

中华生殖与避孕杂志[®]

原刊名《生殖与避孕》

CHINESE JOURNAL OF REPRODUCTION AND CONTRACEPTION

月刊 1980年12月创刊 第42卷 第1期 2022年1月25日出版



主 管

中国科学技术协会

主 办

中华医学会
上海市生物医药技术研究院
复旦大学附属妇产科医院

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《中华医学杂志》社有限责任公司
100710,北京市东四西大街42号
电话(传真):(010)51322059
Email:office@cmaph.org

广告发布登记号

京东市监广登字20200006号

印 刷

上海船舶设备研究所

发 行

范围:公开
国内:中国邮政集团公司
上海分公司
国外:中国国际图书贸易集团
责任有限公司
(北京399信箱,100044)
代号 BM 389

订 购

全国各地邮政局
邮发代号4-928

邮 购

中华生殖与避孕杂志编辑部
200237,上海市老沪闵路779号
电话:(021)64438169,64438975
Email:rande@sibpt.com

定 价

每期35.00元,全年420.00元

中国标准连续出版物号

ISSN 2096-2916

CN 10-1441/R

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本期责任编辑 乔杰 本期责任编辑 宋培培 本期责任编辑 年丽红	

CHINESE JOURNAL OF REPRODUCTION AND CONTRACEPTION

(Original title: *Reproduction and Contraception*)

Monthly

Established in December 1980

Volume 42, Number 1

January 25, 2022



Responsible Institution

China Association for Science and Technology

Sponsor

Chinese Medical Association,
Shanghai Institute for Biomedical and Pharmaceutical Technologies,
Obstetrics and Gynecology Hospital of Fudan University

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Editorial Board of Chinese Journal of Reproduction and Contraception
779 Laohumin Road, Shanghai 200237, China
Tel: 0086-21-64438169
Fax: 0086-21-64438975
Email: rande@sibpt.com
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Publishing

Chinese Medical Journals Publishing House Co., Ltd.
42 Dongsi Xidajie, Beijing 100710, China
Tel(Fax): 0086-10-51322059
Email: office@cmaph.org

Printing

Shanghai Marine Equipment Research Institute

Overseas Distributor

China International Book Trading Corporation
P.O. Box 399, Beijing 100044, China
Code No.M389

Mail-Order

Editorial Board of Chinese Journal of Reproduction and Contraception
779 Laohumin Road, Shanghai 200237, China
Tel: 0086-21-64438169
Fax: 0086-21-64438975
Email: rande@sibpt.com

CSSN

ISSN 2096-2916
CN 10-1441/R

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All articles published represent the opinions of the authors, and do not reflect the official policy of the Chinese Medical Association or the Editorial Board, unless this is clearly specified.

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DOI: 10.3760/cma.j.cn101441-20211227-00573

收稿日期 2021-12-27 责任编辑 宋培培

引用本文: 乔杰. 母婴疾病防治领域的新兴医学科技进展[J]. 中华生殖与避孕杂志, 2022, 42(1): 1-8. DOI: 10.3760/cma.j.cn101441-20211227-00573.

· 特约专论 ·

母婴疾病防治领域的新兴医学科技进展

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【摘要】 提高妇幼健康水平作为建设健康中国的重要任务之一, 需要加强和推动医药健康科技创新, 为保障和改善妇幼健康提供有力的科技支撑。因此, 本文对基因诊断与基因治疗技术、多组学技术、干细胞技术、组织工程技术等前沿生物技术以及机器人技术、大数据与人工智能技术在母婴健康医学科技领域的发展现状和未来趋势作一概述, 对新兴技术在母婴疾病防治中面临的伦理挑战进行了分析, 并提出了母婴疾病防治的重点发展方向, 以期从事母婴疾病防治领域科技创新和技术服务的专业人员提供参考。

【关键词】 母婴疾病; 新兴医学科技; 伦理

基金项目: 北京市科学技术委员会 (Z191100006619073); 中国工程院咨询研究项目 (2020-XZ-22)

Advances in emerging medical technologies in the field of prevention and treatment of maternal and infant diseases

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【Abstract】 As one of the important tasks of building the Healthy China, improving maternal and child health needs to strengthen and promote medical and health scientific and technological innovations, so as to provide strong scientific and technological support for ensuring and improving maternal and child health. Therefore, this paper summarizes the development status and future trend of cutting-edge biotechnology such as gene diagnosis and gene therapy, multiomics technology, stem cell technology and tissue engineering technology, as well as robot technology, big data and artificial intelligence technology in the field of maternal and

infant health medical science and technology, and analyzes the ethical challenges faced by emerging technologies in the prevention and treatment of maternal and infant diseases. It also puts forward the key development direction of maternal and infant disease prevention and control, in order to provide reference for professionals engaged in scientific and technological innovation and technical services in the field of maternal and infant disease prevention and control.

【Key words】 Maternal and infant diseases; Emerging medical technologies; Ethic

Fund program: Beijing Municipal Science & Technology Commission (Z191100006619073); Chinese Academy of Engineering (2020-XZ-22)

·临床研究·

DOI: 10.3760/cmaj.cn101441-20200519-00291

收稿日期 2020-05-25 责任编辑 宋培培

引用本文: 张少娣, 尹轶莎, 李秋圆, 等. 以每取卵周期累积活产率评价拮抗剂方案与 PPOS 方案在波塞冬标准低预后患者的临床效果: 一项回顾性队列研究[J]. 中华生殖与避孕杂志, 2022, 42(1): 9-16. DOI: 10.3760/cmaj.cn101441-20200519-00291.

以每取卵周期累积活产率评价拮抗剂方案与 PPOS 方案在波塞冬标准低预后患者的临床效果: 一项回顾性队列研究

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【摘要】 目的 以评价拮抗剂方案和高孕激素状态下促排卵 (progestin-primed ovarian stimulation, PPOS) 方案在低预后患者中的临床效果。方法 回顾性队列研究分析 2016 年 1 月至 2018 年 12 月期间在河南省人民医院生殖医学中心接受体外受精/卵胞质内单精子注射-胚胎移植 (*in vitro* fertilization/intracytoplasmic sperm injection-embryo transfer, IVF/ICSI-ET) 助孕, 符合波塞冬低预后诊断标准并采用拮抗剂方案或 PPOS 方案治疗的不孕症患者

1419 名, 共 1560 个取卵周期。比较拮抗剂方案组和 PPOS 方案组患者基线特征、临床指标、实验室指标及临床结局。通过多因素 logistic 回归分析调整混杂因素后分析两种促排卵方案的每取卵周期累积活产率。结果 一般情况比较显示, 拮抗剂方案组中患者抗苗勒管激素 (anti-Müllerian hormone, AMH) 和窦卵泡计数 (antral follicle count, AFC) 显著高于 PPOS 方案组 [1.45 (0.68, 3.28) $\mu\text{g/L}$ 比 1.10 (0.55, 2.71) $\mu\text{g/L}$, $P=0.002$; 7.00 (4.00, 11.00) $\mu\text{g/L}$ 比 6.00 (3.00, 9.00) $\mu\text{g/L}$, $P=0.010$], 基础卵泡刺激素 (follicle-stimulating hormone, FSH) 显著低于 PPOS 方案组患者 [7.65 (6.26, 9.99) U/L 比 7.88 (6.29, 10.58) U/L, $P=0.007$]。实验室结局及临床结局指标显示, 拮抗剂方案组人绒毛膜促性腺激素 (human chorionic hormone, hCG) 注射日雌二醇水平 [726.20 (415.30, 1095.00) ng/L] 显著低于 PPOS 方案组 [738.00 (412.55, 1187.75) ng/L, $P=0.028$], hCG 注射日子宫内膜厚度 [(9.31 \pm 2.67) mm]、每取卵周期累积妊娠率 [49.35% (379/768)] 及每取卵周期累积活产率 [38.04% (291/765)] 显著高于 PPOS 方案组 [(6.81 \pm 2.26) mm, $P<0.001$; 37.62% (298/792), $P<0.001$; 26.08% (206/790), $P<0.001$], 差异均有统计学意义。调整混杂因素后, 在波塞冬标准低预后患者中拮抗剂方案组的每取卵周期累积妊娠率 ($OR=1.58$, 95% $CI=1.24\sim 2.01$, $P<0.001$) 及每取卵周期累积活产率 ($OR=1.68$, 95% $CI=1.30\sim 2.17$, $P<0.001$) 均显著高于 PPOS 方案组; 分层分析结果显示, 在不同变量分层中, 拮抗剂方案的每取卵周期累积妊娠率及每取卵周期累积活产率均高于 PPOS 方案组。每取卵周期累积妊娠率及每取卵周期累积活产率在女方年龄 ($P<0.001$, $P<0.001$)、授精方式 ($P<0.001$, $P<0.001$)、AMH 分层 ($P<0.001$, $P<0.001$) 中以及波塞冬组 1 ($P=0.001$, $P<0.001$) 及组 3 分层 ($P=0.008$, $P=0.024$) 中, 差异均有统计学意义。结论 与 PPOS 方案相比, 拮抗剂方案可改善波塞冬低预后患者的每取卵周期累积活产率, 且在波塞冬组 1 及波塞冬组 3 患者中更为显著。

【关键词】 受精, 体外; 胚胎移植; 累积活产率; 波塞冬标准

基金项目: 国家重点研发计划 (2018YFC1002106)

Evaluation of the clinical effects of antagonist protocol and progestin-primed ovarian stimulation protocol in patients with low prognosis according to POSEIDON criteria by cumulative live birth rate per oocyte extraction cycle: a retrospective cohort study

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【Abstract】 **Objective** To evaluate the clinical effects of antagonist protocol and progestin-primed ovarian stimulation (PPOS) protocol in patients with low prognosis. **Methods** A total of 1560 controlled ovarian stimulation cycles of 1419 patients consistent with POSEIDON low prognosis with antagonist protocol or PPOS protocol in the treatment of *in vitro* fertilization/intracytoplasmic sperm injection-embryo transfer (IVF/ICSI-ET) from January 2016 to December 2018 in the Reproductive Medicine Center of Henan Provincial People's Hospital were collected in a retrospective cohort study. The essential characteristic, clinical

characteristics, laboratory index and clinical outcomes of patients in the antagonist protocol group and the PPOS protocol group were compared. Multivariate logistic regression analysis was used to compare cumulative live rate per ovulation cycle after adjusting for confounders of the two controlled ovarian stimulation protocols.

