

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41卷 第9期 2021年9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

乔 杰

编辑部主任

王 健

出 版

《中华医学杂志》社有限责任公司
100710,北京市东西大街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30.00元,全年360.00元

中国标准连续出版物号

ISSN 2096-2916

CN 10-1441/R

2021年版权归主办者所有

未经授权,不得转载、摘编本刊
文章,不得使用本刊的版式设计

除非特别声明,本刊刊出的所有
文章不代表中华医学会和本刊
编委会的观点

本刊如有印装质量问题,请向本刊
编辑部调换

目 次

MDT专家视角专栏

- 子宫腺肌病合并不孕,为何提倡多学科诊疗?陈子江 颜磊 765
如何看待子宫腺肌病的临床影像诊断和分型?陆菁菁 767

临床研究

- 波塞冬分类标准下的不同卵巢刺激方案对卵巢
低反应患者的疗效分析李飞 牛爱琴 冯建兵等 770
长效方案与拮抗剂方案应用于PCOS不孕患者
IVF/ICSI临床妊娠结局比较朱颖春 孙彦欣 刘景瑜等 776
探讨长效生长激素预处理对高龄助孕患者
IVF/ICSI临床结局及安全性的影响熊奕雯 张俊伟 王璐璐等 783
剖宫产术后瘢痕子宫患者行单胚胎移植的
临床结局分析王琳 刁飞扬 王菁等 790
PCOS患者停用复方口服避孕药治疗后
无排卵复发的影响因素分析周红娣 王哲蔚 798

实验研究

- 邻苯二甲酸二丁酯暴露对不孕女性助孕结局及小鼠早期胚胎
发育影响的研究张合龙 崔趁趁 李蕾等 805
miR-3074-5p及其靶基因p27在子痫前期
胎盘组织中的异常表达顾艳 乔磊 范卓然等 812
LncRNA AC000061.1调控CFTR在非梗阻性
无精子症发病机制中的作用杨慧敏 傅赞星 王飞苗等 822

临床报道

- 青春期启动前后行睾丸下降固定术对同周期
ICSI-microTESE临床结局的比较分析周梁 王盛兴 周党侠等 832

综 述

- 双刺激方案在卵巢低反应患者中的应用研究进展李京哲 高敏芝 839
精子鞭毛多发形态异常的相关基因研究进展刘旭东 李彦锋 843
环状RNA在滋养细胞功能障碍相关疾病中的
研究进展谢来娣 刘爱霞 850
Cyclin B家族在哺乳动物卵母细胞减数分裂
成熟过程中的作用郭佳妮 孙青原 857

《中华生殖与避孕杂志》第二届通讯编辑委员会成员名单 821

本刊稿约见本卷第1期封三、第7期封二

本期责任编辑 陈子江、乔杰 本期责任编辑 宋培培 本期责任编辑 年利红

CHINESE JOURNAL OF REPRODUCTION AND CONTRACEPTION

(Original title: *Reproduction and Contraception*)

Monthly

Established in December 1980

Volume 41, Number 9

September 25, 2021



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

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

Copyright © 2021 by the all sponsors

No content published by the journals of Chinese Medical Association may be reproduced or abridged without authorization. Please do not use or copy the layout and design of the journals without permission.

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.

CONTENTS IN BRIEF

MDT expert perspective column

- Why should multi-disciplinary team be advocated in adenomyosis related infertility?765
Chen Zijiang, Yan Lei
- A revisit to the clinical imaging diagnosis and classification of adenomyosis767
Lu Jingjing

Clinical Studies

- Comparison of different ovarian hyperstimulation protocols efficacy in poor ovarian responders classified by Poseidon criteria770
Li Fei, Niu Aiqin, Feng Jianbing, et al
- Comparison of clinical outcome for long GnRH agonist protocol and flexible antagonist protocol in IVF/ICSI for infertile patients with PCOS776
Zhu Yingchun, Sun Yanxin, Liu Jingyu, et al
- Effect of long-acting growth hormone pretreatment on the clinical outcome and safety of IVF/ICSI in women of advanced age783
Xiong Yiwen, Zhang Junwei, Wang Lulu, et al
- Clinical outcome analysis of single embryo transfer in patients with scarred uterus after cesarean790
Wang Lin, Diao Feiyang, Wang Jing, et al
- Analysis on influential factors on the recurrence of anovulation of PCOS patients who stop the treatment of combined oral contraceptive798
Zhou Hongdi, Wang Zhewei

Laboratory Studies

- Effects of exposure to di-n-butyl phthalate on pregnancy outcome in infertile women and early embryo development in mice805
Zhang Helong, Cui Chenchen, Li Lei, et al
- Dysregulated expressions of miR-3074-5p and its target gene *p27* in placenta of pre-eclampsia patients812
Gu Yan, Qiao Lei, Fan Zhuoran, et al
- LncRNA AC000061.1 regulates *CFTR* in the pathogenesis of nonobstructive azoospermia822
Yang Huimin, Fu Yunxing, Wang Feimiao, et al

Clinical Reports

- Effects of orchidopexy operations in different pubertal status on the clinical outcomes of ICSI-micro TESE: a comparative analysis832
Zhou Liang, Wang Shengxing, Zhou Dangxia, et al

Reviews

- Recent advances of double stimulation protocols in poor ovarian responders839
Li Jingzhe, Gao Minzhi
- Progress in the study of the related genes of multiple morphological abnormalities of the sperm flagellum843
Liu Xudong, Li Yanfeng
- Research progress of circular RNA in diseases related to trophoblast dysfunction850
Xie Laidi, Liu Aixia
- The functions of Cyclin B family in mammalian oocyte meiotic maturation857
Guo Jiani, Sun Qingyuan

DOI: 10.3760/cma.j.cn101441-20210609-00262

收稿日期 2021-06-10 本文编辑 宋培培

引用本文: 陈子江, 颜磊. 子宫腺肌病合并不孕, 为何提倡多学科诊疗? [J]. 中华生殖与避孕杂志, 2021, 41(9): 765-766. DOI: 10.3760/cma.j.cn101441-20210609-00262.

