

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40卷 第4期 2020年4月25日出版

主 管

中国科学技术协会

主 办

中华医学会
上海市计划生育科学研究所
复旦大学附属妇产科医院

编 辑

中华生殖与避孕杂志
编辑委员会
200237,上海市老沪闵路779号
电话:(021)64438169
传真:(021)64438975
Email:rande@sippr.org.cn
http://zhshzybyzz.yiigle.com

总编辑

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出 版

《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20170015号

印 刷

上海商务联西印刷有限公司

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@sippr.org.cn

定 价

每期20.00元,全年240.00元

中国标准连续出版物号

ISSN 2096-2916

CN 10-1441/R

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本刊稿约见本卷第1期封二

本期责任编辑乔杰

本期责任编辑孙敏

本期责任编辑张蔚森

CHINESE JOURNAL OF REPRODUCTION AND CONTRACEPTION

(Original title: *Reproduction and Contraception*)

Monthly

Established in December 1980

Volume 40, Number 4

April 25, 2020



Responsible Institution

China Association for Science and Technology

Sponsor

Chinese Medical Association, Shanghai Institute of Planned Parenthood Research, Obstetrics and Gynecology Hospital of Fudan University

Editing

Editorial Board of Chinese Journal of Reproduction and Contraception
779 Laohumin Road, Shanghai 200237, China
Tel: 0086-21-64438169
Fax: 0086-21-64438975
Email: randc@sippr.org.cn
http://zhshzybyzz.yiigle.com
http://www.medline.org.cn

Editor-in-Chief

Qiao Jie

Managing Director

Wang Jian

Publishing

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

Printing

Business Book Printing Shop Shanghai Printing Co., LTD

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: randc@sippr.org.cn

CSSN

ISSN 2096-2916
CN 10-1441/R

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DOI : 10.3760/cma.j.cn101441-20190902-00395

收稿日期 2019-09-18 本文编辑 王李艳

引用本文：代玮, 胡琳莉. 卵泡期长效长方案在卵巢高储备人群中的最佳获卵数分析[J]. 中华生殖与避孕杂志, 2020, 40(4): 265-270. DOI: 10.3760/cma.j.cn101441-20190902-00395.

·临床研究·

卵泡期长效长方案在卵巢高储备人群中的最佳获卵数分析

代玮 胡琳莉

郑州大学第一附属医院生殖医学中心 450052

通信作者：胡琳莉，Email：hulinli1999@163.com，电话：+86-371-66913635

【摘要】 目的 观察卵泡期长效长方案应用于卵巢高储备人群的临床特征及最佳获卵数分析。方法 回顾性分析 2015 年 8 月至 2019 年 7 月期间在郑州大学第一附属医院生殖医学中心接受第一周期体外受精/卵胞质内单精子注射(IVF/ICSI)助孕、采用卵泡期长效长方案助孕的 5168 例卵巢多囊样改变/多囊卵巢综合征(PCO/PCOS)患者的临床资料，根据取卵后是否因卵巢高反应行全部胚胎冷冻分为高反应冷冻胚胎组及对照组，根据移植后是否发生中重度卵巢过度刺激综合征(OHSS)分为中重度 OHSS 组及对照组。根据获卵数分为 6 组：<6、6~10、11~15、16~20、21~25 和 ≥26。比较各分组间的临床特征及不同获卵数分组的临床妊娠率、高反应冷冻胚胎率、中重度 OHSS 率。采用 logistics 回归分析获卵数与卵巢高反应及移植后中重度 OHSS 的相关性。结果 在使用卵泡期长效长方案的 PCO/PCOS 周期中，获卵数 6~10、11~15、16~20 能获得满意的临床妊娠率 (72.05%、74.29%、76.17%) 及较低的高反应冷冻胚胎率 (2.46%、10.01%、23.59%)。矫正混杂因素后，获卵数是影响卵巢高反应全部胚胎冷冻的独立因素 ($OR=2.159$, 95% $CI=2.027\sim2.300$, $P<0.001$)，与移植后中重度 OHSS 无明显相关性 ($OR=0.755$, 95% $CI=0.553\sim1.031$, $P=0.077$)。结论 对于 PCO/PCOS 患者采用卵泡期长效长方案，获卵数 6~20 枚可达到满意的周期结局。

【关键词】 促性腺激素释放激素激动剂长方案； 长效促性腺激素释放激素激动剂； 卵巢高储备； 卵巢高反应； 卵巢过度刺激综合征

Optimum number of oocytes retrieved of follicular phase long-acting long protocol in patients with high ovarian reserve

Dai Wei, Hu Linli

Reproductive Medical Center, the First Affiliated Hospital of Zhengzhou University, Zhengzhou 450052, China

Corresponding author: Hu Linli, Email: hulinli1999@163.com, Tel: +86-371-66913635

【Abstract】 Objective To observe the clinical characteristics and the optimum number of oocytes retrieved of follicular phase long-acting long protocol in patient with high ovarian reserve. **Methods** A total of 5168 patients with polycystic ovary/polycystic ovary syndrome (PCO/PCOS) underwent *in vitro* fertilization/intracytoplasmic sperm injection (IVF/ICSI) in Reproductive Medical Center, the First Affiliated Hospital of Zhengzhou University from August 2015 to July 2019 were retrospectively identified. The cycles were divided into two groups according if “freeze all embryos” for high ovarian response, divided into groups according to whether the patients underwent moderate to severe ovarian hyperstimulation syndrome (OHSS) after embryo transfer, and divided

into six groups for the number of oocytes retrieved: <6 , $6-10$, $11-15$, $16-20$, $21-25$, ≥ 26 . Clinical characteristics, clinical pregnancy rate, freeze-all rate for high response and moderate to severe OHSS rate after embryo transfer in different groups were compared. Logistic regression analysis was used to analyze the correlation of the number of oocytes retrieved to high ovarian response and the moderate or severe OHSS occurrence after embryo transfer. **Results** In IVF cycles stimulated with follicular phase long-acting long protocol , the optimal number of oocytes for achieving clinical pregnancy was $6-10$, $11-15$, $16-20$ (72.05% , 74.29% , 76.17%) , and also had a lower chance of all embryo frozen rate (2.46% , 10.01% , 23.59%) . The number of oocytes retrieved was associated with embryo frozen rate ($OR=2.159$, $95\% CI=2.027-2.300$, $P<0.001$) , and not associated with moderate to severe OHSS after embryo transfer ($OR=0.755$, $95\% CI=0.553-1.031$, $P=0.077$) . **Conclusion** The optimal number of oocytes for PCO/PCOS patient stimulated with follicular phase long-acting long protocol is between 6 and 20.

【Key words】 Gonadotropin-releasing hormone agonist long protocol ; Long-acting gonadotropin-releasing hormone agonist ; High ovarian reverse ; High ovarian response ; Ovarian hyperstimulation syndrome

DOI : 10.3760/cma.j.cn101441-20190508-00186

收稿日期 2019-05-23 本文编辑 王李艳

引用本文：何湘娇, 赵静, 张琼, 等. 血清与卵泡液 25-羟维生素 D 水平与体外受精-胚胎移植妊娠结局的相关性研究[J]. 中华生殖与避孕杂志, 2020, 40(4): 271-278. DOI: 10.3760/cma.j.cn101441-20190508-00186.