Results The comparison of the general conditions of the patients with the two controlled ovarian stimulation protocols showed that anti-Müllerian hormone (AMH) [1.45(0.68, 3.28) $\mu\text{g/L}$] and antral follicle count (AFC) [7.00(4.00,11.00) $\mu\text{g/L}$] in the antagonist protocol group were significantly higher than those in the PPOS protocol group [1.10(0.55, 2.71) $\mu\text{g/L}$, $P=0.002$; 6.00(3.00, 9.00) $\mu\text{g/L}$, $P=0.010$], and basal follicle-stimulating hormone (FSH) [7.65(6.26, 9.99) U/L] was significantly lower than that in the PPOS protocol group [7.88(6.29, 10.58) U/L, $P=0.007$]. The results of laboratory and clinical outcomes showed that the estrogen level [726.20(415.30,1 095.00) ng/L] on human chorionic hormone (hCG) injection day in the antagonist protocol group was significantly lower than that in the PPOS protocol group [738.00(412.55, 1 187.75) ng/L, $P=0.028$], and the endometrial thickness [(9.31 \pm 2.67) mm] on hCG injection day, the cumulative pregnancy rate [49.35% (379/768)] and the cumulative live birth rate per ovulation cycle [38.04% (291/765)] were significantly higher than those in the PPOS protocol group [(6.81 \pm 2.26) mm, $P<0.001$; 37.62% (298/792), $P<0.001$; 26.08% (206/790), $P<0.001$]. After adjusting for confounder factors, the cumulative pregnancy rate ($OR=1.58$, 95% $CI=1.24-2.01$, $P<0.001$) and the cumulative live birth rate ($OR=1.68$, 95% $CI=1.30-2.17$, $P<0.001$) per ovulation cycle in the antagonist protocol group were higher than those in the PPOS protocol group in patients with POSEIDON low prognosis. The results of stratified analysis showed that the cumulative pregnancy rate and the cumulative live birth rate per ovulation cycle of antagonist protocol group per ovulation cycle was higher than that of PPOS protocol group. The cumulative pregnancy rate and the cumulative live birth rate per ovulation cycle in different age ($P<0.001$, $P<0.001$), insemination method ($P<0.001$, $P<0.001$), AMH ($P<0.001$, $P<0.001$) and POSEIDON group 1 ($P=0.001$, $P<0.001$) and POSEIDON group 3 ($P=0.008$, $P=0.024$) were statistically different. **Conclusion** In patients with low prognosis of POSEIDON, the antagonist protocol improved the cumulative live birth rate per ovulation cycle compared with the PPOS protocol, especially for patients in POSEIDON group 1 and POSEIDON group 3.

【Key words】 Fertilization *in vitro*; Embryo transfer; Cumulative live birth rate; POSEIDON standard

Fund program: National Key Research and Development Program (2018YFC1002106)

·临床研究·

DOI: 10.3760/cmaj.cn101441-20200526-00313

收稿日期 2020-05-29 本文编辑 宋培培

引用本文：郑叶, 杜彦博, 王慧丹, 等. 不同黄体支持方案在激素替代周期冻胚移植中的临床疗效及成本分析[J]. 中华生殖与避孕杂志, 2022, 42(1): 17-23. DOI: 10.3760/cma.j.cn101441-20200526-00313.

不同黄体支持方案在激素替代周期冻胚移植中的临床疗效及成本分析

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【摘要】 目的 探究不同黄体支持方案对激素替代周期冻融胚胎移植 (hormone replacement therapy for frozen-thawed embryo transfer, HRT-FET) 妊娠结局的影响及成本差异, 寻找具有低成本-效果比的高性价比的黄体支持方案。方法 采用回顾性队列研究, 选取 2017 年 10 月至 2019 年 4 月期间在山东大学附属生殖医院行 HRT-FET 患者, 共 1009 个周期, 按照移植后不同黄体支持方案分为口服黄体酮胶囊组 (A 组, 504 个周期) 和黄体酮阴道缓释凝胶+地屈孕酮组 (B 组, 505 个周期), 比较两种黄体支持方案患者的妊娠结局、成本-效果比。结果 两组临床妊娠率、胚胎种植率、多胎妊娠率、异位妊娠率、早期流产率、晚期流产率、早产率、活产率、妊娠期并发症发生率、新生儿缺陷率、新生儿出生体质量, 差异均无统计学意义 (均 $P>0.05$); A 组的早期出血率明显低于 B 组 [6.0% (30/504) 比 10.3% (52/505), $P=0.015$]; A 组成本-效果比明显优于 B 组 (17.76 比 77.30)。结论 在 HRT-FET 周期中, 口服黄体酮胶囊在取得和黄体酮阴道缓释凝胶联合地屈孕酮相同的妊娠结局的同时, 可以减少患者阴道出血, 降低了患者的医疗成本, 因此临床上可以作为一种黄体支持方案。

【关键词】 黄体支持; 成本-效果分析; 冻融胚胎移植; 激素替代; 妊娠结局

基金项目: 国家重点研发计划 (2017YFC1703600、2017YFC1703606)

Clinical efficacy and cost-effectiveness analysis in patients with hormone replacement for frozen-thawed embryo transfer under different luteal support scheme

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【Abstract】 Objective To evaluate the differences in pregnancy outcomes of patients and cost variance with hormone replacement therapy for frozen-thawed embryo transfer (HRT-FET) under different luteal support scheme. **Methods** A

retrospective cohort study was performed. A total of 1009 cycles of HRT-FET from October 2017 to April 2019 were collected and the patients were recruited from Reproductive Hospital Affiliated to Shandong University. According to different luteal support protocol, patients in group A ($n=504$) were treated with oral progesterone capsule while patients in group B ($n=505$) were treated with progesterone vaginal sustained release gel and dydrogesterone. The pregnancy outcomes, pregnancy complications and cost-effectiveness ratio were compared between the two groups. **Results** There were no significant differences in embryo implantation rate, clinical pregnancy rate, multiple pregnancy rate, ectopic pregnancy rate, early and late abortion rate, premature birth rate, live birth rate, incidence of pregnancy complications and birth defect rate between the two groups (all $P>0.05$). But the incidence of vaginal bleeding in group B was significantly higher than that in group A [6.0% (30/504) vs. 10.3% (52/505), $P=0.015$], cost-effectiveness ratio (C/E) in group A was better than that in group B (17.76 vs. 77.30). **Conclusion** For patients undergoing HRT-FET cycles, oral progesterone capsule can reduce vaginal bleeding and medical cost, while achieving a pregnancy outcome similar to that of progesterone vaginal sustained release gel and dydrogesterone, so it can be used as a luteal support scheme in clinic.

【Key words】 Luteal support; Cost-effectiveness analysis; Frozen-thawed embryo transfer; Hormone replacement; Pregnancy outcomes

Fund program: National Key R&D Program of China (2017YFC1703600, 2017YFC1703606)

·临床研究·

DOI: 10.3760/cmaj.cn101441-20200523-00303

收稿日期 2020-05-26 本文编辑 宋培培

引用本文: 张俊韦, 杜明泽, 管一春, 等. 薄型子宫内膜是新鲜胚胎移植单胎子代低出生体质量的危险因素[J]. 中华生殖与避孕杂志, 2022, 42(1): 24-29. DOI: 10.3760/cmaj.cn101441-20200523-00303.

