5 and 79.0, respectively. In 2020, the PGD clinical pregnancy rate was 60.2% (10 326/17 158), the delivery rate was 51.1% (8 767/17 158), the multiple delivery rate was 1.9% (163/8 767), totally with 8 904 live births. **Conclusion** After more than 20 years of rapid development of PGD technology in China, the geographical accessibility has been significantly improved. PGD services are small and uneven. Comprehensive hospitals in the capital cities of the eastern and central regions are the main features of the technical configuration, and prefecture-level institutions and institutions in the western regions have also become important providers of PGD technology.

【Key words】 Preimplantation genetic diagnosis; Technology configuration; Service utilization

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循证医学

维生素D改善男性不育患者精液质量的有效性 评估: 系统评价和meta分析

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黄臻伟和张静茹对本文有同等贡献

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【摘要】 目的 系统评价维生素D (vitamin D, VD) 治疗男性不育的有效性。方法 从PubMed、Embase、Web of science、中国知网、万方及维普数据库中鉴定和收集关于VD单用或联合用药治疗男性不育的随机对照试验 (randomized controlled trial, RCT), 患者分为试验组 (给予VD或以VD为主的联合用药治疗) 和对照组 (给予安慰剂治疗)。利用RevMan5.4软件对最终纳入的研究进行meta分析。计算合并效应尺度以加权均数差 (mean difference, MD) 及其95% CI表示。结果 最终纳入6项RCT, 共计673例患者, 研究基线具有可比性。精子总活力 (MD=6.49, 95% CI: 2.75~10.22, $P<0.001$) 和前向运动精子百分率 (MD=5.03, 95% CI: 1.36~8.70, $P=0.007$) 在试验组与对照组之间差异均有统计学意义, 而精子总数 (MD=5.56, 95% CI: 12.62~23.75, $P=0.550$)、精子浓度 (MD=-0.30, 95% CI: -4.81~4.21, $P=0.890$)、精液体积 (MD=-0.04; 95% CI: -0.18~0.09, $P=0.510$) 和精子正常形态 (MD=0.42; 95% CI: -0.05~0.88, $P=0.080$) 在试验组

与对照组间差异均无统计学意义。结论 VD 在改善不育男性的精液质量方面有一定的疗效。但由于纳入 RCT 的样本数量有限, 仍需更大样本的临床试验方案进一步证实这一论点。

【关键词】 维生素 D; 不育, 男性; 随机对照试验; Meta 分析

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Efficacy of vitamin D in treating semen quality in patients with male infertility: a systematic review and meta-analysis

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【Abstract】 Objective To systematically evaluate the efficacy of vitamin D (VD) in the treatment of male infertility. **Methods** Randomized controlled trials (RCT) on male infertility treated with VD alone or in combination were identified and collected from PubMed, Embase, Web of science, CNKI, Wanfang and VIP databases. Patients were divided into experimental group (VD or combination therapy with VD as the main treatment) and control group (placebo treatment). A meta-analysis of the included studies was performed using RevMan5.4 software. The combined effect scale was calculated as the weighted mean difference (MD) and its 95% CI. **Results** Six RCTs with a total of 673 patients were ultimately included, and the study baseline was comparable. Total sperm motility (MD=6.49, 95% CI: 2.75-10.22, $P<0.001$) and percentage of forward motile sperm (MD=5.03, 95% CI: 1.36-8.70, $P=0.007$) were significantly different between the experimental group and control group. Total sperm count (MD=5.56, 95% CI: -12.62-23.75, $P=0.550$), sperm concentration (MD=-0.30, 95% CI: -4.81-4.21, $P=0.890$), semen volume (MD=-0.04, 95% CI: -0.18-0.09, $P=0.510$) and normal sperm morphology (MD=0.42, 95% CI: -0.05-0.88, $P=0.080$) were not significantly different between the experimental group and control group. **Conclusion** VD is effective in improving semen quality in the treatment of male infertility. However, due to the limited number of samples included in RCT, clinical trials with larger samples are still needed to further confirm this thesis.