·MDT 专家视角专栏·

子宫腺肌病合并不孕, 为何提倡多学科诊疗?

陈子江 颜磊

山东大学附属生殖医院, 山东大学齐鲁医学院, 济南 250001

通信作者: 陈子江, Email: chenzijiang@vip.163.com

【摘要】 子宫腺肌病合并不孕症的临床诊疗过程涉及影像科、妇科、生殖科、病理科、介入科等多个学科。推行多学科综合诊疗(multi-disciplinary team, MDT)模式与个体化相结合的综合治疗, 是弥补专业深度细分后诊疗宽度不足的有效办法。针对子宫腺肌病合并不孕, 开辟 MDT 专家视角专栏组织专题述评, 可有效推动子宫腺肌病合并不孕症患者的多学科、个体化的诊疗模式的实施, 为该类患者提供通往活产、优生的最佳诊疗途径。

【关键词】 子宫腺肌病; 不孕症; 多学科综合诊疗

Why should multi-disciplinary team be advocated in adenomyosis related infertility?

Chen Zijiang, Yan Lei

Reproductive Hospital Affiliated to Shandong University, Cheeloo College of Medicine, Shandong University, Jinan 250001, China

Corresponding author: Chen Zijiang, Email: chenzijiang@vip.163.com

【Abstract】 The clinical diagnosis and treatment process of adenomyosis complicated with infertility involves multiple disciplines such as imaging department, gynecology department, reproductive department, pathology department and interventional department. The combination of the multi-disciplinary team (MDT) model and personalized comprehensive treatment is an effective way to make up for the lack of limited diagnosis and treatment breadth after in-depth subdivision. The development of a special topic review from the perspective of MDT experts for adenomyosis related infertility can effectively promote the multi-disciplinary and individualized diagnosis and treatment mode for patients with adenomyosis and provide the best path leading to live and healthy birth for such patients.

【Key words】 Adenomyosis; Infertility; Multi-disciplinary team

DOI: 10.3760/cma.j.cn101441-20210703-00297

收稿日期 2021-07-05 责任编辑 李天琦

引用本文: 陆菁菁. 如何看待子宫腺肌病的临床影像诊断和分型? [J]. 中华生殖与避孕杂志, 2021, 41(9): 767-769. DOI: 10.3760/cma.j.cn101441-20210703-00297.

·MDT 专家视角专栏·

如何看待子宫腺肌病的临床影像诊断和分型?

陆菁菁

北京和睦家医院影像科 100015

通信作者: 陆菁菁, Email: cjr.lujingjing@vip.163.com, 电话: +86-10-59277556

【摘要】 子宫腺肌病是育龄妇女的常见病,其引起的症状包括月经过多、严重痛经和不孕等,对患者身心健康造成严重的影响。其疾病表现多样复杂,累及范围和严重程度迥异。本文拟针对临床和影像诊断中的要点和困惑,分别对子宫腺肌病影像学诊断、结合带的价值以及疾病分型三个方面进行简要归纳与探讨。

【关键词】 子宫腺肌病; 诊断; 影像; 分型

A revisit to the clinical imaging diagnosis and classification of adenomyosis

Lu Jingjing

Department of Radiology, Beijing United Family Hospital, Beijing 100015, China

Corresponding author: Lu Jingjing, Email: cjr.lujingjing@vip.163.com, Tel: +86-10-59277556

【Abstract】 Adenomyosis is a quite common gynecological disease, which presents a spectrum of clinical symptoms such as menorrhagia, severe dysmenorrhea and infertility, which have a serious impact on the physical and mental health of patients. The presentations of clinical symptoms are diverse with varying involvement and disease severity. In this review, the comprehensive diagnosis, value of the junctional zone in diagnosis, and new imaging-based classification of uterine adenomyosis is revisited and discussed in order to address the main concerns existing in diagnosis of uterine adenomyosis.

【Key words】 Adenomyosis; Diagnosis; Imaging; Classification

·临床研究·

DOI: 10.3760/cma.j.cn101441-20200421-00236

收稿日期 2020-04-22 本文编辑 王李艳

引用本文: 李飞, 牛爱琴, 冯建兵, 等. 波塞冬分类标准下的不同卵巢刺激方案对卵巢低反应患者的疗效分析[J]. 中华生殖与避孕杂志, 2021, 41(9): 770-775. DOI: 10.3760/cma.j.cn101441-20200421-00236.