薄型子宫内膜是新鲜胚胎移植单胎子代低出生体质量的危险因素

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【摘要】 目的 探讨薄型子宫内膜厚度(endometrial thickness, EMT)对新鲜胚胎移植周期单胎子代低出生体质量(low birth weight, LBW)的影响。方法 回

回顾性队列研究分析 2015 年 1 月至 2019 年 2 月期间在郑州大学第三附属医院生殖医学科行体外受精 (*in vitro* fertilization, IVF) 或卵胞质内单精子注射 (intracytoplasmic sperm injection, ICSI) 助孕的患者资料, 纳入新鲜卵裂期胚胎移植且分娩单胎子代周期, 共 2247 个周期。根据人绒毛膜促性腺激素 (human chorionic gonadotropin, hCG) 注射日的 EMT 进行分组, A 组: ≤ 7.5 mm; B 组: 7.6~12.0 mm; C 组: >12.0 mm, 分别计算各组单胎子代出生体质量和 LBW 的发生率, 并采用二元逻辑回归校正混杂因素。结果 A 组单胎子代出生体质量 [3000 (2525, 3350) g] 显著低于 B 组和 C 组 [3350 (3050, 3650) g, 3400 (3100, 3690) g; 均 $P<0.001$]。A 组 LBW 的发生率 [24.7% (20/81)] 显著高于 B 组和 C 组 [4.0% (57/1414), 5.3% (40/752); 均 $P<0.001$], 而 B 组和 C 组差异无统计学意义 ($P>0.05$)。经逻辑回归分析, 体质量指数 ($P=0.029$)、hCG 注射日雌激素水平 ($P=0.027$)、EMT ($P<0.001$)、分娩孕周 ($P<0.001$) 及新生儿性别 ($P<0.001$) 是 LBW 的独立影响因素, 即体质量指数较小、分娩孕周越小、hCG 注射日雌激素水平 ≥ 4000 ng/L 以及新生儿为女性时, LBW 的发生率增加。以 B 组为对照组, A 组 LBW 发生率显著增加, 为 LBW 的独立危险因素 (aOR=4.39, 95% CI=1.85~10.46, $P<0.001$), 而 C 组 LBW 发生率差异无统计学意义 (aOR=0.90, 95% CI=0.51~1.59, $P=0.723$)。结论 在新鲜卵裂期胚胎移植周期中, 薄型 EMT 单胎子代出生体质量下降, 为 LBW 的独立危险因素。

【关键词】 胚胎移植; 低出生体质量; 薄型子宫内膜

Thin endometrium is an independent risk factor for low birth weight of singleton in fresh embryo transfer

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【Abstract】 Objective To explore the effect of thin endometrial thickness (EMT) on the low birth weight (LBW) of singleton in fresh embryo transfer cycle. **Methods** It was a retrospective cohort study. The data of singleton deliveries achieved after fresh cleavage embryo transfer in the Reproductive Center of the Third Affiliated Hospital of Zhengzhou University from January 2015 to February 2019 were included. A total of 2247 cycles were included and were divided into three groups depending on the EMT: group A ≤ 7.5 mm, group B 7.6–12.0 mm and group C >12.0 mm. The major outcome measure was LBW. Binary logistic regression was performed to correct for confounding factors. **Results** Singleton birthweight was lower in group A [3000(2525, 3350) g] compared with group B and group C [3350(3050, 3650) g, 3400(3100, 3690) g, all $P<0.001$]. The incidence of LBW in group A [24.7% (20/81)] was significantly higher than that in groups B and C [4.0% (57/1414), 5.3% (40/752), all $P<0.001$], while there was no statistical difference between groups B and C ($P>0.05$). Body mass index ($P=0.029$), estrogen level on the human chorionic gonadotropin (hCG) trigger day ($P=0.027$), EMT ($P<0.001$), gestational age ($P<0.001$) and the gender of the newborn ($P<0.001$) were independent factors of LBW. The incidence of LBW increased when the body mass index and gestational age were smaller and estrogen level on the hCG trigger day was

≥ 4000 ng/L. Taking group B as control group, the incidence of LBW in group A increased significantly and was an independent risk factor for LBW (aOR=4.39, 95% CI=1.85–10.46, $P<0.001$), while the incidence of LBW in group C had no significant difference (aOR=0.90, 95% CI=0.51–1.59, $P=0.723$). **Conclusion** In the fresh cleavage stage embryo transfer cycle, singleton birth weight was lower in thin EMT group. And thin EMT was an independent risk factor for LBW of singleton delivery.

【Key words】 Embryo transfer; Low birth weight; Thin endometrium

DOI: 10.3760/cmaj.cn101441-20200623-00354

收稿日期 2020-06-30 本文编辑 王李艳

引用本文: 田瑜, 张觐宇. 血浆皮质醇水平与 IVF/ICSI 患者生育压力及妊娠结局相关性分析[J]. 中华生殖与避孕杂志, 2022, 42(1): 30-35. DOI: 10.3760/cmaj.cn101441-20200623-00354.

·临床研究·

血浆皮质醇水平与 IVF/ICSI 患者生育压力及妊娠结局相关性分析

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【摘要】 目的 探讨生育压力与血浆皮质醇水平的相关性、生育压力及血浆皮质醇水平与妊娠结局的相关性。方法 本研究为病例对照研究, 采用便利抽样法选取 2019 年 3 月至 2019 年 10 月期间于重庆医科大学附属第二医院妇产科生殖医学中心, 拟行体外受精/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) 助孕的不孕女性行横断面调查, 将患者分为妊娠组和非妊娠组, 对研究对象行一般资料调查, 采用生育压力量表 (fertility problem inventory, FPI) 进行生育压力评估, 同时测定移植前、移植日清晨空腹血浆皮质醇水平, 随访 IVF/ICSI-ET 的妊娠结局, 对妊娠结局的影响因素采用 logistic 回归分析。结果 调查期间共有 169 例研究对象行胚胎移植, 妊娠组患者 80 例, 非妊娠组患者 89 例, 两组患者的人口学特征和临床特征的基线差异均无统计学意义 (均 $P>0.05$)。研究期间共发放问卷 320 份, 回收有效问卷 291 份, Spearman 相关性分析结果显示血浆皮质醇与生育压力呈正相关 ($r=0.234$, $P<0.001$)。回归分析结果显示移植日血浆皮质醇是妊娠结局的独立影响因素 ($OR=1.002$, 95% CI=1.001~1.004, $P=0.003$)。结论 血浆

皮质醇水平可反映不孕患者生育压力水平；移植日血浆皮质醇含量是妊娠结局的独立影响因素，随着血浆皮质醇含量的增加，妊娠的可能性减小。

【关键词】 不孕症； 生育压力； 血浆皮质醇

Correlation analysis of plasma cortisol levels with fertility stress and pregnancy outcome in patients with IVF/ICSI

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【Abstract】 Objective To explore the correlation between fertility stress and plasma cortisol level, the correlation between fertility stress and plasma cortisol level and pregnancy outcome. **Methods** This experiment is a case-control study. Convenience sampling method was used to select infertility women assisted by *in vitro* fertilization/intracytoplasmic sperm injection and embryo transfer (IVF/ICSI-ET) in the Department of Reproductive Medicine, Department of Obstetrics and Gynecology, the Second Affiliated Hospital of Chongqing Medical University between March 2019 and October 2019. A cross-sectional survey was conducted. The patients were divided into pregnancy and non-pregnancy groups and general data survey was conducted on the study subjects, and the fertility problem inventory (FPI) scale was adopted. A fertility stress assessment was performed and fasting plasma cortisol levels were measured in the morning before transplantation during the investigation. The plasma cortisol level before transplantation and the morning of the transplantation day were measured, and their pregnancy outcomes were followed up. Logistic regression analysis was used to determine the factors affecting pregnancy outcomes. **Results** During the investigation, a total of 169 subjects underwent embryo transfer. There were 80 patients in pregnancy group and 89 patients in non-pregnancy group. There was no statistically significant difference in demographic and clinical characteristics between the two groups at baseline (all $P>0.05$). A total of 320 questionnaires were issued during the study period, and 291 valid questionnaires were recovered. The Spearman correlation analysis showed that plasma cortisol was positively correlated ($r=0.234, P<0.001$) with fertility stress. Regression analysis showed that plasma cortisol on the day of transplantation was an independent factor affecting pregnancy outcome ($OR=1.002, 95\% CI=1.001-1.004, P=0.003$). **Conclusion** The level of plasma cortisol can reflect the fertility pressure of infertile patients, the content of plasma cortisol on the day of transplantation is an independent influencing factor of pregnancy outcome. With the increase of the content of plasma cortisol, the possibility of pregnancy decreases.

【Key words】 Infertility; Fertility stress; Plasma cortisol

DOI: 10.3760/cma.j.cn101441-20201219-00681

收稿日期 2020-12-24

责任编辑 宋培培

引用本文：李太旻, 李蓉, 黄锦, 等. 平衡易位携带者性别对复发性流产夫妇胚胎移植结局的影响[J]. 中华生殖与避孕杂志, 2022, 42(1): 36-42. DOI: 10.3760/cma.j.cn101441-20201219-00681.

·临床研究·

平衡易位携带者性别对复发性流产夫妇胚胎移植结局的影响

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【摘要】 目的 分析因染色体平衡易位导致复发性流产 (recurrent miscarriage, RM) 的夫妇中, 携带者性别对正常/平衡囊胚率 (可移植囊胚率) 及活产结局的影响。方法 回顾性病例分析 2012 年 1 月至 2018 年 12 月期间在北京大学第三医院生殖医学中心就诊的携带平衡易位的 RM 夫妇的第一个刺激周期的临床资料, 所有周期均进行胚胎移植前染色体结构重排检测 (preimplantation genetic testing for chromosomal structural rearrangements, PGT-SR), 比较不同性别携带者一个完整周期的妊娠结局。结果 研究纳入 247 个刺激周期, 均为一方携带, 女性携带者 136 例, 男性携带者 111 例。每移植周期临床妊娠率为 47.64% (91/191), 每移植周期活产率为 43.98% (84/191), 累积活产率为 34.71% (84/242), 周期取消率为 38.87% (96/247)。女方平衡易位携带者的囊胚形成率 [31.42% (427/1359)] 低于男性携带者 [36.44% (379/1040), $P=0.010$]; 女方平衡易位携带的夫妇获得的可移植囊胚率 [31.85% (136/427)] 与男方平衡易位携带者的夫妇 [36.15% (137/379)], 差异无统计学意义 ($P=0.198$), 囊胚数是患者获得活产的保护因素 [OR (95% CI) =1.243 (1.002~1.542), $P=0.047$]。结论 女方平衡易位携带者的囊胚形成率低于男方平衡易位携带者, 平衡易位携带者性别对可移植囊胚率没有影响。PGT-SR 后携带者的性别不影响累积活产结局, 需要根据患者获得活产所需的刺激周期数来评估携带者性别对妊娠结局的整体影响。