·临床研究·

血清与卵泡液 25-羟维生素 D 水平与体外受精-胚胎移植妊娠结局的相关性研究

何湘娇 赵静 张琼 侯昭娟 谢诗 郝洁 黄曦 何爱桦 傅婧 李艳萍

中南大学湘雅医院生殖中心 湖南省女性生殖健康临床研究中心, 长沙 410008

何湘娇现工作于湖南省人民医院(湖南师范大学第一附属医院)妇产科

通信作者：李艳萍，Email：liyanp@csu.edu.cn，电话：+86-13607317798

【摘要】 目的 研究血清和卵泡液中 25-羟维生素 D[25(OH)D]水平与体外受精/卵胞质内单精子注射-胚胎移植 (IVF/ICSI-ET) 妊娠结局的关系。方法 2017 年 8 月至 2018 年 6 月期间前瞻性队列研究在中南大学湘雅医院生殖中心因输卵管因素接受 IVF/ICSI-ET 治疗的 201 例不孕症患者的临床资料。血清和卵泡液 25(OH)D 水平的 cut-off 值采用最小化 P 值的方法确定。分析血清与卵泡液 25(OH)D 水平相关性；分组比较血清或卵泡液的 25(OH)D 水平与年龄、体质量指数 (BMI)、既往 IVF 史、人绒毛膜促性腺激素 (hCG) 注射日子宫内膜厚度、促性腺激素(Gn)、孕酮、雌二醇、获卵数、MII 卵数、正常受精率、第 3 日 (D3) 优质胚胎率及与胚胎着床率、临床妊娠率及早期流产率间有无关联。将妊娠结局的影响因素进行二分类 logistic 回归分析。结果 ①血清 25(OH)D 水平为 16.4 (13.1 , 20.2) $\mu\text{g/L}$, 卵泡液 25(OH)D 水平为 15.3 (11.6 , 20.3) $\mu\text{g/L}$, 两者比较呈显著直线相关 ($r=0.78$, $P<0.001$) 。②血清 25(OH)D 低水平组的临床妊娠率

(33.87%)、胚胎着床率 (25.44%) 低于高水平组 (52.52%, $P=0.014$; 40.24%, $P=0.006$) ; 卵泡液 25(OH)D 低水平组的临床妊娠率(39.39%)、胚胎着床率(30.22%)低于高水平组 (53.92%, $P=0.039$; 40.98%, $P=0.032$) , 卵泡液低水平组的早期流产率 (17.95%) 明显高于高水平组 (7.27%, $P=0.002$) , 差异有统计学意义。③二分类 logistic 回归分析显示血清和卵泡液 25(OH)D 水平与临床妊娠结局相关 ($P=0.016$; $P=0.020$) 。结论 血清 25(OH)D 水平高于卵泡液 25(OH)D 水平, 呈显著直线相关性; 血清和卵泡液 25(OH)D 水平与 IVF/ICSI-ET 妊娠结局相关。

【关键词】 受精,体外; 胚胎移植; 25-羟维生素 D; 妊娠结局

临床试验注册: 中国临床试验注册中心 (ChiCTR-ROC-17013441)

Relationship between serum and follicular fluid 25-hydroxyvitamin D levels and pregnancy outcome after *in vitro* fertilization and embryo transfer

He Xiangjiao , Zhao Jing , Zhang Qiong , Hou Zhaojuan , Xie Shi , Hao Jie , Huang Xi , He

Aihua , Fu Jing ,

Li Yanping

Department of Reproductive Medicine, Xiangya Hospital, Central South University, Clinical Research Center for Women's Reproductive Health in Hunan Province, Changsha 410008, China

He Xiangjiao is now working at Department of Gynecology and Obstetrics, Hunan Provincial People's Hospital (The First Hospital Affiliated with Hunan Normal University)

Corresponding author: Li Yanping, Email: liyanp@csu.edu.cn, Tel: +86-13607317798

【Abstract】 Objective To investigate the relationship between 25-hydroxy vitamin D [25(OH)D] in blood and follicular fluid and pregnancy outcome after *in vitro* fertilization/intracytoplasmic sperm injection-embryo transfer (IVF/ICSI-ET). **Methods** A prospective cohort study of 201 infertility patients who were treated with IVF/ICSI-ET due to fallopian tube factors in Department of Reproductive Medicine, Xiangya Hospital, Central South University was performed. The cut-off values of 25(OH)D levels in serum and follicular fluid were determined by the method of minimizing P value. The correlations was studied between serum or follicular fluid levels of 25(OH)D and age, body mass index (BMI), past IVF history, endometrial thickness. On human chorionic gonadotropin (hCG) injection day, gonadotropin (Gn), progesterone, estradiol, number of retrieved oocytes, and MII oocytes, normal fertilization rate, day 3 high-quality embryo rate, embryo implantation rate, clinical pregnancy rate and early abortion rate. Binary logistic regression analysis of influencing factors of pregnancy outcome was done. **Results** 1) The serum 25(OH)D level was 16.4(13.1, 20.2) $\mu\text{g/L}$ and the follicular fluid 25(OH)D was 15.3(11.6, 20.3) $\mu\text{g/L}$. There was a significant linear correlation between the two groups ($r=0.78$, $P<0.001$). 2) The clinical pregnancy rate (33.87%) and the embryo implantation rate (25.44%) in the low level group of 25(OH)D in serum were lower than those in the high level group (52.52%, $P=0.014$; 40.24%, $P=0.006$). The clinical pregnancy rate (39.39%) and the embryo implantation rate (30.22%) in the low level group of 25(OH)D in follicular fluid were lower than those in the high level group (53.92%, $P=0.039$; 40.98%, $P=0.032$). The early abortion rate in the low level group of 25(OH)D in follicular fluid (17.95%) was higher than that in the high level group (7.27%, $P=0.002$). 3) The results of two classification logistic regression analysis showed that the levels of 25(OH)D in serum and follicular fluid were related to clinical pregnancy outcome ($P=0.016$, $P=0.020$). **Conclusion** There was a significant linear correlation between 25(OH)D in serum and that in follicular fluid. The levels of 25(OH)D in serum and follicular fluid were correlated with the pregnancy outcome of IVF/ICSI-ET.

【Key words】 Fertilization *in vitro* ; Embryo transfer ; 25-hydroxy vitamin D ; Pregnancy outcome

Clinical trial registration: China Clinical Trials Registration Center (ChiCTR-ROC-17013441)

DOI : 10.3760/cma.j.cn101441-20190529-00216

收稿日期 2019-06-11 本文编辑 王李艳

引用本文: 杜琛, 赵杰, 梁琳, 等. 多囊卵巢综合征患者颗粒细胞 miRNA 及 mRNA 表达谱的构建[J]. 中华生殖与避孕杂志, 2020, 40(4): 279-286. DOI: 10.3760/cma.j.cn101441-20190529-00216.

·实验研究·

多囊卵巢综合征患者颗粒细胞 miRNA 及 mRNA 表达谱的构建

杜琛 赵杰 梁琳 爱伦高娃 陈秀娟

内蒙古医科大学附属医院妇产科生殖医学中心, 呼和浩特 010050

通信作者: 陈秀娟, Email: 90098687@sina.com, 电话: +86-471-3451651

【摘要】 目的 构建多囊卵巢综合征(polycystic ovary syndrome, PCOS)患者卵巢颗粒细胞中的微小 RNA(miRNA)和 mRNA 表达谱。方法 采用标准长方案, 收集 2017 年至 2018 年在内蒙古医科大学附属医院生殖医学中心接受体外受精/卵胞质内单精子显微注射(IVF/ICSI)助孕的 PCOS 患者(PCOS 组)和正常排卵女性(对照组)的卵巢颗粒细胞, 整合高通量 mRNA 和 miRNA 表达谱数据, 通过 Gene Ontology 功能富集和 KEGG Pathway 分析差异表达基因富集的生物学过程, 同时利用 miRNA 靶向调控基因的关系构建 PCOS 发病过程中核心调控网络, 预测 PCOS 相关的 mRNA 与 miRNA。结果 与对照组相比, PCOS 组中 66 个差异表达 miRNA, 其中 42 个表达上调, 24 个表达下调; mRNA 转录谱筛选出 416 个表达显著差异基因, 其中 236 个基因上调, 180 个基因下调($P<0.05$, $|\log_2FC|\geq 2$)。通过联合分析得到 miRNA-26b、miRNA-423-3p、miRNA-219a、miRNA-326、miRNA-3928-3p 和 miRNA-194-5p 关联到 107 个靶基因, 差异有统计学意义($P<0.01$)。这些靶基因涉及离子转运、细胞黏附和炎症反应等多方面功能, 以及紧密连接丝裂原活化蛋白激酶(MAPK)、Wnt 和磷脂酰肌醇-3-激酶/丝氨酸蛋白激酶 B (PI3K-Akt) 等多个信号通路。结论 PCOS 患者卵巢颗粒细胞中差异表达的 miRNA 及其调控的靶基因与其病理生理过程密切相关。