波塞冬分类标准下的不同卵巢刺激方案对卵巢低反应患者的疗效分析

李飞¹ 牛爱琴¹ 冯建兵² 王晨晨² 冯兴梅¹ 张亚莉¹ 陈莹²

¹ 商丘市第一人民医院生殖医学中心 470000; ² 郑州大学第一临床学

院生殖医学中心 450000

陈莹现在商丘市第一人民医院生殖医学中心 470000

通信作者: 陈莹, Email: cici1873680@163.com, 电话: +86-370-

3255052

【摘要】 目的 探讨基于波塞冬分类标准下的卵泡期长效方案、黄体期短效方案和拮抗剂方案在卵巢低反应人群中的治疗效果, 为卵巢低反应患者提供合适的治疗方案。方法 回顾性队列研究分析 2013 年 3 月至 2018 年 12 月期间在郑州大学第一临床学院生殖医学中心行体外受精 (*in vitro fertilization*, IVF) / 卵胞质内单精子注射 (*intracytoplasmic sperm injection*, ICSI) 治疗的, 且根据波塞冬分类标准筛选卵巢低反应预期患者的临床资料, 按年龄因素分为低年龄组 (<35 岁组) 和高年龄组 (≥35 岁组), 进行不同治疗方案的临床疗效对比。结果 本研究共纳入患者 1249 例, 其中低年龄组 410 例, 高年龄组 839 例。在低年龄组中, 卵泡期长效方案相对于黄体期短效方案和拮抗剂方案, 可获得更多的卵母细胞数 [(5.6±3.6) 枚比 (4.6±3.2) 枚比 (2.4±1.7) 枚, $P<0.001$] 和可移植胚胎数 [(2.2±1.6) 枚比 (1.6±1.6) 枚比 (1.1±1.1) 枚, $P<0.001$], 更低的移植周期取消率 [20.8% (33/159) 比 39.5% (49/124) 比 69.3% (88/127), $P<0.001$], 更高的妊娠率 [40.9% (65/159) 比 29.0% (36/124) 比 15.7% (20/127), $P<0.001$] 和活产率 [31.4% (50/159) 比 23.4% (29/124) 比 12.6% (16/127), $P<0.001$], 三种治疗方案的种植率和流产率差异均无统计学意义 ($P>0.05$)。在高年龄组中, 卵泡期长效方案相对于黄体期短效方案和拮抗剂方案, 可获得更多的卵母细胞数 [(3.9±2.8) 枚比 (3.1±2.3) 枚比 (2.5±1.8) 枚, $P<0.001$] 和可移植胚胎数 [(2.8±2.0) 枚比 (2.4±2.0) 枚比 (2.1±1.7) 枚, $P<0.001$], 但三种治疗方案在种植率、妊娠率、流产率和活产率方面差异均无统计学意义 ($P>0.05$)。结论 对于预期卵巢低反应的年轻患者, 卵泡期长效方案比黄体期短效方案和拮抗剂方案拥有更好的临床结局。值得强调的是年龄越

大，妊娠结局越差，另外应根据卵巢低反应患者的特点和个体差异针对性制定治疗方案。

【关键词】 波塞冬标准； 卵巢低反应； 控制性卵巢刺激方案； 受精，体外； 活产

基金项目：河南省科技攻关项目（212102310049）；河南省部联合共建项目（LHGJ20200933）；河南省研究生科研创新项目（HNGRI2018091）

Comparison of different ovarian hyperstimulation protocols efficacy in poor ovarian responders classified by Poseidon criteria

Li Fei¹, Niu Aiqin¹, Feng Jianbing², Wang Chenchen², Feng Xingmei¹, Zhang Yali¹, Chen Ying²

¹Center for Reproductive Medicine, the First People's Hospital of Shangqiu, Shangqiu 470000, China; ²Reproductive Medicine Center, the First Clinical College of Zhengzhou University, Zhengzhou 450000, China

Chen Ying is working in Center for Reproductive Medicine, the First People's Hospital of Shangqiu, Shangqiu 470000, China

Corresponding author: Chen Ying, Email: cici1873680@163.com, Tel: +86-370-3255052

【Abstract】 Objective To compare the efficiency of the early-follicular phase long-acting gonadotropin-releasing hormone agonist (GnRH-a) long protocol, the mid-luteal phase short-acting GnRH-a long protocol and the gonadotropin-releasing hormone antagonist (GnRH-A) protocol in poor ovarian responders classified by Poseidon criteria, and to explore the most appropriate and effective ovarian hyperstimulation protocol in each Poseidon criteria. **Methods** The clinical data from poor ovarian responders according to the Poseidon criteria who underwent *in vitro* fertilization (IVF)/intracytoplasmic sperm injection (ICSI) in the Reproductive Medicine Center of the First Clinical College of Zhengzhou University were retrospectively analyzed by a cohort study. The patients were further divided into lower age group (<35 years) and high age group (≥35 years). The data of baseline characteristics and clinical outcomes in each ovarian hyperstimulation protocol group were analyzed and compared. **Results** Totally 1249 eligible subjects were recruited in the study, including 410 patients in lower age group and 839 patients in high age group. In lower age group, early-follicular phase long-acting GnRH-a long protocol was associated with higher oocyte number (5.6 ± 3.6 vs. 4.6 ± 3.2 vs. 2.4 ± 1.7 , $P < 0.001$) and No. of transferable embryos (2.2 ± 1.6 vs. 1.6 ± 1.6 vs. 1.1 ± 1.1 , $P < 0.001$), lower cancellation rate of embryo transfer [20.8% (33/159) vs. 39.5% (49/124) vs. 69.3% (88/127), $P < 0.001$], higher pregnancy rate per transfer [40.9% (65/159) vs. 29.0% (36/124) vs. 15.7% (20/127), $P < 0.001$], and higher live birth rate [31.4% (50/159) vs. 23.4% (29/124) vs. 12.6% (16/127), $P < 0.001$] than mid-luteal phase short-acting GnRH-a long protocol and GnRH-A protocol. However, there was no significant difference in implantation rate and abortion rate among three protocols ($P > 0.05$). In high age group, the early-follicular phase long-acting GnRH-a long protocol was associated with higher oocyte number (3.9 ± 2.8 vs. 3.1 ± 2.3 vs. 2.5 ± 1.8 , $P < 0.001$) and No. of transferable embryos (2.8 ± 2.0 vs. 2.4 ± 2.0 vs. 2.1 ± 1.7 ,