【关键词】 复发性流产; 胚胎移植前染色体结构重排检测; 染色体易位; 平衡易位

基金项目: 国家重点研发计划 (2018YFC1003104); 国家科技重大专项课题 (2017ZX09304012-012)

Influence of the gender of reciprocal translocation carrier on the clinical outcomes of couples with recurrent miscarriage

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【Abstract】 Objective To analyze the influence of carrier gender on normal/balanced blastocyst rate (transferable blastocyst rate) and live birth outcome in couples with recurrent miscarriage (RM) due to reciprocal translocation. **Methods** The clinical data of the first stimulated cycle of RM couples carried with the reciprocal translocation were retrospectively analyzed. Preimplantation genetic testing for chromosomal structural rearrangements (PGT-SR) were performed in all stimulated cycles. All patients were treated at the Reproductive Medicine Center of Peking University Third Hospital from January 2012 to December 2018. The pregnancy outcome of a full cycle was compared among carriers of different genders. **Results** Totally 247 stimulated cycles were included. Only one partner of couples was the carrier including 136 female carriers and 111 male carriers. The clinical pregnancy rate per transfer cycle was 47.64% (91/191), the live birth rate per transfer cycle was 43.98% (84/191). The cumulative live birth rate (multiple live birth) was 34.71% (84/242), and the cycle cancellation rate was 38.87% (96/247). The blastocyst formation rate of female carriers with reciprocal translocation [31.42% (427/1359)] was lower than that of male carriers [36.44% (379/1040), $P=0.010$]. There was no statistically difference between the transferable blastocyst rate of female carriers with reciprocal translocation [31.85% (136/427)] and that of couples of male carriers [36.15% (137/379), $P=0.198$]. The number of blastocysts was a protective factor for achieving a live birth [$OR(95\% CI)=1.243(1.002-1.542)$, $P=0.047$]. **Conclusion** The blastocyst formation rate was lower in female reciprocal translocation carriers than in male carriers. The gender of reciprocal translocation carriers had no effect on transferable blastocyst rate. The gender of the carrier did not affect the cumulative live birth outcome after PGT-SR. The overall impact of the carrier's gender on pregnancy outcome should be evaluated according to the number of stimulation cycles required for the patient to achieve a live birth.

【Key words】 Recurrent miscarriage; Preimplantation genetic testing for chromosomal structural rearrangements; Chromosomal translocation; Reciprocal translocation

Fund program: National Key R&D Program (2018YFC1003104); National Science and Technology Major Project of China (2017ZX09304012-012)

DOI: 10.3760/cmaj.cn101441-20200602-00324

收稿日期 2020-06-04 本文编辑 王李艳

引用本文：涂文娇, 许世艳, 朱科衡, 等. 精子透明质酸结合试验阳性率与诱发顶体反应率预测精子形态异常对受精的影响[J]. 中华生殖与避孕杂志, 2022, 42(1): 43-49. DOI: 10.3760/cmaj.cn101441-20200602-00324.

·临床研究·

精子透明质酸结合试验阳性率与诱发顶体反应率预测精子形态异常对受精的影响

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【摘要】 目的 探讨精子形态异常对受精影响的原因, 为畸形精子症患者受精方式的选择提供参考。方法 回顾性队列研究分析 2016 年 1 月至 2020 年 3 月期间于深圳市人民医院生殖医学中心首次进行常规体外受精 (*in vitro* fertilization, IVF) 的助孕周期, 根据精子正常形态率 (normal sperm morphology rate, NSMR) 分为 4 组, A 组: IVF 精子形态正常 (NSMR \geq 4%, 750 个周期), B 组: IVF 轻度畸形精子症 (2% \leq NSMR $<$ 4%, 277 个周期), C 组: IVF 中度畸形精子症 (1% \leq NSMR $<$ 2%, 110 个周期), D 组: IVF 重度畸形精子症 (0% \leq NSMR $<$ 1%, 49 个周期), 比较各组的正常受精率、受精失败率 (受精率 $<$ 30%)、完全受精失败率 (受精率=0) 以及受精功能相关指标: 2 h 酪氨酸磷酸化率、透明质酸结合试验 (hyaluronan-binding assay, HBA) 阳性率、顶体酶含量、自发顶体反应率、诱发顶体反应率。结果 ①D 组 IVF 正常受精率 [52.4% (18.3%, 69.0%)] 显著低于 A 组 [60.0% (45.5%, 75.0%)], $P=0.008$ 和 B 组 [60.0% (42.9%, 75.0%)], $P=0.028$; IVF 受精失败率 [22.4% (11/49)] 显著高于 A 组 [5.5% (41/750)], $P<0.001$ 和 B 组 [8.3% (23/277)], $P=0.018$; IVF 完全受精失败率 [14.3% (7/49)] 显著高于 A 组 [2.7% (20/750)], $P=0.006$ 。多因素 logistics 回归分析也显示 D 组 IVF 正常受精率显著低于 A 组 ($OR=0.433$, $P=0.008$), 受精失败风险 ($OR=5.426$, $P<0.001$)、完全受精失败风险 ($OR=8.194$, $P<0.001$) 显著高于 A 组。②B、C、D 组 HBA 阳性率 [75.0% (62.3%, 83.0%), 71.0% (58.0%, 81.0%), 68.0% (48.0%, 76.5%)] 均显著低于 A 组 [80.0% (71.0%, 85.0%)], 均 $P<0.001$; C、D 组诱发顶体反应率 [32.3% (26.5%, 40.8%), 28.8% (24.2%, 43.0%)] 均显著低于 A 组 [37.8% (30.5%, 46.8%)], $P<0.001$, $P=0.009$ 。③Spearman 相关分析结果显示精子正常形态率与 HBA 阳性率 ($r=0.259$, $P<0.001$) 和诱发顶体反应率 ($r=0.202$, $P<0.001$) 正相关。④以精子 HBA 阳性率、诱发顶体反应率、NSMR 为自变量, 对 NSMR $<$ 4% 的 IVF 周期受精率 (IVF 受精率 $<$ 30%) 的受试者工作特征

(receiver operator characteristic, ROC) 曲线分析, HBA 阳性率的截断值是 73.5%, 敏感度为 51.4%, 特异度为 73.8%, 曲线下面积 (area under curve, AUC) (95% CI) = 0.643 (0.559~0.726), $P=0.002$; 诱发顶体反应率的截断值是 28.9%, 敏感度为 72.1%, 特异度为 50%, AUC (95% CI) = 0.599 (0.497~0.700), $P=0.036$; 正常形态率的截断值是 1.45, 敏感度为 77.8%, 特异度为 42.9%, AUC (95% CI) = 0.605 (0.509~0.701), $P=0.025$ 。结论 畸形精子可能通过影响受精功能指标 HBA 阳性率、诱发顶体反应率从而影响 IVF 受精, 建议对于畸形精子症患者, 尤其重度畸形精子症 ($0\% \leq \text{NSMR} < 1\%$) 患者, 进入促排卵周期后, 男方行精子受精功能检测, 包括 HBA 阳性率、诱发顶体反应率, 如果取卵当日处理后精液符合常规 IVF 受精的要求, 但前期受精功能检测 HBA 阳性率 $< 73.5\%$, 诱发顶体反应率 $< 28.9\%$, 建议行短时受精观察、卵胞质内单精子注射 (intracytoplasmic sperm injection, ICSI) 或 half-ICSI, 以降低 IVF 受精失败的风险。

【关键词】 顶体反应; 透明质酸结合试验; 精子正常形态率; 受精, 体外; 受精率

Sperm-hyaluronan binding assay rate and induced acrosome reaction rate to predict the influence of abnormal sperm morphology on fertilization

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【Abstract】 **Objective** To explore the cause of abnormal morphology sperm on fertilization from insemination function and provide reference for the selection of fertilization methods for teratozoospermia patients. **Methods** Through a retrospective cohort study of their first *in vitro* fertilization (IVF) treatment cycles in Reproductive Medicine Center of Shenzhen People's Hospital from January 2016 to March 2020, all patients were divided into four groups according to the normal sperm morphology rate (NSMR), group A: IVF normal sperm morphology ($\text{NSMR} \geq 4\%$, $n=750$), group B: mild teratozoospermia ($2\% \leq \text{NSMR} < 4\%$, $n=277$), group C: moderate teratozoospermia ($1\% \leq \text{NSMR} < 2\%$, $n=110$), group D: severe teratozoospermia ($0\% \leq \text{NSMR} < 1\%$, $n=49$). We compared normal fertilization rate, fertilization failure rate (fertilization rate $< 30\%$) and total fertilization failure rate (fertilization rate = 0) among the four groups and we also compared insemination function indexes: 2 h tyrosine phosphorylation rate, hyaluronan-binding assay (HBA) positive rate, content of acrosin, spontaneous acrosome reaction rate and induced acrosome reaction rate. **Results** 1) The normal fertilization rate of group D [52.4% (18.3%, 69.0%)] was significantly lower than that of group A [60.0% (45.5%, 75.0%), $P=0.008$] and group B [60.0% (42.9%, 75.0%), $P=0.028$]; the fertilization failure rate [22.4% (11/49)] was significantly higher than that of group A [5.5% (41/750), $P<0.001$] and group B [8.3% (23/277), $P=0.018$]; the total fertilization failure rate [14.3% (7/49)] was significantly higher than that of group A [2.7% (20/750), $P=0.006$]. Multivariate logistic regression models: the normal fertilization rate of group D was significantly lower than that of group A ($OR=0.433$, $P=0.008$), and the risk of fertilization failure ($OR=5.426$, $P<0.001$) and