【Key words】 Vitamin D; Infertility, male; Randomized controlled trials; Meta-analysis

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综述

铜稳态及铜死亡与多囊卵巢综合征发病关系的研究进展

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【摘要】 环境铜暴露问题日益显现, 近十余年学术界聚焦铜与人类疾病发病关系的研究以及铜复合物在疾病诊疗方面的应用研究。多囊卵巢综合征 (polycystic ovary syndrome, PCOS) 是一种多因素多基因导致的生殖内分泌代谢紊乱疾病, 许多研究报道了 PCOS 患者机体铜离子发生了显著变化。故本文对铜稳态及铜死亡与 PCOS 中的胰岛素抵抗、卵巢颗粒细胞功能障碍、卵泡发育异常、氧化应激/线粒体功能障碍之间的关系进行综述。

【关键词】 多囊卵巢综合征; 铜; 铜稳态; 铜诱导的细胞死亡; 微量元素

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Research progress on copper homeostasis and copper-induced cell death in the pathogenesis of polycystic ovary syndrome

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【Abstract】 The problem of environmental copper exposure has become increasingly apparent. In the past ten years, academic circles have focused on the research on the relationship between copper and human diseases and the application of copper compounds in disease diagnosis and treatment. Polycystic ovary syndrome (PCOS) is a disorder of reproductive endocrine metabolism caused by multiple factors and multiple genes. Many studies have reported significant

changes in copper ions in PCOS patients. In this paper, the relationship between copper homeostasis and copper-induced death and insulin resistance, ovarian granulosa cell dysfunction, follicular dysplasia, oxidative stress/mitochondrial dysfunction in PCOS was reviewed.

【Key words】 Polycystic ovary syndrome; Copper; Copper homeostasis; Copper-induced cell death; Trace element

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综述

HSP70 在早期胚胎发育中作用的研究进展

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【摘要】 热休克蛋白 (heat shock proteins, HSPs) 是一组高度保守且功能多样的分子伴侣蛋白, 对维持细胞稳态和应对多种应激反应起着至关重要的作用。HSP70 是 HSPs 家族的重要成员之一, 参与蛋白质的正确折叠、防止聚集, 并在早期胚胎发育中对生殖细胞的形成、DNA 损伤修复、受精过程以及胚胎植入等方面发挥关键作用。HSP70 通过促进受精卵的正常发育和细胞稳态, 维护胚胎健康发育并在各种应激条件下保护细胞免受伤害。通过深入研究 HSP70 的复杂功能和潜在机制, 有望揭示其在原因不明性不孕症、反复着床失败以及复发性流产等疾病中的作用。

【关键词】 热休克蛋白 70; 受精卵; 胚胎植入; 早期胚胎发育

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Research progress on the role of HSP70 in early embryonic development

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【Abstract】 Heat shock proteins (HSPs) are a group of highly conserved and functionally diverse molecular chaperones that play a crucial role in maintaining cellular homeostasis and coping with a variety of stress responses. HSP70 is one of the important members of the HSPs family, which is involved in the correct folding of proteins, preventing aggregation, and plays a key role in the formation of germ cells, DNA damage repair, fertilization process and embryo implantation in early embryonic development. HSP70 maintains the healthy development of embryos and protects cells from injury under various stress conditions by promoting the normal development and cellular homeostasis of fertilized eggs after fertilization. Through in-depth study of the complex functions and potential mechanisms of HSP70, it is expected to reveal its role in unexplained infertility, recurrent implantation failure, recurrent abortion and other diseases.

【Key words】 Heat shock protein 70; Zygote; Embryo implantation; Early embryonic development

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综述

线粒体自噬影响卵巢储备功能减退女性卵母细胞发育的研究进展

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【摘要】 卵巢储备功能减退 (diminished ovarian reserve, DOR) 是女性常见的生殖内分泌疾病,是导致女性生育力下降的重要影响因素。DOR 女性卵母细胞的数量和质量随年龄增长逐渐下降,从而导致女性出现生育力的减退,其中线粒体功能障碍是造成卵母细胞质量下降的重要诱因。近年来,研究表明线粒体自噬作为细胞内重要的自我修复和代谢平衡机制,与卵母细胞发育密切相关。本文围绕线粒体 DNA 拷贝数及突变、ATP 含量、线粒体活性氧含量、线粒体膜电位变化对线粒体自噬的调控,进而对卵母细胞发育产生的影响及药物对卵母细胞线粒体自噬产生的调节作用展开综述。

【关键词】 线粒体自噬; 卵巢储备功能减退; 卵母细胞

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Research progress on the effects of mitophagy on oocyte development in women with diminished ovarian reserve

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【Abstract】 Diminished ovarian reserve (DOR) is a common reproductive endocrine disease in women, which is an important factor leading to the decline of female fertility. The number and quality of oocytes in DOR women gradually decrease with age, which leads to the decline of fertility in women. Mitochondrial dysfunction is an important cause of oocyte quality decline. In recent years, studies have found that mitophagy, as an important mechanism of self-repair and metabolic balance in cells, is closely related to oocyte development. This article focuses on the regulation of mitochondrial DNA copy number and mutation, ATP content, mitochondrial reactive oxygen species content, mitochondrial membrane potential changes on mitophagy, and the effects on oocyte development and the regulation of drugs on oocyte mitophagy.