$P<0.001$), lower cancellation rate of embryo transfer [19.5% (60/307) vs. 28.7% (102/355) vs. 53.3% (56/105), $P<0.001$] than mid-luteal phase short-acting GnRH-a long protocol and GnRH-A protocol. However, there was no statistical significance in implantation rate, pregnancy rate, abortion rate and live birth rate among the three protocols ($P>0.05$). **Conclusion** It seems that the early-follicular phase long-acting GnRH-a long protocol was more effective in clinical outcomes than the mid-luteal phase short-acting GnRH-a long protocol and the GnRH-A protocol for young patients with POR. It is worth emphasizing that the older the patient is, the lower the live birth rate will be. The characteristics and prognosis of patients should be used to develop clinical management strategies especially for the POR crowd.

【Key words】 Poseidon criteria; Poor ovarian response; Controlled ovarian stimulation; Fertilization *in vitro*; Live birth

Fund program: The Key Science and Technology Foundation of Henan Province (212102310049); the Medical Science and Technology Co-construction Project of Henan Province (LHGJ20200933); Graduate Research Innovation Project of Henan Province (HNGRI2018091)

DOI: 10.3760/cma.j.cn101441-20210112-00014

收稿日期 2021-01-14 本文编辑 王李艳

引用本文: 朱颖春, 孙彦欣, 刘景瑜, 等. 长效长方案与拮抗剂方案应用于 PCOS 不孕患者 IVF/ICSI 临床妊娠结局比较[J]. 中华生殖与避孕杂志, 2021, 41(9): 776-782. DOI: 10.3760/cma.j.cn101441-20210112-00014.

·临床研究·

长效长方案与拮抗剂方案应用于 PCOS 不孕患者 IVF/ICSI 临床妊娠 结局比较

朱颖春 孙彦欣 刘景瑜 梅洁
南京大学医学院附属鼓楼医院生殖医学中心, 南京大学分子生殖医学中心 210008

通信作者: 梅洁, Email: meijie560@163.com, 电话: +86-25-68183322

【摘要】 目的 探讨长效长方案或拮抗剂方案对多囊卵巢综合征 (polycystic ovary syndrome, PCOS) 患者行体外受精/卵胞质内单精子注射 (*in*

vitro fertilization/intracytoplasmic sperm injection, IVF/ICSI) 临床妊娠结局的影响。方法 回顾性队列研究分析 2018 年 1 月至 2019 年 12 月期间于南京大学医学院附属鼓楼医院生殖医学中心行首次 IVF/ICSI 助孕的 1286 例 PCOS 患者 (1286 个 IVF/ICSI 周期) 的临床资料, 根据患者促排卵方案的不同将所有周期分为长效长方案组 (1106 例) 和拮抗剂方案组 (180 例), 分别比较两组的基线资料、促排卵治疗过程和首次移植 (包括新鲜周期或复苏周期移植) 临床结局的差异。结果 拮抗剂方案组基础卵泡刺激素 (basal follicle-stimulating hormone, bFSH) $[(6.37 \pm 1.70) \text{ IU/L}]$ 显著低于长效长方案组 $[(6.84 \pm 1.69) \text{ IU/L}]$ ($P=0.001$), 基础窦卵泡计数 (34.52 ± 11.23) 多于长效长方案组 (27.63 ± 8.24) ($P<0.001$), 故使用倾向评分匹配法将两组数据进行匹配, 匹配后长效长方案组和拮抗剂组分别纳入 165 个和 166 个取卵周期。拮抗剂方案组促性腺激素 (gonadotropin, Gn) 使用时间 $[(9.43 \pm 1.78) \text{ d}]$ 、Gn 使用总量 $[(1\ 648.95 \pm 524.15) \text{ IU}]$ 低于长效长方案组 $[(13.85 \pm 3.45) \text{ d}]$, $P<0.001$; $(2\ 391.14 \pm 826.55) \text{ IU}$, $P<0.001$], 且卵泡发育率 $[53.21\% (3095/5817)]$ 、获卵数 $[(20.72 \pm 8.55) \text{ 个}]$ 、囊胚形成率 $[72.77\% (1291/1774)]$ 和可利用胚胎数 $[(8.20 \pm 5.09) \text{ 个}]$ 显著高于长效长方案组 $[43.24\% (2599/6011)]$, $P<0.001$; $(16.42 \pm 6.14) \text{ 个}$, $P<0.001$; $63.06\% (840/1332)$, $P<0.001$; $(6.39 \pm 3.35) \text{ 个}$, $P<0.001$], 但两组间卵子利用率、中重度卵巢过度刺激综合征 (ovarian hyperstimulation syndrome, OHSS) 发生率差异均无统计学意义 (P 均 >0.05)。同时, 长效长方案组和拮抗剂方案组患者首次移植 (新鲜或复苏周期移植) 后临床妊娠率、胚胎种植率、早期流产率和持续妊娠率差异均无统计学意义 (P 均 >0.05)。结论 PCOS 患者 IVF/ICSI 助孕时应用拮抗剂方案促排卵存在 Gn 使用总量少、刺激时间短、囊胚形成率高、可利用胚胎数多等优势, 但其中重度 OHSS 发生率和首次移植妊娠结局与长效长方案相同。