total fertilization failure ($OR=8.194$, $P<0.001$) were significantly higher than those of group A. 2) HBA positive rate in groups B, C, D [75.0%(62.3%, 83.0%), 71.0%(58.0%, 81.0%), 68.0%(48.0%, 76.5%)] was significantly lower than that in group A [80.0%(71.0%, 85.0%), all $P<0.001$] and induced acrosome reaction rate in group C and group D [32.3%(26.5%, 40.8%), 28.8%(24.2%, 43.0%)] was significantly lower than that in group A [37.8%(30.5%, 46.8%), $P<0.001$, $P=0.009$]. 3) Spearman correlation analysis showed that sperm normal morphology rate was positively correlated with HBA positive rate ($r=0.259$, $P<0.001$) and induced acrosome reaction rate ($r=0.202$, $P<0.001$). 4) Receiver operating characteristic (ROC) curve analysis was performed to determine a cut-off value using HBA positive rate, induced acrosome reaction rate and sperm normal morphology rate as independent variables with the fertilization rate of IVF cycles (normal sperm morphology rate $<4\%$) dichotomized at 30%. The best cut-off value of HBA positive rate obtained was 73.5% with a sensitivity of 51.4% and specificity of 73.8% [area under curve (AUC) (95% CI)=0.643 (0.559–0.726), $P=0.002$]; the cut-off value of induced acrosome reaction rate was 28.9% with a sensitivity of 72.1% and specificity of 50% [AUC (95% CI)=0.599 (0.497–0.700), $P=0.036$]; the cut-off value of normal sperm morphology rate was 1.45% with a sensitivity of 77.8% and specificity of 42.9% [AUC (95% CI)=0.605 (0.509–0.701), $P=0.025$]. **Conclusion** Abnormal morphology sperm may affect IVF fertilization by HBA positive rate and induced acrosome reaction rate. For teratozoospermia patients, especially for the severe teratozoospermia ($0\%\leq NSMR<1\%$), we recommend that HBA positive rate and induced acrosome reaction rate are tested after ovulation induction treatment. If the post-treatment sperm meets the requirements of routine IVF fertilization on the day of retrieved oocytes, but HBA positive rate $<73.5\%$, induced acrosome reaction rate $<28.9\%$, short time IVF or intracytoplasmic sperm injection (ICSI) or half-ICSI is recommended to minimize IVF fertilization failure.

【Key words】 Acrosome reaction; Hyaluronan-binding assay; Normal sperm morphology rate; Fertilization *in vitro*; Fertilization rate

DOI: 10.3760/cmaj.cn101441-20200519-00294

收稿日期 2020-06-01 本文编辑 王李艳

引用本文: 毛献宝, 王世凯, 谭卫红, 等. 培养液对胚胎早期发育动态表型和动力学参数的影响: 一项 time-lapse 研究[J]. 中华生殖与避孕杂志, 2022, 42(1): 50-57. DOI: 10.3760/cmaj.cn101441-20200519-00294.

·实验研究·

培养液对胚胎早期发育动态表型和动力学参数的影响：一项 time-lapse 研究

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【摘要】 目的 探讨胚胎早期发育动态表型和动力学参数是否受培养液组分差异的影响。方法 回顾性队列研究分析广西壮族自治区人民医院生殖医学与遗传中心 2016 年 10 月至 2018 年 12 月期间收治的体外受精 (*in vitro* fertilization, IVF) 周期患者的临床资料，根据使用的培养液品牌不同，将 IVF 周期分为 Cook 组和 Vitrolife 组，经 1:1 倾向性评分匹配后，每组纳入 59 个，采用延时成像技术分析正常受精卵裂胚胎授精后 68 h 内的早期发育形态动力学。记录胚胎发育动态表型，比较两组胚胎 7 种发育动态表型构成的差异；计算正常表型胚胎的 13 个早期发育动力学参数，比较两组之间动力学参数的差异；基于两个已发表的 time-lapse 胚胎筛选模型，比较两组正常动态表型胚胎的等级分布差异。结果 ①Cook 组胚胎发育动态表型构成如下：正常表型 54.0%、胞质异常波动 (abnormal first cytokinesis, A1^{qt}) 3.0%、不规则卵裂 (abnormal cleavage, AC) 17.4%、逆向卵裂 (reverse cleavage, RC) 5.2%、无序卵裂 (chaotic cleavage, CC) 3.2%、多核 (multinucleation, Mn) 3.5% 以及混合表型 13.7%；Vitrolife 组胚胎发育动态表型构成如下：正常表型 49.3%、A1^{qt} 4.0%、AC 19.1%、RC 7.5%、CC 2.1%、Mn 6.4% 以及混合表型 11.6%，两组间表型构成差异没有统计学意义 ($P>0.05$)。②相较于 Vitrolife 组，Cook 组正常动态表型胚胎 13 个发育动力学参数 (tPNa、tPNf、t2、t3、t4、t5、t6、t7、t8、cc2、s2、t5_PNf 和 t8_PNf) 均略长，授精后 68 h 胚胎平均卵裂球数略少，但差异均无统计学意义 (均 $P>0.05$)。③基于模型 A，Vitrolife 组与 Cook 组胚胎等级分布差异没有统计学意义 ($P>0.05$)；基于模型 B，两组胚胎等级分布差异存在统计学意义 ($P=0.040$)，其中 Vitrolife 组 A⁺ 级胚胎比例较 Cook 组高 [59.8% (125/209) 比 43.3% (94/217)]，而 C 级胚胎比例较 Cook 组低 [9.6% (20/209) 比 20.3% (44/217)]。结论 胚胎早期发育动态表型及动力学参数不受 Cook 与 Vitrolife 序贯培养液差异的影响，但不同 time-lapse 胚胎筛选模型对不同培养液体系的适用性存在差异，选择或建立模型时应充分考虑所使用的胚胎培养液体系。

【关键词】 培养基； 延时成像； 胚胎动力学； 动态表型； 胚胎评估

基金项目：广西自然科学基金 (2018GXNSFAA138112、2019GXNSFAA185056)；
广西重点研发计划 (桂科 AB18050024)；广西卫健委科研课题 (Z20180742)；南

Effects of culture media on early developmental dynamic phenotypes and kinetic parameters of embryos: a time-lapse study

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【Abstract】 Objective To investigate whether the early developmental dynamic phenotypes and kinetic parameters of embryos used for embryo selection are affected by the differences in the components of culture media utilized. **Methods** The clinical data of patients undergoing *in vitro* fertilization (IVF) at Center for Reproductive Medicine and Genetics of People's Hospital of Guangxi Zhuang Autonomous Region from October 2016 to December 2018 were analyzed in a retrospective cohort study. According to the different culture media utilized, IVF cycles were divided into Cook group and Vitrolife group. After 1 : 1 propensity-score matching (PSM), 59 IVF cycles were included in each group. Time-lapse imaging technology was used to analyze the early developmental dynamics of normal fertilized embryos between insemination and 68 h post insemination. Seven developmental dynamic phenotypes of embryos were annotated and the differences in the composition of dynamic phenotypes were compared between the two groups. Thirteen early developmental kinetic parameters were calculated, and the differences in the kinetic parameters of normal dynamic phenotypic embryos between the two groups were compared. According to the two published time-lapse embryo selection algorithms, the hierarchical distribution of normal dynamic phenotypic embryos of two groups was compared. **Results** 1) In Cook group, the composition of developmental dynamic phenotypes of embryos were 54.0% normal phenotype, 3.0% abnormal first cytokinesis (A1^{cut}), 17.4% abnormal cleavage (AC), 5.2% reverse cleavage (RC), 3.2% chaotic cleavage (CC), 3.5% multinucleation (Mn) and 13.7% mixed phenotype, which were 49.3%, 4.0%, 19.1%, 7.5%, 2.1%, 6.4% and 11.6% in Vitrolife group, respectively. No statistically significant differences were observed between the two groups for the composition of dynamic developmental phenotypes ($P>0.05$). 2) Compared with Vitrolife group, the 13 developmental kinetic parameters (tPNa, tPNf, t2, t3, t4, t5, t6, t7, t8, cc2, s2, t5_PNf and t8_PNf) of normal dynamic phenotype embryos in Cook group were slightly longer, and the average number of blastomeres in 68 h post insemination (EB68hpi) was less, but the differences were not statistically significant (all $P>0.05$). 3) No significant difference in hierarchical distribution of embryos was observed between Vitrolife group and Cook group according to algorithm A ($P>0.05$). The difference of embryo hierarchical distribution between the two groups was statistically significant according to algorithm B ($P=0.040$), the proportion of grade A+ embryos in Vitrolife group was higher than that in Cook group [59.8% (125/209) vs. 43.3% (94/217)],

and grade C proportion was lower [9.6% (20/209) vs. 20.3% (44/217)]. **Conclusion** Although the early developmental dynamic phenotypes and kinetic parameters of embryos were not affected by the differences between Cook and Vitrolife sequential culture media, the applicability of different time-lapse embryo selection algorithms to the culture media is different, the embryo culture media utilized should be considered when selecting or constructing the algorithms.