【关键词】 多囊卵巢综合征; 高通量测序; 卵巢颗粒细胞; mRNA; 微小 RNAs

基金项目: 内蒙古自治区科技厅自然科学基金(2015BS0802、2019MS08121); 内蒙古教育厅高校自然科学项目(NJZY19104)

Construction of microRNA and mRNA expression profiles in granulosa cells of patients with polycystic ovary syndrome

Du Chen, Zhao Jie, Liang Lin, Airuka, Chen Xiujuan

Reproductive Medicine Center, Obstetrics and Gynecology, Inner Mongolia Medical University Affiliated Hospital, Huhehot 010050, China

Corresponding author: Chen Xiujuan, Email: 90098687@sina.com, Tel: +86-471-3451651

【Abstract】 Objective To construct the expression profiles of microRNA (miRNA) and mRNA in ovarian granulosa cells in patients with polycystic ovary syndrome (PCOS) in search of the molecular markers of PCOS. **Methods** A standard length scheme was used to collect ovarian granulosa cells of PCOS patients (PCOS group) and normal ovulating women (control group) who received *in vitro* fertilization/intracytoplasmic sperm injection (IVF/ICSI) in the Reproductive Medicine Center of the Affiliated Hospital of Inner Mongolia Medical University from 2017 to 2018, integrate high-throughput mRNA and miRNA expression profiles, and the biological processes involved in differential expression genes were analyzed through Gene Ontology's functional enrichment and KEGG Pathway. At the same time, the core regulatory network during the pathogenesis of PCOS was constructed by using the relationship between miRNA target regulatory genes, and PCOS-related mRNAs and miRNAs were predicted. **Results** Compared with control group, 66 miRNAs with differential expression were screened in PCOS group, among which 42 miRNAs were up-regulated and 24 miRNAs were down-regulated. Totally 416 differentially expressed genes were screened by transcription profiling, among which 236 genes were up-regulated and 180 genes were down-regulated ($P<0.05$, $|\log_2FC|\geq 2$). Highly significantly

differentially expressed miRNAs (miRNA-26b, miRNA-423-3p, miRNA-219a, miRNA-326, miRNA-3928-3p and miRNA-194-5p) were associated with 107 differentially targeted genes by joint analysis, with significant differences ($P<0.01$). These target genes involve many functions such as ion transport, cell adhesion and inflammatory reactions, and multiple signal pathways such as mitogen-activated protein kinase (MAPK), Wnt and phosphatidylinositol-3-kinase/serine-threonine kinase (PI3K-Akt). **Conclusion** The expression of miRNA and its regulatory target genes in ovarian granulosa cells in patients with PCOS are closely related to their pathophysiological processes.

【Key words】 Polycystic ovary syndrome ; High-throughput sequencing ; Ovarian granulosa cells ; mRNA ; MicroRNAs

Fund program : Inner Mongolia Autonomous Region Natural Science Foundation (2015BS0802, 2019MS08121); Inner Mongolia Education Department Foundation (NJZY19104)

DOI : 10.3760/cma.j.cn101441-20190326-00122

收稿日期 2019-06-06 本文编辑 李天琦

引用本文: 马璎璇, 管海云, 王璐, 等. 多囊卵巢综合征患者颗粒细胞 mTOR 通路改变与生殖内分泌异常的相关性[J]. 中华生殖与避孕杂志, 2020, 40(4): 287-293. DOI: 10.3760/cma.j.cn101441-20190326-00122.

·实验研究·

多囊卵巢综合征患者颗粒细胞 mTOR 通路改变与生殖内分泌异常的相关性

马璎璇 管海云 王璐 张炜

复旦大学附属妇产科医院, 上海 200011

通信作者: 张炜, Email: zhangwei623@hotmail.com, 电话: +86-21-63455050

【摘要】 目的 探讨多囊卵巢综合征(PCOS)患者颗粒细胞 mTOR 和下游靶分子 p-S6k1 变化与血清性激素异常的相关性。方法 本实验收集人原代颗粒细胞进行体外培养, 测定 PCOS 组和对照组颗粒细胞 mTOR 通路的差异。培养液中添加睾酮、卵泡刺激素(FSH)、胰岛素, 并检测外源性激素对于颗粒细胞 mTOR 通路的影响。结果 PCOS 组颗粒细胞磷酸化 mTOR 水平高于对照组, 其中 PCOS 组 p-mTOR 水平(0.66 ± 0.29)高于对照组(0.34 ± 0.32), 差异存在统计学意义($P=0.02$); PCOS 组 p-S6k1 水平(0.95 ± 0.42)高于对照组(0.62 ± 0.29), 但差异无统计学意义($P>0.05$); 颗粒细胞 p-mTOR 与 p-S6k1 水平与血清睾酮相关(P 均 $=0.001$), 与血清 FSH($P=0.67$, $P=0.75$)、促黄体生成素(LH)($P=0.75$, $P=0.37$)无关。结论 PCOS 患者颗粒细胞 mTOR 信号分子存在异常活化, 睾酮与胰岛素可能参与了 PCOS 患者颗粒细胞 mTOR 通路异常磷酸化, 从而导致颗粒细胞功能障碍, 造成卵泡发育异常。

【关键词】 多囊卵巢综合征; mTOR 通路; 睾酮; 颗粒细胞

基金项目: 国家自然科学基金(81771587); 上海市科委医学引导项目(16411963400)

Correlation between changes of mTOR signaling pathway in granulosa cells and reproductive endocrine abnormalities in polycystic ovary syndrome patients

Ma Yingxuan, Guan Haiyun, Wang Lu, Zhang Wei

Obstetrics and Gynecology Hospital of Fudan University, Shanghai 200011, China
Corresponding author: Zhang Wei, Email: zhangwei623@hotmail.com, Tel: +86-21-63455050

[Abstract] Objective To evaluate the changes of mTOR signaling molecules in granulosa cells from polycystic ovary syndrome (PCOS) patients, and whether the change of mTOR signaling is related to serum hormones. **Methods** The phosphorylation levels of mTOR signaling molecules in primary granulosa cells were compared between PCOS group and control group. The correlation between phosphorylation levels of mTOR signaling and serum hormones was also analyzed. Then effects of exogenous testosterone and insulin on mTOR signaling were investigated *in vitro*. **Results** Granulosa cells from PCOS patients (0.66 ± 0.29) had higher phosphorylation levels of mTOR compared with control group (0.34 ± 0.32 , $P=0.02$). The level of p-s6k1 in PCOS group (0.95 ± 0.42) was higher than that in control group (0.62 ± 0.29), but the difference was not statistically significant ($P>0.05$). The serum testosterone was associated with p-mTOR and p-S6k1 ($P=0.01$, $P=0.01$). Serum follicle-stimulating hormone (FSH) ($P=0.67$, $P=0.75$) and luteinizing hormone (LH) ($P=0.75$, $P=0.37$) levels were irrelevant with p-mTOR and p-S6k1. **Conclusion** Granulosa cells from PCOS patients had higher activated mTOR signaling. Testosterone and insulin could elevate the phosphorylation levels of mTOR signaling of granulosa cells *in vitro*, which maybe contributed to the dysfunction of granulosa cells and follicular development stagnation of PCOS.

[Key words] Polycystic ovary syndrome ; mTOR signaling ; Testosterone ; Granulosa cells

Fund program : National Natural Science Foundation of China (81771587); Leading Project of Shanghai Municipal Science and Technology Commission (16411963400)

DOI : 10.3760/cma.j.cn101441-20190711-00301

收稿日期 2019-07-15 本文编辑 李天琦

引用本文：金海霞, 王赛赛, 石森林, 等. 不同胚胎培养试剂胚胎发育时间动力学参数、胚胎发育潜能及临床结局的比较[J]. 中华生殖与避孕杂志, 2020, 40(4): 294-300. DOI: 10.3760/cma.j.cn101441-20190711-00301.