【关键词】 多囊卵巢综合征; 受精, 体外; 胚胎移植

基金项目: 国家自然科学基金面上项目 (82071646); 辅助生殖中青年医生研究项目 (2019); 南京市卫生科技发展专项资金 (YKK18090)

Comparison of clinical outcome for long GnRH agonist protocol and flexible antagonist protocol in IVF/ICSI for infertile patients with PCOS

Zhu Yingchun, Sun Yanxin, Liu Jingyu, Mei Jie

Reproductive Medicine Center of Nanjing Drum Tower Hospital, Center for Molecular Reproductive Medicine of Nanjing University, Nanjing 210003, China

Corresponding author: Mei Jie, Email: meijie560@163.com, Tel: +86-25-68183322

【Abstract】 **Objective** To compare the clinical outcomes of *in vitro* fertilization/intracytoplasmic sperm injection (IVF/ICSI) in infertility patients with polycystic ovary syndrome (PCOS) using the long gonadotropin-releasing hormone agonist (GnRH-a) protocol and flexible antagonist protocol. **Methods** We used a retrospective cohort study to analyze the clinical data of 1286 IVF/ICSI cycles in Reproductive Medicine Center of Nanjing Drum Tower Hospital from January 2018 to December 2019. All patients were undergoing their first IVF/ICSI cycle and divided into long GnRH-a protocol group ($n=1106$) and GnRH antagonist protocol group ($n=180$). Laboratory and clinical outcomes were compared between the two groups. **Results** Since the significant differences have been found in basal follicle-

stimulating hormone (bFSH) [(6.37±1.70) IU/L vs. (6.84±1.69) IU/L]($P=0.001$) and antral follicle count (AFC)(34.52±11.23 vs. 27.63±8.24) between GnRH antagonist protocol group and GnRH-a protocol group ($P<0.001$), the propensity score matching method was used to match the two groups of data. After the matching, 165 and 166 oocyte retrieved cycles were included in long GnRH-a protocol group and GnRH antagonist protocol group, respectively. The dosage of gonadotropin (Gn) used [(1 648.95±524.15) IU] and Gn used duration [(9.43±1.78) d] were lower in GnRH antagonist protocol group than in long GnRH-a protocol group [(2 391.14±826.55) IU, $P<0.001$; (13.85±3.45) d, $P<0.001$]. The number of oocytes retrieved (20.72±8.55), the rate of follicle development [53.21% (3095/5817)], blastocyst formation rate [72.77% (1291/1774)] and the number of transplantable embryos (8.20±5.09) were higher in GnRH antagonist protocol group than in long GnRH-a protocol group [43.24% (2599/6011), $P<0.001$; 16.42±6.14, $P<0.001$; 63.06% (840/1332), $P<0.001$; 6.39±3.35, $P<0.001$]. However, no statistical difference of oocyte utilization and incidence of moderate to severe ovarian hyperstimulation syndrome (OHSS) was found between the two groups. Besides, there were no significant differences in clinical pregnancy rate, implantation rate, miscarriage rate and ongoing pregnancy rate between the two groups undergoing their first embryo transfer cycle. **Conclusion** The usage of GnRH antagonist protocol in PCOS patients during IVF/ICSI cycles has the advantages of less total Gn used, short stimulation time, higher blastocyst formation rate and more embryos available. However, there was no significant difference in the incidence of moderate to severe OHSS and clinical outcomes between long GnRH-a protocol and GnRH antagonist protocol in their first embryo transfer cycles.

【Key words】 Polycystic ovary syndrome; Fertilization *in vitro*; Embryo transfer

Fund program: Surface Program of National Natural Science Foundation of China (82071646); Assisted Reproduction Research Program for Young and Middle-aged Doctors (2019); Medical Science and Technology Development Foundation, Nanjing Department of Health (YKK18090)

DOI: 10.3760/cmaj.cn101441-20200930-00541

收稿日期 2020-10-14 责任编辑 宋培培

引用本文: 熊奕雯, 张俊韦, 王璐璐, 等. 探讨长效生长激素预处理对高龄助孕患者 IVF/ICSI 临床结局及安全性的影响[J]. 中华生殖与避孕杂志, 2021, 41(9): 783-789. DOI: 10.3760/cmaj.cn101441-20200930-00541.