【Key words】 Culture media; Time-lapse imaging; Embryo kinetics; Dynamic phenotype; Embryo assessment

Fund program: Natural Science Foundation of Guangxi Zhuang Autonomous Region (2018GXNSFAA138112, 2019GXNSFAA185056); Key Research and Development Plan of Guangxi Zhuang Autonomous Region (AB18050024); Scientific Research Project of the Guangxi Zhuang Autonomous Region Health Commission (ZZ0180742); Key Research and Development Plan of Qingxiu District of Nanning (2018025); Youth Foundation of People's Hospital of Guangxi Zhuang Autonomous Region (QN2019-1)

DOI: 10.3760/cmaj.cn101441-20200608-00335

收稿日期 2020-06-16 本文编辑 王李艳

引用本文: 李晓虹, 汤惠茹, 李雨珊, 等. 不同玻璃液冻存人卵巢组织的近期异种移植效果的比较[J]. 中华生殖与避孕杂志, 2022, 42(1): 58-64. DOI: 10.3760/cmaj.cn101441-20200608-00335.

·实验研究·

不同玻璃液冻存人卵巢组织的近期 异种移植效果的比较

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【摘要】 目的 通过研究不同的玻璃液对人卵巢组织冻存后的近期异种移植效果, 以筛选出较优的玻璃化冷冻方案。方法 收集 2018 年 3 月至 2019 年 12 月期间在北京大学深圳医院因妇科疾病行手术治疗的 4 例患者卵巢组织, 将卵巢组织分割成 5~10 mm×10 mm×1 mm 的小块, 分为新鲜对照组和 4 个处理组, 4 个处理组分别放入 G1、G2、G3、G4 不同的玻璃液中, 经过 4 组玻璃液预平衡和平衡

后冻存 4 周后复苏, 复苏后的组织移植到胚龄 10 d 的鸡卵绒毛尿囊膜 (chorioallantoic membrane, CAM) 上培养, 培养 5 d 后取出移植于 CAM 的卵巢组织, HE 染色比较移植后 4 组卵巢组织的正常原始卵泡率, 免疫组织化学法检测 CD105 标记的 4 组卵巢组织的新生血管并比较其微血管密度; Western blotting 法检测并比较 4 组卵巢组织 Bcl-2 和 Bax 蛋白的表达。结果 经过 G1、G2、G3、G4 玻璃液冻融并移植于鸡胚 5 d 后的卵巢组织, 正常原始卵泡率分别为 63.2% (24/38)、68.3% (28/41)、61.9% (26/42)、69.6% (32/46), 新鲜对照组的正常卵泡率为 82.8% (82/99), 5 组间的差异有统计学意义 ($P=0.044$), 进一步两两比较, 各处理组间正常原始卵泡率均低于新鲜对照组 (均 $P<0.05$), 而各处理组间的正常卵泡率差异无统计学意义 ($P>0.05$)。G1 组、G2 组、G3 组和 G4 组鸡胚移植后的卵巢组织均可见 CD105 表达量增加, CD105 标记的微血管密度 (microvascular density, MVD) 在新鲜对照组和 G1 组、G2 组、G3 组、G4 组分别为 $6.51\pm 1.30/\text{mm}^2$ 、 $11.10\pm 1.62/\text{mm}^2$ 、 $13.04\pm 1.84/\text{mm}^2$ 、 $9.11\pm 1.09/\text{mm}^2$ 、 $11.28\pm 1.62/\text{mm}^2$, 各处理组的 MVD 均高于新鲜对照组, 差异有统计学意义 ($P<0.001$, $P<0.001$, $P=0.022$, $P<0.001$), G1 组、G2 组和 G4 组的 MVD 均高于 G3 组 ($P=0.024$, $P<0.001$, $P=0.034$)。Western blotting 检测结果显示 G1 组、G2 组、G3 组、G4 组和新鲜对照组的 Bcl-2/Bax 的比值分别为 0.71 ± 0.37 、 0.84 ± 0.29 、 0.45 ± 0.18 、 0.84 ± 0.29 和 0.44 ± 0.21 , 差异有统计学意义 ($P=0.013$), G2 组 Bcl-2/Bax 的比值明显高于新鲜对照组和 G3 组 ($P=0.025$, $P=0.038$)。结论 玻璃化冷冻保存的人卵巢组织, 在移植早期原始卵泡丢失较多。经过 G2 和 G4 玻璃液冷冻复融后的人卵巢组织, 在移植 5 d 后血管化程度较高, 抗凋亡能力强, 是适用于人卵巢组织冷冻的较优的玻璃化冷冻方案。

【关键词】 卵巢组织; 玻璃化冷冻; 凋亡; 微血管密度

基金项目: 深圳市“医疗卫生三名工程”项目 (SZSM202011016); 深圳市科创委技术攻关项目 (JSGG20180703164202084)

Comparison of short-term transplantation effect of different vitrification solution on human ovarian tissue

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【Abstract】 **Objective** To investigate the short-term transplantation effect of different vitrification solutions in order to optimize the cryopreservation protocol on human ovarian tissue. **Methods** Ovarian tissues came from 4 patients who were treated surgically due to gynecological diseases in Peking University Shenzhen Hospital from March 2018 to December 2019. The size of 5–10 mm×10 mm×1 mm ovarian tissues were distributed to fresh control group and four experimental groups (G1, G2, G3 and G4). After equilibrium and thawing, the frozen ovarian tissues were grafted into chorioallantoic membrane (CAM). The transplanted ovarian tissues were collected 5 d after transplantation. The morphology of follicles was assessed by HE, the expression of CD105 protein was detected by immunohistochemistry and the microvascular density was recorded.

The expression of Bcl-2 and Bax proteins was detected by Western blotting. **Results** There was a significantly difference in the percentage of morphologically normal primordial follicles (MNPF) among G1 [63.2% (24/38)], G2 [68.3% (28/41)], G3 [61.9% (26/42)], G4 [69.6% (32/46)] and fresh control groups [82.8% (82/99), $P=0.044$]. Compared with fresh control group, the percentages of MNPF were statistically lower in the treatment groups (all $P<0.05$). The CD105-microvascular density (MVD) in fresh control group, G1, G2, G3 and G4 groups were $6.51\pm1.30/\text{mm}^2$, $11.10\pm1.62/\text{mm}^2$, $13.04\pm1.84/\text{mm}^2$, $9.11\pm1.09/\text{mm}^2$, $11.28\pm1.62/\text{mm}^2$, respectively. The CD105-MVD in four treatment groups after transplantation was significantly higher than that of fresh control group ($P<0.001$, $P<0.001$, $P=0.022$, $P<0.001$), and the CD105-MVD of G1, G2 and G4 groups was higher than that of G3 group ($P=0.024$, $P<0.001$, $P=0.034$). The ratio of Bcl-2/Bax in G1, G2, G3, G4 groups and fresh control group were 0.71 ± 0.37 , 0.84 ± 0.29 , 0.45 ± 0.18 , 0.84 ± 0.29 and 0.44 ± 0.21 , respectively. The ratio of Bcl-2/Bax of G2 group was statistically higher than that of fresh control group and G3 group ($P=0.025$, $P=0.038$). **Conclusion** After 5 d of transplantation into CAM, the percentage of normal primordial follicles is lower. According to the higher vascularization and anti-apoptotic ability, G2 and G4 are the optimal vitrification protocol for human ovarian tissue cryopreservation.

【Key words】 Human ovarian tissue; Vitrification; Apoptosis; Microvessel density

Fund program: Sanming Project of Medicine in Shenzhen (SZSM202011016); Technical Key Project of Shenzhen Science and Innovation Commission (JSGG20180703164202084)

·实验研究·

DOI: 10.3760/cma.j.cn101441-20200515-00285

收稿日期 2020-05-19 本文编辑 王李艳

引用本文: 梅忆媛, 王晓博, 谢青贞. 骨桥蛋白在体外对小鼠子宫内膜蜕膜化的调节作用[J]. 中华生殖与避孕杂志, 2022, 42(1): 65-71. DOI: 10.3760/cma.j.cn101441-20200515-00285.

骨桥蛋白在体外对小鼠子宫内膜蜕膜化的调节作用

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【摘要】 目的 探讨骨桥蛋白(osteopontin, OPN)是否参与体外诱导小鼠子宫内膜基质细胞(mouse endometrial stromal cells, mESCs)蜕膜化的过程及其调节作用。方法 采用雌激素(10 nmol/L)和孕酮(1 μmol/L)处理 mESCs 进行体外诱导蜕膜化,检测 OPN 的表达变化。设立 *Opn* 质粒过表达组及 *Opn* shRNA 敲减组,分别将 *Opn* 过表达质粒和 *Opn* shRNA 转染 mESCs,同时设立阴性对照组,采用实时定量 PCR 及 Western blotting 法检测转染效率;CCK-8 法检测每组的增殖情况;采用实时定量 PCR 和 Western blotting 法检测小鼠子宫内膜蜕膜化标志分子蜕膜/滋养层催乳素相关蛋白(decidual/trophoblast-layer prolactin related protein, Dtprp)和血管内皮生长因子 A(vascular endothelial growth factor A, Vegfa)及其受体 2(vascular endothelial growth factor A receptor 2, Vegfr2)表达情况。结果 雌激素+孕酮诱导蜕膜化 mESCs 中 *Dtprp* ($P<0.001$)、*Vegfa* ($P=0.004$)和 *Vegfr2* ($P=0.002$) mRNA 水平显著增加,同时 *Opn* mRNA ($P=0.002$)和 OPN 蛋白 ($P<0.001$)的表达水平也显著增加;*Opn* 过表达可促进 mESCs 细胞增殖 ($P=0.004$),而敲减 *Opn* 可抑制 mESCs 细胞增殖 ($P=0.008$);转染 *Opn* 过表达质粒可进一步促进蜕膜化 mESCs 中 *Dtprp* ($P<0.001$)、*Vegfa* ($P=0.021$)和 *Vegfr2* ($P=0.012$)的 mRNA 表达,同时 Vegfa 蛋白水平也显著增加 ($P=0.001$);敲减 *Opn* 后,则可降低蜕膜化 mESCs 中 *Dtprp* ($P=0.009$)、*Vegfa* ($P=0.007$)和 *Vegfr2* ($P=0.001$)的 mRNA 表达,VEGFA 蛋白的表达水平也相应降低 ($P<0.001$)。结论 OPN 参与调节小鼠子宫内膜基质细胞蜕膜化进程及功能。