·实验研究·

不同胚胎培养试剂胚胎发育时间动力学参数、胚胎发育潜能及临床结局的比较

金海霞 王赛赛 石森林 宋文妍 刘艳 闻爽 吴翌婷

郑州大学第一附属医院生殖中心, 河南省郑州大学第一附属医院生殖与遗传重点实验室 450052

通信作者: 金海霞, Email: jinhx@zzu.edu.cn, 电话: +86-13523488589

[摘要] 目的 比较不同胚胎培养试剂对胚胎发育时间动力学参数、胚胎发育潜能及临床妊娠结局影响。方法 回顾性分析 2016 年 9 月至 2018 年 5 月期间于郑州大学第一附属医院生殖医学中心行体外受精/卵胞质内单精子注射(IVF/ICSI)助孕患者资料, 按照胚胎培养试剂不同, 分为 Vitrolife 组和 Cook 组, 比较符合入选标准的 470 个新鲜移植周期患者的胚胎时间动力学参数、胚胎发育潜能及临床妊娠结局。结果 与 Cook 组比较, Vitrolife 组原核出现时间、消失时间、发育到 3-细胞和 8-细胞时间更快[tPNa: (7.12 ± 2.71) h 比 (7.40 ± 2.61) h, tPNf: (23.83 ± 4.33) h 比 (24.21 ± 4.74) h, t3: (35.75 ± 6.03) h 比 (36.64 ± 6.16) h, t4: (38.30 ± 6.25) h 比 (38.92 ± 6.06) h, t5: (47.59 ± 7.85) h 比 (49.01 ± 7.86) h, t6: (50.77 ± 7.17) h 比 (52.12 ± 6.99) h, t7: (53.05 ± 6.31) h 比 (54.33 ± 6.37) h, t8: (55.35 ± 6.89) h 比

(56.31 ± 6.41) h], 差异均有统计学意义(P 均 <0.05); 细胞周期 s2 差异无统计学意义, 在细胞周期同步性比较中, cc2 [(9.71 ± 4.60) h 比 (10.33 ± 4.28) h] 差异有统计学意义, Cook 组具有更长的细胞周期, 细胞发育时间间隔 t5-t4 [(10.60 ± 5.65) h 比 (11.20 ± 5.90) h], t8-t4 [(18.45 ± 5.76) h 比 (19.28 ± 5.18) h], 差异均有统计学意义(P 均 <0.05), 然而 t2、t4-t2 差异无统计学意义。两种胚胎培养试剂胚胎发育潜能比较显示, Cook 组胚胎利用率(59.9%)、第 3 日 (D3) 优质胚胎率(65.4%)高于 Vitrolife 组(63.9%, $P=0.017$; 69.5%, $P=0.011$); 两组种植率、胚胎种植率、囊胚种植率、受精率、卵裂率差异均无统计学意义 (P 均 >0.05); 临床妊娠率、持续妊娠率、流产率、分娩率、活产率、胎儿畸形率、活产男女比例、胚胎妊娠率、囊胚妊娠率组间比较差异均无统计学意义 (P 均 >0.05)。结论 各中心应根据本中心的实际情况, 摸索出适合本中心的胚胎培养试剂的胚胎时间动力学参数, 制定符合最佳胚胎培养试剂选择标准, 提高本中心患者临床妊娠率及活产率。

【关键词】 延时成像; 胚胎培养试剂; 胚胎发育潜能; 时间动力学; 临床结局

Comparison of embryonic development time kinetic parameters, embryo development potential and clinical outcomes of different embryo culture reagents

Jin Haixia, Wang Saisai, Shi Senlin, Song Wenyan, Liu Yan, Wen Shuang, Wu Zhaoting

Center for Reproductive Medicine of the First Affiliated Hospital of Zhengzhou University, Henan Key Laboratory of Reproduction and Genetics, the First Affiliated Hospital of Zhengzhou University, Zhengzhou 450052, China

Corresponding author: Jin Haixia, Email: jinhx@zzu.edu.cn, Tel: +86-13523488589

【Abstract】 Objective To compare the effects of two embryo culture reagents on embryonic developmental time dynamics, embryonic development potential and clinical pregnancy outcomes. **Methods** The data of patients undergoing *in vitro* fertilization/intracytoplasmic sperm injection (IVF/ICSI) were retrospectively analyzed at the Center for Reproductive Medicine of the First Affiliated Hospital of Zhengzhou University from September 2016 to May 2018. According to the different embryo culture reagents, they were divided into Vitrolife group and Cook group, comparing the embryonic time dynamics parameters, embryo development potential and clinical pregnancy outcomes of 470 patients who met the criteria. **Results** There were significant differences in the kinetic parameters of embryo development between the two different embryo culture reagents. Compared with Cook group, Vitrolife group had shorter time in pronuclei appearance and disappearance, and time of development to 3-cell and 8-cell embryos [tPNa: (7.12 ± 2.71) h vs. (7.40 ± 2.61) h, tPNf: (23.83 ± 4.33) h vs. (24.21 ± 4.74) h, t3: (35.75 ± 6.03) h vs. (36.64 ± 6.16) h, t4: (38.30 ± 6.25) h vs. (38.92 ± 6.06) h, t5: (47.59 ± 7.85) h vs. (49.01 ± 7.86) h, t6: (50.77 ± 7.17) h vs. (52.12 ± 6.99) h, t7: (53.05 ± 6.31) h vs. (54.33 ± 6.37) h, t8: (55.35 ± 6.89) h vs. (56.31 ± 6.41) h, all $P<0.05$]. There was no significant difference in cell cycle s2 and had a significant difference in cc2 [9.71 ± 4.60) h vs. (10.33 ± 4.28) h, $P<0.001$], synchronized in cell cycle in the sexual comparison. Cook group had a longer cell cycle, cell development time interval t5-t4 [(10.60 ± 5.65) h vs. (11.20 ± 5.90) h], t8-t4 [(18.45 ± 5.76) h vs. (19.28 ± 5.18) h] with statistically significant differences, all $P<0.05$, but there was no significant difference at t2 and t4-t2. Comparing the embryo development potential of the two embryo culture reagents, embryo utilization rate (59.9% vs. 63.9%, $P=0.017$) and day 3 (D3) high-quality embryo rate (65.4% vs. 69.5%, $P=0.011$) in Cook group were higher than those in Vitrolife group. There were no significant differences in implantation rate, embryo implantation rate, blastocyst implantation rate, fertilization rate and cleavage rate ($P>0.05$). The clinical pregnancy rate, the continuous pregnancy rate (OPR), the abortion rate, the delivery rate, the live birth rate, the fetal malformation rate, the male to female ratio, the embryo pregnancy rate, and the blastocyst pregnancy rate were not statistically different ($P>0.05$). **Conclusion** According to the actual situation of the center, each center should find out the embryo time kinetic parameters suitable for the embryo culture reagent of the center, and establish the selection standard of the best embryo culture reagent, so as to improve the clinical pregnancy rate and live birth rate of the patients in the center.

【Key words】 Time-lapse imaging; Embryo culture media; Embryonic development potential; Time dynamics; Clinical outcome

DOI: 10.3760/cma.j.cn101441-20200128-00050

收稿日期 2020-01-30 本文编辑 孙敏

引用本文: 袁冬, 李玉艳, 张慧英. 中国妇女产后 2 年内避孕措施使用及意外妊娠率影响因素分析[J]. 中华生殖与避孕杂志, 2020, 40(4): 301-308. DOI: 10.3760/cma.j.cn101441-20200128-00050.