·临床研究·

探讨长效生长激素预处理对高龄助孕患者 IVF/ICSI 临床结局及安全性的影响

熊奕雯 张俊韦 王璐璐 杜明泽 管一春 孙丽君

郑州大学第三附属医院生殖医学科 450052

通信作者：孙丽君，Email：docslj@163.com，电话：+86-

13253528099

【摘要】 目的 探讨长效生长激素预处理对高龄不孕患者体外受精/卵胞质内单精子显微注射 (*in vitro* fertilization/intracytoplasmic sperm injection, IVF/ICSI) 临床结局和安全性的影响。方法 采用前瞻性、自身前后对照研究分析 2018 年 5 月至 2019 年 11 月期间在郑州大学第三附属医院生殖医学科进行 IVF/ICSI 助孕患者的临床资料。选取女方年龄 35~39 岁, 单侧基础窦卵泡数 ≥ 5 个, 基础卵泡刺激素 (follicle-stimulating hormone, FSH) <10 IU/L, 且前次 IVF/ICSI 周期 $\geq 50\%$ 的 IV 级胚胎为 A1 组, 再次助孕添加生长激素 6 周以上预处理为 A2 组。平行对照选取同期行 IVF/ICSI 助孕患者, 入组标准同上, 第一周期常规 IVF/ICSI 助孕, 未使用生长激素 (B1 组); 第二周期采用与第一周期相同的控制性超促排卵方案, 未使用生长激素 (B2 组), 主要观察指标为累积活产率 (cumulative live birth rate, CLBR)。结果 促性腺激素 (gonadotropin, Gn) 使用时间、人绒毛膜促性腺激素 (human chorionic gonadotropin, hCG) 注射日子宫内膜厚度、hCG 注射日雌激素、hCG 注射日孕酮水平及 IVF 受精比例前后自身对照比较差异均无统计学意义 (P 均 >0.05)。A2 组的 Gn 用量高于 A1 组 [$(3\ 880.4\pm 902.0)$ IU 比 $(3\ 485.6\pm 1\ 054.0)$ IU, $P=0.012$], B2 组的 Gn 用量高于 B1 组 [$(3\ 377.7\pm 899.2)$ IU 比 $(3\ 117.8\pm 891.3)$ IU, $P=0.025$]。A2 组的可利用胚胎率 [55.17% (160/290)]、优质胚胎率 [21.38% (62/290)]、冻融胚胎移植临床妊娠率 [60.87% (14/23)]、累积妊娠率 [61.11% (22/36)] 和 CLBR [50.00% (18/36)] 均显著高于 A1 组 [45.98% (120/261), $P=0.031$; 12.64% (33/261), $P=0.007$; 17.39% (4/23), $P=0.003$; 17.50% (7/40), $P<0.001$; 2.50% (1/40), $P<0.001$], 差异均有统计学意义。B2 组与 B1 组比较, 可利用胚胎率、优质胚胎率、新鲜周期临床妊娠率、冻融胚胎移植临床妊娠率差异均无统计学意义 (P 均 >0.05), 累积妊娠率 [34.21% (13/38) 比 12.50% (5/40), $P=0.023$]、CLBR [26.32% (10/38) 比 2.50% (1/40), $P=0.003$] 增加, 差异均有统计学意义。A2 组与 B2 组比较, 可利用胚胎率 [55.17% (160/290) 比 45.56% (113/248), $P=0.026$]、优质胚胎率 [21.38% (62/290) 比 13.31% (33/248), $P=0.014$]、累积妊娠率 [61.11% (22/36) 比 34.21% (13/38), $P=0.021$] 和 CLBR [50.00% (18/36) 比 26.32% (10/38), $P=0.036$] 显著

增高，差异均有统计学意义。A2 组卵巢过度刺激综合征（ovarian hyperstimulation syndrome, OHSS）发生率、多胎妊娠率和异位妊娠率较 A1 组差异均无统计学意义，但 A2 组流产率小于 A1 组，差异有统计学意义 [18.18% (4/22) 比 71.43% (5/7), $P=0.016$]。A2 组应用生长激素前、后 Gn 启动日和取卵日空腹血糖组间比较差异无统计学意义 ($P>0.05$)。结论 生长激素可能改善高龄患者的助孕结局，临床应用相对安全。

【关键词】 生长激素； 高龄； 生殖技术，辅助； 累积活产率

Effect of long-acting growth hormone pretreatment on the clinical outcome and safety of IVF/ICSI in women of advanced age

Xiong Yiwen, Zhang Junwei, Wang Lulu, Du Mingze, Guan Yichun, Sun Lijun

Reproductive Center of the Third Affiliated Hospital of Zhengzhou University, Zhengzhou 450052, China

Corresponding author: Sun Lijun, Email: docslj@163.com, Tel: +86-13253528099

【Abstract】 Objective To investigate the effect of long-acting growth hormone (GH) pretreatment on the clinical outcome and safety of *in vitro* fertilization/intracytoplasmic sperm injection (IVF/ICSI) in women of advanced age. **Methods** It was a prospective, self-controlled study. The patients who underwent IVF/ICSI-embryo transfer (ET) in the Department of Reproductive Center of the Third Affiliated Hospital of Zhengzhou University from May 2018 to November 2019 were included. The patients with age between 35 and 39 years, number of unilateral basal antral follicles ≥ 5 , the basic follicle-stimulating hormone (FSH) <10 IU/L, and $\geq 50\%$ of the embryos in the previous IVF/ICSI-ET cycle belong to IV grade embryos were collected in group A1, and in the next IVF/ICSI cycle, GH was added for more than 6 weeks of pretreatment (group A2). The parallel control group was selected for IVF/ICSI during the same period, the criteria for inclusion in the group are the same as above, group B1: the first cycle of routine IVF/ICSI without GH treatment; group B2: adopt the same controlled ovarian hyperstimulation (COH) protocol as the first cycle, without GH treatment. The main outcome measure was the cumulative live birth rate (CLBR). **Results** The duration of gonadotropin (Gn) used, the thickness of the endometrium on human chorionic gonadotropin (hCG) injection day, the levels of estrogen and progesterone on hCG injection day, and IVF ratio were not statistically significantly different between before and after self-control groups ($P>0.05$). The dosage of Gn used in group A2 was higher than that in group A1 [(3 880.4 \pm 902.0) IU vs. (3 485.6 \pm 1 054.0) IU, $P=0.012$], and the dosage of Gn used in group B2 was higher than that in group B1 [(3 377.7 \pm 899.2) IU vs. (3 117.8 \pm 891.3) IU, $P=0.025$]. Available embryo rate [55.17% (160/290)], high-quality embryo rate [21.38% (62/290)], clinical pregnancy rate of frozen-thawed embryo transfer [60.87% (14/23)], cumulative pregnancy rate [61.11% (22/36)] and CLBR [50.00% (18/36)] of group A2 were significantly higher than those of group A1 [45.98% (120/261), $P=0.031$; 12.64% (33/261), $P=0.007$; 17.39% (4/23), $P=0.003$; 17.50% (7/40), $P<0.001$; 2.50% (1/40), $P<0.001$], the difference was statistically significant. Comparing group B2 with group B1, there were no statistical differences in available embryo rate, high-quality embryo rate, clinical pregnancy rate of fresh cycle, and