【关键词】 骨桥蛋白; 小鼠子宫内膜; 蜕膜化

基金项目: 国家自然科学基金(81471456)

Regulation of osteopontin on decidualization of mouse endometrium *in vitro*

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【Abstract】 Objective To explore whether osteopontin (OPN) is involved in the regulation of mouse endometrial stromal cells (mESCs) decidualization *in vitro*. **Methods** Primary mESCs were treated with estrogen (10 nmol/L) and progesterone (1 μmol/L) to induce decidualization *in vitro*, and to detect the expression of OPN during mESCs decidualization. mESCs were transfected with over-expression vector of *Opn*, *Opn* shRNA, or with blank group as a negative control. The transfection efficiency was detected by real time PCR and Western blotting. The cell proliferation was detected by CCK-8 kit. Expressions of decidual/trophoblast-layer prolactin related protein (Dtprp), vascular endothelial growth factor A (Vegfa) and its receptor 2 (Vegfr2) were detected by real time PCR and Western blotting. **Results** The mRNA levels of *Dtprp* ($P<0.001$), *Vegfa* ($P=0.004$) and *Vegfr2* ($P=0.002$) in decidualized mESCs were significantly increased, accompanied with the upregulated of *Opn* mRNA ($P=0.002$) and OPN protein ($P<0.001$) levels. *Opn* overexpression promoted mESCs proliferation ($P=0.004$), while *Opn* knockdown can inhibit mESCs proliferation ($P=0.008$). In addition, *Opn* overexpression further increased the mRNA levels of *Dtprp* ($P<0.001$), *Vegfa* ($P=0.021$), and *Vegfr2* ($P=0.012$)

in decidualized mESCs, as well as the protein level of VEGFA ($P=0.001$). *Opn* knockdown, on the other hand, inhibited the mRNA expression levels of *Dtprp* ($P=0.009$), *Vegfa* ($P=0.007$), and *Vegfr2* ($P=0.001$) in decidualized mESC, and the protein level of VEGFA ($P<0.001$). **Conclusion** OPN may play an important role in the regulation of mouse endometrial stromal cell decidualization.

【Key words】 Osteopontin; Mouse endometrium; Decidualization

Fund program: National Natural Science Foundation of China (81471456)

DOI: 10.3760/cmaj.cn101441-20200507-00264

收稿日期 2020-05-11 本文编辑 王李艳

引用本文: 张瑞, 王丽蓉, 袁月, 等. 甘肃省汉、回、藏族女性围绝经期综合征发生及其影响因素研究[J]. 中华生殖与避孕杂志, 2022, 42(1): 72-79. DOI: 10.3760/cmaj.cn101441-20200507-00264.

·流行病学研究·

甘肃省汉、回、藏族女性围绝经期综合征发生及其影响因素研究

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【摘要】 目的 探讨甘肃省汉族、回族、藏族女性围绝经期综合征的发生及相关影响因素。方法 运用分层整群抽样法选取 7290 例 40~55 岁女性为研究对象进行横断面调查, 以问卷方式调查人口学特征、婚育月经史, 并采用改良 Kupperman 评分对围绝经期综合征相关症状进行评估。资料采用 SPSS20.0 软件进行统计分析。结果 甘肃省女性自然绝经年龄为 (47.43 ± 3.99) 岁, 其中回族女性最早, 为 (47.08 ± 4.29) 岁; 职业、受教育程度以及居住地, 三个民族之间的差异均具有统计学意义 ($P<0.001$, $P=0.001$, $P=0.005$); 围绝经期综合征发生率回族为 58.85% (246/418), 藏族为 44.16% (136/308), 汉族为 41.06% (2695/6564), 三个民族之间差异具有统计学意义 ($P<0.001$); 相关症状汉族轻度人员占比最多, 回族、藏族中度人员占比最多, 三个民族之间轻度和重度的发生率差异均具有统计学意义 (均 $P<0.001$)。logistic 回归分析显示从事重体力劳动是三个民族女性发生围绝经期综合征共同的危险因素。结论 促进和帮助欠发达地区经济发展、改善农村居住条件、改变落后生活劳作模式, 加大教育及医疗卫生的投入、加强生殖健康

知识的普及, 针对各民族围绝经期综合征发生的相关危险因素逐项改善, 将有助于围绝经期综合征预防和诊治工作的开展, 对促进各民族女性健康工作起到积极作用。

【关键词】 民族; 绝经; 自然绝经年龄; 围绝经期综合征

A study on the occurrence and influencing factors of perimenopausal syndrome among Han, Hui and Tibetan women in Gansu Province

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【Abstract】 Objective To explore the occurrence and influencing factors of perimenopausal syndrome among Han, Hui and Tibetan women in Gansu Province.

Methods A stratified cluster sampling method was used to select 7290 women aged 40–55 years as the research subjects for cross-sectional survey. The questionnaire was used to investigate demographic characteristics, marriage and childbearing menstrual history, and the modified Kupperman score was used to investigate the symptoms related to perimenopausal syndrome. The data were statistically analyzed using SPSS20.0 software. **Results** The natural menopausal age of women in Gansu Province was (47.43±3.99) years old, Hui women had the earliest age of menopause (47.08±4.29). There were statistically significant differences in occupation, education level and residence among the three ethnic groups ($P<0.001$, $P=0.001$, $P=0.005$). The incidence of perimenopausal syndrome was 58.85% (246/418) for Hui, 44.16% (136/308) for Tibetans, and 41.06% (2695/6564) for Hans. The incidence of perimenopausal syndrome and the grade of related symptoms were significantly different among the three ethnic groups (all $P<0.001$). Han women had the highest proportion of mild symptoms, while Hui women and Tibetan women had the highest proportion of moderate symptoms. The differences of the incidence of mild and severe symptoms among the three ethnic groups were statistically significant (all $P<0.001$). Logistic regression analysis showed that engaging in heavy physical labor is a common risk factor for the incidence of perimenopausal syndrome in the three ethnic groups. **Conclusion** The prevention and treatment of perimenopausal syndrome can be carried out from the following aspects: promoting economic development, improving living conditions, changing life and work patterns, increasing investment in education, medical and health care, and strengthening knowledge popularization.

【 Key words 】 Ethnicity; Menopause; Age of natural menopause; Menopausal syndrome

DOI: 10.3760/cmaj.cn101441-20200707-00383

收稿日期 2020-07-15 责任编辑 宋培培

引用本文: 陈镒, 谢雅婷, 郭闻亚, 等. POSEIDON 标准及其在辅助生殖中的应用[J]. 中华生殖与避孕杂志, 2022, 42(1): 80-85. DOI: 10.3760/cmaj.cn101441-20200707-00383.

POSEIDON 标准及其在辅助生殖中的应用

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【摘要】 卵巢低反应 (poor ovarian response, POR) 通常被认为是卵巢储备低下以及卵巢对外源性促性腺激素的反应较差。欧洲人类生殖与胚胎学学会 (European Society of Human Reproduction and Embryology, ESHRE) 2011 年制定的 Bologna 标准对 POR 的诊断标准达成了首次共识, 但该人群存在异质性, 给其治疗带来了许多困难和疑惑。2016 年提出的 POSEIDON 标准, 可根据 POR 人群异质性特征进行分层, 精确定义各层人群的临床特征和诊断标准, 从而对 POR 各层人群进行精准治疗, 改善其临床治疗结局。本文就最新的 POSEIDON 标准的提出背景、人群分层特点和对应治疗研究进展做一综述。

【关键词】 卵巢低反应; POSEIDON; 累积活产率; 低预后; 临床诊疗

基金项目: 国家自然科学基金 (31400970)

POSEIDON stratification and its application in assisted reproduction

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【Abstract】 Poor ovarian response (POR) is usually defined as low ovarian reserve and poor ovarian response to exogenous gonadotropins. The Bologna criteria proposed by the European Society of Human Reproduction and Embryology (ESHRE) in 2011 reached the initial consensus on the diagnostic criteria for POR, but the heterogeneity of these patients has posed many difficulties and doubts on treatment. The POSEIDON criteria, proposed in 2016, allow for stratification based on the heterogeneous features of POR patients and the accurate definition of clinical characteristics and diagnostic criteria for each stratum, leading to precise treatment and improved clinical outcomes for POR patients. This article reviews the background of the latest POSEIDON criteria, the characteristics of the stratified population and the progress of corresponding treatment studies.

【Key words】 Poor ovarian response; POSEIDON; Cumulative live birth rate; Low prognosis; Clinical treatment

Fund program: National Natural Science Foundation of China (31400970)

·综述·

DOI: 10.3760/cmaj.cn101441-20200614-00343

收稿日期 2020-06-22 本文编辑 宋培培

引用本文: 张晨露, 潘宇, 龙亚玲, 等. 卵巢低反应人群的个体化控制性卵巢刺激的研究进展[J]. 中华生殖与避孕杂志, 2022, 42(1): 86-90. DOI: 10.3760/cmaj.cn101441-20200614-00343.