·流行病学研究·

中国妇女产后 2 年内避孕措施使用及意外妊娠率影响因素分析

袁冬¹ 李玉艳² 张慧英¹

¹天津医科大学总医院 300052; ²复旦大学生殖与发育研究院上海市计划生育科学研究所, 国家卫生健康委员会计划生育药具重点实验室 200237

通信作者: 张慧英, Email: huiying_zhang@163.com, 电话: +86-15900320106

【摘要】 目的 分析中国妇女产后 2 年内避孕措施及意外妊娠风险影响因素。方法 在我国东、中、西部地区 15 个省区市 60 家医院, 通过电话各随机调查 2015 年 7 月至 2016 年 6 月期间 300 名分娩产妇, 内容包括产后母乳喂养、月经和性生活恢复、避孕措施以及是否意外妊娠等情况。分析其产后 2 年内避孕措施及意外妊娠风险因素。结果 共调查 18 045 名产妇, 其中有 15 328 名(84.9%)产妇产后 2 年内使用了避孕措施。使用避孕措施的产妇 2 年内意外妊娠率为 7.16%, 71.88%发生于产后 7~18 个月, 产后不同时间段发生意外妊娠率差异具有统计学意义($P<0.001$)。除体外排精/安全期避孕措施外, 避孕套、长效避孕方法、短效口服避孕药和其他(紧急避孕/杀精剂)4 种避孕措施在不同地区的构成比差异均有统计学意义($P<0.001$, $P<0.001$, $P=0.01$, $P<0.001$)。单因素分析显示, 产妇年龄、民族、教育程度、地域、分娩方式、产次、孕次、产后避孕方式、产后避孕启动时间、产后性生活恢复时间、产后月经恢复时间、母乳喂养时间与产后 2 年内意外妊娠率有关(P 均 <0.001)。多元 logistic 回归分析显示, 地域($P<0.001$)、产妇年龄($P<0.001$)、教育程度($P<0.001$)、民族($P=0.01$)、孕次($P=0.04$)、产次($P=0.02$)、母乳喂养时间($P<0.001$)、分娩方式($P=0.01$)、产后避孕方法($P<0.001$)、产后月经恢复时间($P=0.01$)和产后避孕启动时间($P=0.02$)是产后 2 年内意外妊娠的独立风险因素。结论 我国妇女产后 2 年内意外妊娠较高, 存在显著的地理差异, 易受产妇个人特征的影响。我国应进一步完善产后避孕宣教和服务制度, 推广以服务对象为中心的避孕咨询方法和个体化避孕方案, 切实降低意外妊娠对母婴健康的伤害。

【关键词】 产后; 避孕方法; 意外妊娠率; 危险因素

基金项目: 上海市计划生育科学研究所攀登计划项目资助 (PD2017-10)

Analysis of contraceptive use and the influencing factors of accidental pregnancy rate in Chinese women within 2 years after delivery

Yuan Dong¹, Li Yuyan², Zhang Huiying¹

¹ Tianjin Medical University General Hospital, Tianjing 300052, China; ² Key Lab of Reproduction Regulation of NHFPC, SIPPR, IRD, Fudan University, Shanghai 200237, China

Corresponding author: Zhang Huiying, Email: huiying_zhang@163.com, Tel: +86-15900320106

【Abstract】 Objective To analyze the contraceptive measures and the risk factors of accidental pregnancy in Chinese women within 2 years after delivery. **Methods** In 60 hospitals in 15 provinces in eastern, central and western China, 300 pregnant women were randomly surveyed in each hospital by telephone from July 2015 to June 2016, including postpartum breast-feeding, menstrual and sexual recovery, contraceptive measures, and accidental pregnancy. The contraceptive measures and risk factors of accidental pregnancy in 2 years after delivery were analyzed. **Results** Of the 18 045 women surveyed, 15 328 women (84.9%) had used contraception within 2 years after delivery. The rate of 2-year accidental pregnancy was 7.16% and 71.88% occurred between 7 and 18 months postpartum. The rate of accidental pregnancy at different postpartum periods was statistically significant ($P<0.001$). There were statistically significant differences in the composition ratio of condoms, long-acting contraceptive methods, combination oral contraceptives and other (emergency contraception/spermicide) contraceptive methods in eastern, central and western regions ($P<0.001$, $P<0.001$, $P=0.01$, $P<0.001$). Single factor analysis showed that maternal age, nationality, education level, region, delivery way, delivery times, No. of pregnancies, postpartum contraceptive method, postpartum contraceptive start time, postpartum sexual recovery time, postpartum menstrual recovery time, and breastfeeding time were related to the rate of 2-year accidental pregnancy (all $P<0.001$). Multivariate logistic regression analysis showed that the region ($P<0.001$), maternal age ($P<0.001$), education level ($P<0.001$), nationality ($P=0.01$), No. of pregnancies ($P=0.04$), delivery times ($P=0.02$), breastfeeding time ($P<0.001$), delivery way ($P=0.01$), postpartum contraceptive methods ($P<0.001$), postpartum menstruation recovery time ($P=0.01$) and postpartum contraception startup time ($P=0.02$) were the risk factor of 2-year accidental pregnancy. **Conclusion** Accidental pregnancy rate in 2 years after delivery is higher in Chinese women. In order to reduce the harm of accidental pregnancy to maternal and child health, China should further improve the postpartum contraception education and service system, promote the service object-centered contraceptive counseling method and individual contraception plan.

【Key words】 Postpartum ; Contraception ; Accidental pregnancy rate ; Risk factors

Fund program : Pandeng Program of Shanghai Institute of Planned Parenthood Research (PD2017-10)

DOI : 10.3760/cma.j.cn101441-20190807-00349

收稿日期 2019-08-18 本文编辑 孙敏

引用本文 : 谷保霞, 王璐, 尚小改, 等. 赠受卵双方体外受精-胚胎移植助孕结局的临床分析[J]. 中华生殖与避孕杂志, 2020, 40(4): 309-313. DOI: 10.3760/cma.j.cn101441-20190807-00349.

·临床报道·

赠受卵双方体外受精-胚胎移植助孕结局的临床分析

谷保霞 王璐 尚小改 王珂 李妍 崔趁趁 张翠莲

河南省人民医院生殖医学中心, 郑州大学人民医院, 河南大学人民医院 450003

通信作者: 张翠莲, Email: luckyzcl@qq.com, 电话: +86-371-87160762

【摘要】 目的 探讨赠受卵双方体外受精-胚胎移植(IVF-ET)患者的临床结局。 **方法** 回顾性分析 2011 年 1 月到 2016 年 12 月期间在河南省人民医院生殖医学中心行赠卵 IVF-ET 的 31 例卵巢高反应患者和受卵的 30 例患者的妊娠结局。 **结果** 受卵和赠卵组冻融胚胎移植(FET)周期的种植率(52.05%比 58.70%)、临床妊娠率(69.23%比 73.91%)、移植周期活产率(61.54%比 65.22%)、取卵周期累积妊娠率(87.10%比 100.00%)、双胎率(40.74%比 48.39%)、活产率

(77.42%比 96.77%)差异均无统计学意义($P>0.05$)。受卵者<38 岁组和≥38 岁组相比, 种植率(58.70%比 40.74%)、临床妊娠率(76.00%比 57.14%)及早期流产率(5.26%比 12.50%)差异均无统计学意义($P>0.05$); 移植周期活产率(72.00%比 42.86%)差异无统计学意义($P>0.05$); 取卵周期累积妊娠率(100.00%比 66.67%)和活产率(94.74%比 50.00%)差异均有统计学意义($P=0.037$, $P=0.007$)。结论 赠卵 IVF-ET 是卵巢早衰、围绝经期、染色体异常及反复 IVF-ET 失败等不孕患者的有效助孕方法。受卵患者妊娠成功率与赠卵患者相似, 不同年龄组的受卵者均可以获得较好的妊娠结局, 年轻受卵者活产率更高。

【关键词】 受精, 体外; 胚胎移植; 受卵; 冻融胚胎移植; 活产率

基金项目: 国家自然科学基金面上项目(81571407)

Clinical analysis of pregnancy outcome assisted by *in vitro* fertilization-embryo transfer between donor and recipient

Gu Baoxia, Wang Lu, Shang Xiaogai, Wang Ke, Li Yan, Cui Chenchen, Zhang Cuilian
Reproductive Medicine Center of Henan Provincial People's Hospital, People's Hospital of Zhengzhou University, People's Hospital of Henan University, Zhengzhou 450003, China
Corresponding author: Zhang Cuilian, Email: luckyzcl@qq.com, Tel: +86-371-87160762