clinical pregnancy rate of frozen-thawed embryo transfer (all $P>0.05$). The cumulative pregnancy rate [34.21% (13/38) vs. 12.50% (5/40), $P=0.023$] and CLBR [26.32% (10/38) vs. 2.50% (1/40), $P=0.003$] were significantly different. Compared with group B2, available embryo rate [55.17% (160/290) vs. 45.56% (113/248), $P=0.026$], high-quality embryo rate [21.38% (62/290) vs. 13.31% (33/248), $P=0.014$], cumulative pregnancy rate [61.11% (22/36) vs. 34.21% (13/38), $P=0.021$] and CLBR [50.00% (18/36) vs. 26.32% (10/38), $P=0.036$] in group A2 were significantly higher, and the differences were statistically significant. The group A2 had no significant difference in the incidence of ovarian hyperstimulation syndrome (OHSS), the rate of multiple pregnancy, and the rate of ectopic pregnancy compared with group A1, but the abortion rate of group A2 was significantly lower than that of group A1 [18.18% (4/22) vs. 71.43% (5/7), $P=0.016$]. There were no significant differences in fasting blood glucose before the use of GH on Gn start day and oocyte retrieval day in group A2 ($P>0.05$). **Conclusion** GH may improve the outcome of assisted pregnancy in advanced age patients. The clinical application of GH is relatively safe.

【Key words】 Growth hormone; Advanced age; Reproductive technology, assisted; Cumulative live birth rate

DOI: 10.3760/cmaj.cn101441-20200831-00467

收稿日期 2020-10-09 本文编辑 李天琦

引用本文: 王琳, 刁飞扬, 王菁, 等. 剖宫产术后瘢痕子宫患者行单胚胎移植的临床结局分析[J]. 中华生殖与避孕杂志, 2021, 41(9): 790-797. DOI: 10.3760/cmaj.cn101441-20200831-00467.

·临床研究·

剖宫产术后瘢痕子宫患者行单胚胎移植的临床结局分析

王琳 刁飞扬 王菁 吴春香 刘嘉茵

南京医科大学第一附属医院生殖医学科 210029

通信作者: 刘嘉茵, Email: jyliu_nj@126.com, 电话: +86-25-

68302608

【摘要】 目的 探讨瘢痕子宫以及瘢痕憩室对行单胚胎移植 (single embryo transfer, SET) 的再生育妇女妊娠结局的影响。方法 回顾性队列研究分析 2016 年 1 月至 2018 年 4 月期间在南京医科大学第一附属医院生殖医学科行 SET 的再生育妇女的临床数据, 根据既往分娩方式分为剖宫产分娩 (cesarean delivery, CD) 组及经阴道分娩 (vaginal delivery, VD) 组, 根据移植胚胎的时

期分成两个亚组, 分别比较移植卵裂期胚胎 CD1 组(928 例)和 VD1 组(928 例), 移植囊胚期胚胎 CD2 组(570 例)和 VD2 组(480 例)的妊娠结局。将 CD 组进一步分为憩室组和无憩室组, 观察子宫瘢痕憩室对妊娠结局的影响。结果 无论移植卵裂期胚胎或囊胚期胚胎, CD 组同 VD 组两组之间的活产率、妊娠率、种植率、流产率、早产率等指标差异均无统计学意义(P 均 >0.05)。同 VD 组相比, CD 组妊娠期并发症如前置胎盘、产后出血、妊娠期糖尿病、妊娠期高血压等疾病的发生率差异均无统计学意义(P 均 >0.05)。同剖宫产术后无憩室患者相比, 合并憩室的患者, 移植囊胚期胚胎活产率下降 [30.00% (12/40) 比 51.32% (272/530), $P=0.013$], 移植卵裂期胚胎的妊娠率 [18.97% (11/58) 比 32.30% (281/870), $P=0.034$] 和种植率 [18.97% (11/58) 比 31.26% (272/870), $P=0.049$] 均下降。结论 采用 SET 策略, 具有剖宫产史的患者同阴道分娩史患者获得相似的妊娠结局, 并且没有增加围产期并发症的风险。但是瘢痕憩室影响体外受精-胚胎移植的妊娠结局。推荐对瘢痕子宫患者行单囊胚移植。

【关键词】 单胚胎移植; 瘢痕子宫; 瘢痕憩室; 妊娠结局

基金项目: 江苏省妇幼专项课题 (FYX201901); 江苏省科教强卫工程 (YXZXB2016001)

Clinical outcome analysis of single embryo transfer in patients with scarred uterus after cesarean

Wang Lin, Diao Feiyang, Wang Jing, Wu Chunxiang, Liu Jiayin

Reproductive Medicine Center of the First Affiliated Hospital, Nanjing Medical University, Nanjing 210029, China