卵巢低反应人群的个体化控制性卵巢刺激的研究进展

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【摘要】 卵巢低反应 (poor ovarian response, POR) 人群主要表现为对促性腺激素反应不良, 周期结局较差, 它的管理是辅助生殖技术中面临的主要难题之一。近几年提出的基于博洛尼亚标准的波塞冬标准对 POR 患者进行分层, 更有利于患者的个体化管理, 在一定程度上有利于改善患者的妊娠结局。本文将从 POR 患者的诊断、排卵方案的制定、排卵的触发、个体化的辅助治疗等方面对最新的基于波塞冬标准的个体化治疗的研究进展进行总结。

【关键词】 生殖技术, 辅助; 排卵诱导; 卵巢低反应; 个体化治疗; 博洛尼亚标准; 波塞冬标准

Progress of individualized controlled ovarian stimulation in people with poor ovarian response

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【Abstract】 Women with poor ovarian response (POR) is really hard to respond to controlled ovarian stimulation, which leads to lower success rates in *in vitro* fertilization. The management of these special group of people has been proved to be one of the main difficulties in assisted reproductive technology (ART). Compared with the Bologna Criteria, POSEIDON criteria which has suggested a new

categorization of ART in patients with POR, is much better in individuation patient management and is significant to improve the pregnancy outcome of patients to some extent. The review aims to summarize recent insights on individualized management of POR patients, including the diagnosis, controlled ovarian stimulation plans, triggering of ovulation and individual assisted therapy.

【Key words】 Reproductive techniques, assisted; Ovulation induction; Poor ovarian response; Individualization; Bologna criteria; POSEIDON criteria

·综述·

DOI: 10.3760/cmaj.cn101441-20200531-00320

收稿日期 2020-06-08 本文编辑 孙敏

引用本文: 高玲芸, 王文君. 卵泡刺激素受体信号调节及相关生物学功能研究进展[J]. 中华生殖与避孕杂志, 2022, 42(1): 91-95. DOI: 10.3760/cmaj.cn101441-20200531-00320.

卵泡刺激素受体信号调节及相关生物学功能研究进展

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【摘要】 卵泡刺激素 (follicle-stimulating hormone, FSH) 是调节卵巢颗粒细胞和睾丸支持细胞功能的重要激素, 其作用由卵泡刺激素受体 (follicle-stimulating hormone receptor, FSHR) 介导。FSHR 下游信号通路包括 G 蛋白介导的下游信号、辅助信号分子参与激活的下游信号、与其他胞质膜信号分子相互作用产生的信号等。近年来随着科学技术的发展, FSHR 信号的精细调节方式被进一步揭示, 组学技术的广泛应用也为信号调控机制的研究提供了更多的方法和可能性。此外, 大量最新研究显示非性腺组织中广泛分布具有生物学活性的 FSHR, 可能与绝经后相关并发症如骨质疏松和代谢综合征有关, 肿瘤组织、生殖系统非性腺组织以及胎儿组织等部位的 FSHR 可能也具有促血管生成等生物学功能, 提示 FSH 可能在多系统生理病理过程中均发挥作用, 这为 FSHR 的相关研究开展提供了全新的视角, 本文就此进行综述。

【关键词】 卵泡刺激素受体; 颗粒细胞; 信号通路; 蛋白激酶 A; G 蛋白偶联受体

Research progress in follicle-stimulating hormone receptor signaling regulation and biological functions

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【 Abstract 】 Follicle-stimulating hormone (FSH), functioning through binding to follicle-stimulating hormone receptors (FSHR), is the key hormone regulating biological functions of granulosa cells and Sertoli cells. Signals intermediated by FSHR mainly transduced by G protein, adaptor proteins and other membrane receptors. With rapid development of analytical chemistry and multi-omics technologies, detailed regulation mode of FSHR signaling have been unveiled in recent years. From a macroscopic view, recent researches have indicated the existence of FSHR in various extra-gonadal tissues, which play biological functions in various diseases including postmenopausal related diseases, chronic renal insufficiency, and lipid metabolic disorder. FSHR in other extra-gonadal tissues such as malignant tumor and reproductive tissue may also exert functional effects like angiogenesis. These evidences suggest a systematic role of FSHR beyond gonadal tissue and provide a brand-new perspective to view this classical G protein-coupled receptor. Current work reviews recent research progress in FSH/FSHR signaling regulation and new biological functions regarding FSHR expression beyond gonadal tissue.

【 Key words 】 Follicle-stimulating hormone receptor; Granulosa cells; Signaling pathway; Protein kinase A; G protein-coupled receptor

·综述·

DOI: 10.3760/cma.j.cn101441-20201125-00639

收稿日期 2020-12-02 本文编辑 孙敏

引用本文: 王阳, 陈小攀, 舒静. 卵泡刺激素受体基因失活突变导致卵巢功能减退的研究进展[J]. 中华生殖与避孕杂志, 2022, 42(1): 96-103. DOI: 10.3760/cma.j.cn101441-20201125-00639.

卵泡刺激素受体基因失活突变导致卵巢功能减退的研究进展

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【摘要】 卵泡刺激素 (follicle-stimulating hormone, FSH) 通过激活靶细胞上特定的 FSH 受体 (FSH receptor, FSHR) 而发挥作用。FSHR 对女性卵泡的发育和雌二醇生成, 以及对男性睾丸支持细胞的功能维持和精子形成具有至关重要的作用。在过去的二十余年中, 已通过较多的病例鉴定了 *FSHR* 基因失活、激活的突变位点以及单核苷酸多态性。*FSHR* 基因型-表型的相关性研究和突变受体体外功能实验研究有助于了解患者不孕的遗传学原因。本综述总结已报道的 *FSHR* 基因不同部位的失活突变及其对女性生殖系统的功能影响。

【关键词】 卵泡刺激素受体; 失活突变; 早发型卵巢功能不全; 卵巢抵抗综合征; 卵巢早衰; 闭经

基金项目: 国家自然科学基金 (81701460); 浙江省医药卫生科技计划 (2019KY033、2019KY021、2020KY414、2020KY448); 生殖遗传教育部重点实验室 (浙江大学) 开放基金 (ZDFY2020-RG-0006)

Research advances in the decreased ovarian function of follicle-stimulating hormone receptor inactivating mutations

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【Abstract】 Follicle-stimulating hormone (FSH) brings about physiological actions by activating specific FSH receptor (FSHR) on target cells. FSHR plays an important role in the development of follicles, the production of estradiol in females, the maintenance of the function of testicular Sertoli cells and the spermatogenesis in males. In the past two decades, a large number of cases have been used to identify the inactivating/activating mutations and single nucleotide polymorphisms of *FSHR* gene. According to the genotype-phenotype correlation research and *in vitro* functional experiments of *FSHR* gene may help to understand the causes of infertility in affected patients. This review summarizes the inactivating mutations which have been reported in different parts of *FSHR* and their impacts on female reproductive system.

【Key words】 Follicle-stimulating hormone receptor; Inactivating mutation; Premature ovarian insufficiency; Resistant ovary syndrome; Premature ovarian failure; Amenorrhea

Fund program: National Natural Science Foundation of China (81701460); General Research Program for Medicine and Health of Zhejiang Province (2019KY033, 2019KY021, 2020KY414, 2020KY448); Open Fund of Key Laboratory of

DOI: 10.3760/cmaj.cn101441-20200615-00344

收稿日期 2020-06-17 本文编辑 王李艳

引用本文: 唐芷菁, 张炜. CD55 对子宫内膜的影响及可能机制[J]. 中华生殖与避孕杂志, 2022, 42(1): 104-108. DOI: 10.3760/cmaj.cn101441-20200615-00344.

CD55 对子宫内膜的影响及可能机制

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【摘要】 妊娠的建立依赖于子宫内膜正常的功能状态, CD55 在分泌期子宫内膜表达逐渐上调并在分泌中期达到峰值, 而 CD55 的异常表达与反复流产和着床失败、子宫内膜异位症、内膜癌等多种子宫内膜相关疾病有关。除了作为补体调节蛋白抑制补体介导的细胞杀伤作用以外, CD55 在子宫内膜中还参与调节细胞周期, 促进细胞增殖抑制凋亡, 促进细胞侵袭迁移与黏附等生物学行为; 此外, CD55 还可结合其配体 CD97 作为 T 细胞及自然杀伤细胞的抑制性调节信号, 在非免疫细胞则参与促进细胞的侵袭迁移。本文通过对 CD55 在子宫内膜中的作用及可能机制进行综述, 为探究 CD55 在子宫内膜容受性建立和胚胎着床中的作用提供更多依据。

【关键词】 CD55; 子宫内膜; 妊娠; 生物学行为

基金项目: 国家自然科学基金 (81771587)

Function and potential mechanism of CD55 in endometrium

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【Abstract】 The establishment of pregnancy depends on the normal function of endometrium. CD55 is up-regulated in the secretory endometrium and reaches the peak during the window of implantation, while abnormal expression of CD55 is associated with recurrent abortion, repeated implantation failure, endometriosis, endometrial cancer and other endometria-related diseases. Besides inhibiting the complement-dependent cytotoxicity as a complement regulatory protein, CD55 in endometrium also plays a role in regulating cell cycle, promoting cell proliferation, inhibiting apoptosis, and promoting cell invasion, migration and adhesion. CD55 can

also bind its ligand CD97 as inhibitory signals of T cells and natural killer (NK) cells and participate in promoting cell invasion and migration in non-immune cells. This review summarizes the role of CD55 in endometrium and its potential regulatory mechanism, providing more evidence for exploring the function of CD55 in endometrial receptivity establishment and embryo implantation.

【Key words】 CD55; Endometrium; Gestation; Biological behavior

Fund program: National Natural Science Foundation of China (81771587)