【Abstract】 **Objective** To investigate the clinical outcomes of *in vitro* fertilization-embryo transfer (IVF-ET) between donor and recipient. **Methods** Pregnancy outcomes of 31 donors of infertility patients of ovarian hyperresponsiveness and 30 recipients receiving by IVF-ET from January 2011 to December 2016 in the Reproductive Center of Henan Provincial People's Hospital were retrospectively analyzed. **Results** The implantation rate of frozen-thawed embryo transfer (FET) cycle (52.05% vs. 58.70%), the clinical pregnancy rate (69.23% vs. 73.91%), the live birth rate per transplant cycle (61.54% vs. 65.22%), the cumulative pregnancy rate per oocyte pick-up cycle (87.10% vs. 100.00%), the twin rate (40.74% vs. 48.39%), and the live birth rate (77.42% vs. 96.77%) were slightly higher in donor group than in recipient group, while there were no significant differences ($P>0.05$). There were no significant differences in implantation rate (58.70% vs. 40.74%), clinical pregnancy rate (76.00% vs. 57.14%), early abortion rate (5.26% vs. 12.50%) and live birth rate per transplant cycle (72.00% vs. 42.86%) between group of <38 years old and group of ≥38 years old ($P>0.05$). There were significant differences in cumulative pregnancy rate (100.00% vs. 66.67%) and live birth rate per oocyte pick-up cycle (94.74% vs. 50.00%) ($P=0.037$, $P=0.007$). **Conclusion** Oocyte donation IVF-ET is an effective method to assist infertility patients such as premature ovarian failure, perimenopausal period, chromosomal abnormalities, and repeated failure of IVF-ET. The success rate of pregnancy in the recipients of oocyte is similar to that in the donors. All different age groups of recipients can obtain good pregnancy outcomes, and the young recipients have a higher live birth rate.

【Key words】 Fertilization *in vitro*; Embryo transfer; Oocyte recipient; Frozen-thawed embryo transfer; Live birth rate

Fund program: General Program of National Natural Science Foundation of China(81571407)

DOI: 10.3760/cma.j.cn101441-20190507-00184

收稿日期 2019-05-24 本文编辑 王李艳

引用本文: 王跃会, 燕虹, 李十月. “全面二孩”政策下流动人口二孩生育意愿及其影响因素分析——基于 2016 年全国流动人口卫生计生动态监测调查湖北省数据[J]. 中华生殖与避孕杂志, 2020, 40(4): 314-319. DOI: 10.3760/cma.j.cn101441-20190507-00184.

·现场调查·

“全面二孩”政策下流动人口二孩生育意愿及其影响因素分析

——基于 2016 年全国流动人口卫生计生动态监测调查湖北省数据

王跃会 燕虹 李十月

武汉大学健康学院 430071

通信作者：燕虹，Email：yanhmjxr@aliyun.com，电话：+86-27-68759118

【摘要】 目的 本文欲探究“全面二孩”政策实施后流动人口的二孩生育意愿及其影响因素。

方法 利用 2016 年全国流动人口卫生计生动态监测调查湖北省数据，了解 15~49 周岁有配偶且已育一孩流动人口的二孩生育意愿，并通过多分类 logistic 回归模型对其影响因素进行分析。结果表明 20.10% 的流动人口明确计划生育二孩。性别、年龄、户口性质、教育水平、就业身份、一孩性别、家庭平均月总收入、医疗保险、本次流动原因、流动累计时间、于流入地长期居住意愿影响流动人口的二孩生育意愿。**结论** 流动人口二孩生育意愿偏低，受多种因素影响。建议通过加强政策宣传，降低二孩生育抚养的经济压力，完善抚育二孩相关资源设施，以提高流动人口二孩生育意愿。

【关键词】 “全面二孩”政策； 流动人口； 二孩生育意愿； 影响因素； 多分类 logistic 回归

基金项目：武汉大学人文社会科学青年学者学术团队建设计划资助

The second child bearing willingness and its influencing factors under the universal two-child policy: based on the Hubei provincial data of the 2016 National Migrant Population Dynamic Monitoring Survey

Wang Yuehui , Yan Hong , Li Shiyue

School of Health Sciences, Wuhan University, Wuhan 430071, China

Corresponding author: Yan Hong, Email: yanhmjxr@aliyun.com, Tel: +86-27-68759118

【Abstract】 Objective To explore the second child bearing willingness of migrants after the policy of “comprehensive two children” and analyze the influencing factors. **Methods** Based on the Hubei provincial data of 2016 National Migrant Population Dynamic Monitoring Survey, the second child bearing willingness of 15 to 49 years old migrants who have had one child already were surveyed and the influencing factors through multinomial logistic regression model were analyzed. **Results** About 20.10% of the migrant population had a clear family planning of the second child. Gender, age, the nature of household registration, educational level, employment status, gender of the first child, income, medical insurance, reason for this current migration, cumulative floating time, long-term residence planning in inflow place affected the second child bearing willingness on migrant population. **Conclusion** The migrant population has a low fertility willingness of the second child, and it's affected by many factors. It is suggested that various measures should be taken to enhance the migrant populations' desire to have a second child by strengthening the propaganda of the universal two-child policy, reducing the economic pressure, and improving the related resources and facilities for bearing and raising of the second child.

【Key words】 The universal two-child policy ; Migrant population ; The second child bearing willingness ; Influencing factors ; Multinomial logistic regression

Fund program : The Academic Team Building Program of Young Scholars in Humanities and Social Sciences of Wuhan University

DOI: 10.3760/cma.j.cn101441-20190620-00267

收稿日期 2019-09-02 本文编辑 宋培培

引用本文: 段培, 王青尔, 黄丽旋, 等. 慢性肾脏病育龄期女性患者避孕现状及影响因素[J]. 中华生殖与避孕杂志, 2020, 40(4): 320-324. DOI: 10.3760/cma.j.cn101441-20190620-00267.

·现场调查·

慢性肾脏病育龄期女性患者避孕现状及影响因素

段培¹ 王青尔² 黄丽旋² 李卉² 吕桂兰²

¹ 南京大学医学院 210093; ² 东部战区总医院(原南京军区南京总医院)国家肾脏疾病临床医学研究中心, 南京 210002

通信作者: 吕桂兰, Email: 2271500539@qq.com, 电话: +86-18205160808

【摘要】 目的 了解慢性肾脏病(CKD)育龄期女性患者避孕现状及影响因素, 为提高其生殖健康水平提供依据。方法 对东部战区总医院国家肾脏疾病临床医学研究中心 2018 年 11 月至 2019 年 2 月期间 256 例 CKD 育龄期女性患者进行现况调查, 对调查结果进行统计分析。结果 共调查 256 例, 回收有效问卷 246 份。其中, 36.18% 未采用避孕措施, 53.25% 采用 1 种避孕措施, 10.57% 采取 2 种或以上的避孕措施。避孕措施使用比例依次为避孕套 51.59%、宫内节育器 45.86%、口服药物 7.01%、安全期 7.01%、体外射精 5.10%、避孕针剂 0.64%。3.25% 明确使用仅含孕酮的避孕制剂, 包括宫内节育器及口服药物。单因素分析显示, 不同年龄、婚姻状态、是否为独生子女、生育情况、伴侣对避孕的态度、是否接受避孕指导、是否存在水肿、意愿生育数目与是否采用避孕措施有关, 差异均有统计学意义($P < 0.05$)。多因素分析显示, 已婚、现有 2 个及以上子女数量、接受避孕指导、伴侣对避孕态度积极者更多的采取避孕措施($P < 0.05$)。结论 CKD 育龄期女性患者避孕措施尤其有效避孕措施使用率较低, 易发生意外妊娠。应加强相应患者避孕咨询, 提高其有效避孕措施的使用。

【关键词】 慢性肾脏病; 女性; 避孕

Contraceptive situation and influencing factors of women in childbearing age with chronic kidney disease

Duan Pei¹, Wang Qing'er², Huang Lixuan², Li Hui², Lyu Guilan²

¹ Medical School of Nanjing University, Nanjing 210093, China; ² National Clinical Research Center of Kidney Diseases, Jinling Hospital, Nanjing 210002, China