【Key words】 Mitophagy; Diminished ovarian reserve; Oocyte

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综述

DNA 甲基化调控在早发性卵巢功能不全发生、发展中的研究进展

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【摘要】 早发性卵巢功能不全 (premature ovarian insufficiency, POI) 是一种严重影响育龄期女性的生殖障碍性疾病, 其发生、发展机制尚不完全清楚。近年来, 随着表观遗传学领域的深入研究, DNA 甲基化逐渐成为 POI 病理生理机制的新视角。研究表明, DNA 甲基化修饰调控与 POI 密切相关, DNA 甲基化异常及其引起的基因表达失调可能会影响卵泡的发育过程, 最终导致 POI 的发生、发展。本文综述 DNA 甲基化调控在 POI 发生、发展中的研究进展, 以期为 POI 的临床诊疗提供新思路。

【关键词】 DNA 甲基化; 表观遗传; 早发性卵巢功能不全

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Research progress on the regulation of DNA methylation in the occurrence and development of POI

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【 Abstract 】 Premature ovarian insufficiency (POI) is a reproductive disorder which seriously affects women of childbearing age, and the mechanisms of its development are not fully understood. In recent years, with the intensive research in the field of epigenetics, DNA methylation has gradually become a new perspective on the pathophysiological mechanisms of POI. Studies have shown that the regulation of DNA methylation modification is closely related to POI. Both DNA methylation abnormalities and the dysregulation of gene expression may affect the follicular development process, ultimately leading to the development of POI. This article reviews the research progress of DNA methylation regulation in the development of POI, with a view to providing new ideas for the clinical diagnosis and treatment of POI.

【 Key words 】 DNA methylation; Epigenetic; Premature ovarian insufficiency

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综述

颗粒细胞程序性死亡在卵巢衰老中的研究进展

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【摘要】 卵巢衰老是育龄女性最常见的生殖内分泌疾病之一, 发病率逐年上升。其特征为卵巢功能包括卵泡数量和/或质量下降或耗竭, 根据卵巢功能下降程度, 可分为卵巢储备功能下降、早发性卵巢功能不全、卵巢早衰等疾病, 临床表现为排卵障碍、生殖内分泌激素紊乱, 并最终导致女性生育力下降。其发病机制复杂多样, 迄今为止具体机制尚不清楚。颗粒细胞功能在卵巢激素合成、卵泡发育等过程中作用关键, 目前多项研究表明诸多颗粒细胞程序性死亡方式(凋亡、焦亡、自噬、铁死亡、铜死亡等)均可能与卵巢衰老的发生发展密切相关。本文对上述相关文献进行系统综述, 旨在探讨颗粒细胞程序性死亡与卵巢衰老的关系。

【关键词】 卵巢衰老; 颗粒细胞; 细胞程序性死亡; 卵巢储备功能下降

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Progress of programmed death of granulosa cells in ovarian aging

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【 Abstract 】 Ovarian aging is one of the most common reproductive endocrine disorders in women of reproductive age, with an increasing incidence over the years. It is characterized by a decline or depletion of ovarian function, including follicle quantity and/or quality. Depending on the degree of ovarian function decline, it can be classified into diseases including diminished ovarian reserve, premature ovarian insufficiency, premature ovarian failure, etc., which are clinically characterized by ovulatory dysfunction, reproductive endocrine hormone disruption, and ultimately lead to a decline in female fertility. The pathogenesis is complex and varied, and the exact mechanism is unknown to date. Granulosa cells play a key role in ovarian hormone synthesis and disruption development, and many studies have shown that the programmed death of granulosa cells (apoptosis, pyroptosis, autophagy, ferroptosis, cuproptosis, etc.) may be closely related to the occurrence and development of ovarian aging. In this article, we present a systematic review of the relevant literature with the aim of exploring the relationship between programmed cell death in granulosa cells and ovarian aging.

【 Key words 】 Ovarian aging; Granulosa cell; Programmed cell death; Diminished ovarian reserve

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