Corresponding author: Lyu Guilan, Email: 2271500539@qq.com, Tel: +86-18205160808

【Abstract】 Objective To investigate the contraceptive status and influencing factors of women at reproductive age of chronic kidney disease (CKD), so as to provide evidence for improving reproductive health of women with CKD. **Methods** A total of 256 female patients of reproductive age of CKD from November 2017 to February 2019 at National Clinical Research Center of Kidney Diseases, Jinling Hospital were selected to investigate the contraceptive status. And the investigation results were analyzed. **Results** A total of 256 patients were investigated, and 246 valid questionnaires were collected. Eighty-nine (36.18%) patients did not use contraceptive methods, 131 (53.25%) patients used one contraceptive method, and 26 (10.57%) patients used two or more contraceptive methods. The proportion of contraceptive users in order were condoms 51.59%,

intrauterine devices 45.86%, oral drugs 7.01%, safe period 7.01%, external ejaculation 5.10%, and contraceptive injection 0.64%. Univariate analysis showed that age, marital status, one-child status, birth status, partner's attitude towards contraception, whether to accept contraceptive guidance, whether to have edema, and the number of children they intended to have were all related to the use of contraceptive measures, with statistically significant differences ($P<0.05$). Multivariate regression analysis showed that those who were married, had 2 or more children, received contraceptive guidance, and had a positive attitude towards contraception were more likely to take contraceptive measures ($P<0.05$). **Conclusion** Child-bearing age women with CKD have a lower rate of contraceptive use, especially long-duration contraception, and a higher risk of unintended pregnancy. Nurses should strengthen the propaganda and education of contraceptive knowledge of CKD patients, and take targeted intervention measures to improve the utilization rate of contraceptive tools.

【Key words】 Chronic kidney disease ; Females ; Contraception

DOI : 10.3760/cma.j.cn101441-20190425-00171

收稿日期 2019-06-12 本文编辑 李天琦

引用本文：楚琪, 张欣, 李茂林, 等. 薄型子宫内膜与辅助生殖技术妊娠结局的研究进展[J]. 中华生殖与避孕杂志, 2020, 40(4): 325-329. DOI: 10.3760/cma.j.cn101441-20190425-00171.

· 综 述 ·

薄型子宫内膜与辅助生殖技术妊娠结局的研究进展

楚琪¹ 张欣² 李茂林¹ 徐影¹

¹ 吉林大学第二医院妇产科生殖中心, 长春 130000; ² 吉林大学第二医院麻醉科, 长春 130000

通信作者: 徐影, Email: 30245188@qq.com, 电话: +86-18686445757

【摘要】 在人类辅助生殖技术(assisted reproductive technology, ART)周期中, 子宫内膜容受性是胚胎植入并获得妊娠的关键条件, 而薄型子宫内膜是影响子宫内膜容受性的一个重要因素。目前, 有关薄型子宫内膜的定义尚不十分明确, 大部分学者认为子宫内膜厚度 ≤ 7 mm 即可认为是薄型子宫内膜。在行 ART 的女性中, 薄型子宫内膜患者约占其周期的 2.4%。ART 周期中子宫内膜薄的问题一直困扰着众多临床医生。本文从薄型子宫内膜的容受性、病因、ART 周期中的妊娠结局等方面进行阐述, 供临床总结、参考以提高 ART 周期中的临床妊娠率。

【关键词】 薄型子宫内膜; 子宫内膜容受性; 辅助生殖技术; 妊娠率; 活产率

Research advances in thin endometrium and pregnancy outcomes with assisted reproductive technology

Chu Qi¹, Zhang Xin², Li Maolin¹, Xu Ying¹

¹ Department of Obstetrics and Gynecology, Jilin University Second Hospital, Changchun 130000, China; ² Department of Anesthesiology, Jilin University Second Hospital, Changchun 130000, China

Corresponding author: Xu Ying, Email: 30245188@qq.com, Tel: +86-18686445757

【Abstract】 In the human assisted reproductive technology (ART) cycle, endometrial receptivity is a key condition for embryo implantation and pregnancy, and thin endometrium is an important factor affecting endometrial receptivity. At present, the definition of thin endometrium is not very clear, most scholars believe that the thickness of endometrium ≤ 7 mm can be considered as thin endometrium. In women with ART, patients with thin endometrium account for about 2.4% of their cycles. The problem of thin endometrium in the ART cycle has been troubling many clinicians.

In this paper, we review the receptivity of thin endometrium, etiology, pregnancy outcome in ART cycles, so as to provide a clinical summary and reference for improving the clinical pregnancy rate in the ART cycle.

【Key words】 Thin endometrium ; Endometrial receptivity ; Reproductive technology, assisted ; Pregnancy rate ; Live birth rate

DOI : 10.3760/cma.j.cn101441-20190601-00234

收稿日期 2019-06-18 本文编辑 王李艳

引用本文：杨琰, 姚桂东, 孙莹璞. ADAMTS1 参与卵巢功能调控的研究现状[J]. 中华生殖与避孕杂志, 2020, 40(4): 330-334.

DOI: 10.3760/cma.j.cn101441-20190601-00234.

· 综 述 ·

ADAMTS1 参与卵巢功能调控的研究现状

杨琰 姚桂东 孙莹璞

郑州大学第一附属医院生殖医学中心 450052

通信作者：孙莹璞，Email：syp2008@vip.sina.com，电话：+86-371-66913114

【摘要】 ADAMTS1 属于含 I 型血小板结合蛋白基序的解聚蛋白样金属蛋白酶(A disintegrin and metalloproteinase with thrombospondin motifs, ADAMTS)家族成员，广泛参与生物体内的炎症反应、组织纤维化等病理生理过程。卵巢在女性生殖系统中最为关键，是产生类固醇激素和雌性配子的场所。而 ADAMTS1 与卵巢功能正常发挥关系密切：ADAMTS1 参与卵巢整体形态结构的维持；在卵泡发育阶段，ADAMTS1 参与颗粒细胞的功能调控，并介导卵母细胞-颗粒细胞“对话”，对于促进卵母细胞的成熟至关重要；在卵泡发育后期的排卵阶段，ADAMTS1 通过裂解多功能蛋白聚糖和聚集蛋白聚糖等细胞外基质，影响卵丘细胞扩展，调控排卵的顺利进行；此外，ADAMTS1 对排卵后的黄体生成、功能维持及退化也具有十分重要的作用。ADAMTS1 的表达异常也与卵巢功能异常如多囊卵巢综合征、卵巢早衰等密切相关。本文就 ADAMTS1 参与卵巢功能调控方面做一综述。

【关键词】 ADAMTS1； 卵巢功能； 卵泡发育； 颗粒细胞

基金项目：国家自然科学基金(81501228)

ADAMTS1 is involved in the regulation of ovarian function

Yang Guang, Yao Guidong, Sun Yingpu

Reproductive Medical Center, the First Affiliated Hospital of Zhengzhou University, Zhengzhou 450052, China

Corresponding author: Sun Yingpu, Email: syp2008@vip.sina.com, Tel: +86-371-66913114

【Abstract】 ADAMTS1 is a member of the disintegrin and metalloproteinase with thrombospondin motifs (ADAMTS) protein family. It is widely involved in the pathophysiological processes *in vivo*, such as inflammation and fibrosis. The ovary is the most critical part of the female reproductive system and the place where steroid hormone is secreted and female gametes are produced. ADAMTS1 is closely related to normal ovarian function. It is involved in maintaining the entire morphological structure of ovary. During the process of follicular development, ADAMTS1 takes part in regulating the function of granulosa cells and mediating "conversation" between oocyte and granulocyte, which is essential to the promotion of oocyte maturation. In the ovulation stage, ADAMTS1 has a significant impact on the full expansion of cumulus cells by cleaving extracellular matrix such as versican and aggrecan, thereby making sure the ovulation goes smoothly. In addition, ADAMTS1 also plays a very important role in forming, maintaining function and degenerating the

corpus luteum after ovulation. The abnormal expression of ADAMTS1 is also intimately associated with ovarian dysfunction, such as polycystic ovarian syndrome (PCOS) and premature ovarian failure (POF). This article gives a review of the role of ADAMTS1 involved in regulating ovarian function.

【Key words】 ADAMTS1 ; Ovarian function ; Follicular development ; Granulosa cell

Fund program : National Natural Science Foundation of China (81501228)

DOI : 10.3760/cma.j.cn101441-20190424-00169

收稿日期 2019-05-07 本文编辑 孙敏

引用本文 : 安慧慧, 曹佳, 周妮娅. 内源性大麻素系统在生殖系统中的作用研究进展[J]. 中华生殖与避孕杂志, 2020, 40(4): 335-339. DOI: 10.3760/cma.j.cn101441-20190424-00169.

· 综 述 ·

内源性大麻素系统在生殖系统中的作用研究进展

安慧慧¹ 曹佳² 周妮娅²

¹ 陆军军医大学第二附属医院血液科, 重庆 400038 ; ² 陆军军医大学军事预防医学系毒理学研究所, 重庆 400038

通信作者 : 周妮娅, Email : zhouniya428@163.com, 电话 : +86-23-68771532

【摘要】 内源性大麻素系统(endocannabinoid system, ECS)主要由大麻素受体(cannabinoid receptors, CBR)、内源性大麻素(endogenous cannabinoids)以及合成降解的酶组成, 在神经、免疫等系统中发挥多种病理生理功能。大量的研究表明, ECS 在性腺功能以及生殖调控中也起着关键作用, 本文就 ECS 在雌/雄生殖系统中的表达分布及作用进行综述。

【关键词】 内源性大麻素系统 ; 生殖系统 ; 大麻素受体

基金项目 : 国家自然科学基金(81502788)

Research progress on the role of endocannabinoid system in the reproductive system

An Huihui¹, Cao Jia², Zhou Niya²

¹ Department of Hematology, the Second Affiliated Hospital of Army Medical University, Chongqing 400038, China ; ² Institute of Toxicology, Department of Military Preventive Medicine, Army Military University, Chongqing 400038, China

Corresponding author: Zhou Niya, Email: zhouniya428@163.com, Tel: +86-23-68771532

【Abstract】 The endocannabinoid system (ECS) is mainly composed of cannabinoid receptors (CBR), endogenous cannabinoids, and synthetically degraded enzymes. It exerts a variety of pathophysiological functions in nervous, immune and other systems. A large number of studies have shown that the ECS also plays a key role in gonadal function and reproductive regulation. At present, the function of ECS on reproduction has been paid more and more attention. Therefore, the research progress on the expression distribution and the role of ECS in female/male reproductive system is summarized in this paper.

【Key words】 Endocannabinoid system ; Reproductive system ; Cannabinoid receptors

Fund program : National Natural Science Foundation of China (81502788)

DOI : 10.3760/cma.j.cn101441-20190423-00167

收稿日期 2019-05-05 本文编辑 宋培培

引用本文：麻婷, 孙小燕, 张学红. N6-甲基腺苷(m6A)修饰调控配子发生、胚胎发育和性别决定的研究进展[J]. 中华生殖与避孕杂志, 2020, 40(4): 340-343. DOI: 10.3760/cma.j.cn101441-20190423-00167.

·综述·

N6-甲基腺苷(m6A)修饰调控配子发生、胚胎发育和性别决定的研究进展

麻婷 孙小燕 张学红

兰州大学第一医院生殖医学专科医院 甘肃省生殖医学与胚胎重点实验室 730000

通信作者：张学红，Email：zhangxueh@lzu.edu.cn，电话：+86-931-8357358

【摘要】 N6-甲基腺苷(m6A)是真核生物 mRNA 中含量最为丰富的甲基化修饰形式，甲基转移酶(writers)、脱甲基酶(erasers)、甲基结合蛋白(readers)3 种蛋白共同保证着 m6A 的动态可逆修饰。最近的研究显示，m6A 的差异表达与配子发生相关，并且对胚胎发育和性别决定也显示出重要作用。对 m6A 的研究明显改变了对胚胎种植、分化和发育的认识，为此，本文就 m6A 与配子发生、胚胎发育及性别决定的相关研究进行综述。

【关键词】 N6-甲基腺苷； 配子发生； 胚胎发育； 性别决定

Advances in the regulation of gametogenesis, embryonic development and sex determination by N6-methyladenosine (m6A) modification

Ma Ting, Sun Xiaoyan, Zhang Xuehong

Reproductive Medicine Special Hospital of the First Hospital of Lanzhou University, Key Laboratory for Reproductive Medicine and Embryo of Gansu Province, Lanzhou 730000, China

Corresponding author: Zhang Xuehong, Email: zhangxueh@lzu.edu.cn, Tel: +86-931-8357358

【Abstract】 N6-methyladenosine (m6A) is the most abundant methylation modification form in eukaryotic mRNA. Methyl transferase (writers), demethylase (erasers) and methyl binding protein (readers) jointly guarantee the dynamic reversible modification of m6A. Recent studies have shown that differential expression of m6A is associated with gametogenesis and plays an important role in embryo development and sex determination. The study of m6A has significantly changed the understanding of embryo implantation, differentiation and development. Therefore, this paper reviews the related studies on m6A and gametogenesis, embryo development and sex determination.

【Key words】 N6-methyladenosine； Gametogenesis； Embryonic development； Sex determination

DOI：10.3760/cma.j.cn142-20190104-00013

收稿日期 2019-06-04 本文编辑 李天琦

引用本文：张巧利, 吴瑞芳. 英国生育协会“医源性原因女性生育力保存策略与实践指南 (2018 版)”解读[J]. 中华生殖与避孕杂志, 2020, 40(4): 344-351. DOI: 10.3760/cma.j.cn142-20190104-00013.

·指南解读·

英国生育协会“医源性原因女性生育力保存策略与实践指南（2018版）”解读

张巧利¹ 吴瑞芳²

¹ 首都医科大学附属北京妇产医院生殖医学中心 100026；² 北京大学深圳医院妇产中心 518036

通信作者：吴瑞芳，Email：wuruf100@126.com，电话：+86-755-83923333

【摘要】 近年来，医学研究取得了长足发展，肿瘤治疗技术的发展使年轻肿瘤患者的生存率提高。但是肿瘤的化疗、放疗、内分泌或手术治疗，可导致卵巢功能低下甚至卵巢衰竭，如何有效保护和保存这些患者的生育力显得尤为重要。本文对英国生育力协会(British Fertility Society，BFS)最新发布的《医源性原因女性生育力保存的策略与实践指南》循证医学证据进行解读。

【关键词】 生育力保存； 胚胎冻存； 卵母细胞冻存； 卵巢组织冻存； 肿瘤
基金项目：北京市属医院科研培育计划项目(PX2019053)

Interpretation to “Fertility preservation for medical reasons in girls and women: British fertility society policy and practice guideline 2018”

Zhang Qiaoli¹ , Wu Ruifang²

¹ Department of Human Reproductive Medicine, Beijing Obstetrics and Gynecology Hospital, Capital Medical University, Beijing 100026, China ; ² Department of Gynecology and Obstetrics, Peking University Shenzhen Hospital, Shenzhen 518036, China

Corresponding author: Wu Ruifang, Email: wuruf100@126.com , Tel: +86-755-83923333

【Abstract】 In recent years, medical research has made great progress. Advances in oncology treatments increased survival rates in young cancer patients. However, the treatments of chemotherapy, radiotherapy, hormone therapy and surgery for oncology can result in diminished ovarian reserve and premature ovarian failure. How to effectively protect and preserve the fertility of these patients is particularly important. This article explains the evidence-based medical evidence from "Fertility preservation for medical reasons in girls and women: British fertility society policy and practice guideline".

【Key words】 Fertility preservation ; Embryo cryopreservation ; Oocyte cryopreservation ; Ovarian tissue cryopreservation ; Oncology

Fund program : Beijing Municipal Administration of Hospitals Incubating Program (PX2019053)