Corresponding author: Liu Jiayin, Email: jyliu_nj@126.com, Tel: +86-25-68302608

【Abstract】 **Objective** To explore the effect of scarred uterus and cesarean scar defect (CSD) on the reproductive outcomes of patients with previous cesarean delivery undergoing single embryo transfer (SET). **Methods** A retrospective cohort study was conducted to analyze the data of patients with a history of cesarean delivery (CD) who accepted SET between January 2016 and April 2018 in Reproductive Medicine Center of the First Affiliated Hospital, Nanjing Medical University. According to the previous mode of delivery, patients were divided into CD group and vaginal delivery (VD) group. The pregnancy outcomes were analyzed in each embryo stage respectively. Furthermore, according to embryonic development stage, patients were divided into cleavage-stage embryo group (CD1 group, $n=928$ and VD1 group, $n=928$) and blastocyst-stage embryo group (CD2 group, $n=570$ and VD2 group, $n=480$). The CD population were further divided into two groups according to the presence of CSD to investigate the effect of CSD on pregnancy outcomes. **Results** Regardless of women undergoing transfer of a cleavage-stage embryo or a blastocyst-stage embryo, there were no statistical differences in live birth rate, pregnancy rate, implantation rate, abortion rate and premature birth rate between CD group and VD group (all $P>0.05$). Compared with VD group, the risk of gestational complications such as placenta previa, postpartum hemorrhage, gestational diabetes, and gestational hypertension were not significantly increased in CD group (all $P>0.05$). The live birth rate was lower in CSD group than in non-CSD group in women undergoing the transfer of blastocyst-stage

embryo [30.00% (12/40) vs. 51.32% (272/530), $P=0.013$]. The pregnancy rate and the implantation rate were lower in CSD group than in non-CSD group in women undergoing the transfer of the cleavage-stage embryo [18.97% (11/58) vs. 32.30% (281/870), $P=0.034$; 18.97% (11/58) vs. 31.26% (272/870), $P=0.049$]. **Conclusion** With SET strategy, patients with a history of cesarean section have similar pregnancy outcomes to those with VD, and there is no increased risk of perinatal complications. However, the pregnancy outcomes of *in vitro* fertilization-embryo transfer are hampered in women with CSD. Single blastocyst-stage embryo transfer strategy is recommended for patients with scarred uterus.

【Key words】 Single embryo transfer; Scarred uterus; Cesarean scar defect; Pregnancy outcomes

Fund program: Special Project of Women and Children in Jiangsu Province (FYX201901); The Project of Strengthening Health Through Science and Education in Jiangsu Province (YXZXB2016001)

DOI: 10.3760/cmaj.cn101441-20200708-00384

收稿日期 2020-07-13 本文编辑 王李艳

引用本文: 周红娣, 王哲蔚. PCOS 患者停用复方口服避孕药治疗后无排卵复发的影响因素分析[J]. 中华生殖与避孕杂志, 2021, 41(9): 798-804. DOI: 10.3760/cmaj.cn101441-20200708-00384.

·临床研究·

PCOS 患者停用复方口服避孕药治疗后无排卵复发的影响因素分析

周红娣 王哲蔚

同济大学附属第一妇婴保健院妇科, 上海 200092

通信作者: 王哲蔚, Email: wangzhewei99@163.com, 电话: +86-21-20261641

【摘要】 目的 研究多囊卵巢综合征(polycystic ovary syndrome, PCOS)患者停用复方口服避孕药(combined oral contraceptive, COC)治疗后无排卵复发的影响因素。方法 从2018年4月至2020年4月期间,对259例在同济大学附属第一妇婴保健院就诊的原无排卵并经3个月COC降雄激素治疗的PCOS患者开展前瞻性观察研究,进行无排卵复发的随访,使用生存分析法进行统计,分析无排卵复发的影响因素。结果 COX多元回归显示,对COC治疗前超重者来说,治疗期间减重幅度达5%以上($HR=0.539$, $P=0.001$)可推迟复发,停用COC时存在糖和胰岛素代谢异常($HR=1.829$, $P=0.008$)为促进复发因素;对COC治

疗前非超重者来说,停用 COC 时仍存在高雄激素血症 ($HR=2.268$, $P=0.030$) 为促进复发因素。K-M 检验显示, 50 例 COC 治疗期间减重幅度达 5% 及以上的原超重患者中, 停用 COC 后体重反增者, 复发时间更早 [1.0 (1.0, 2.0) 个周期比 3.0 (2.0, 8.0) 个周期, $P=0.001$]; 35 例停用 COC 时糖和胰岛素代谢恢复正常者, 其中停药后继续维持剂量口服二甲双胍者的复发时间晚于未再服用二甲双胍者 [2.0 (1.0, 4.0) 个周期比 1.0 (0.0, 3.0) 个周期, $P=0.022$]。结论 为推迟 PCOS 停用 COC 后无排卵复发, 建议超重患者减重一定幅度, 并纠正糖和胰岛素代谢异常后再停药; 停用 COC 时糖和胰岛素代谢恢复正常者, 宜继续口服维持剂量二甲双胍; 非超重患者待雄激素水平降至正常后停药。

【关键词】 多囊卵巢综合征; 胰岛素抵抗; 无排卵; 复发

基金项目: 同济大学附属第一妇婴保健院院级课题 (2017B11)

Analysis on influential factors on the recurrence of anovulation of PCOS patients who stop the treatment of combined oral contraceptive

Zhou Hongdi, Wang Zhewei

Gynecologic Department of Shanghai First Maternity and Infant Hospital, School of Medicine, Tongji University, Shanghai 20092, China

Corresponding author: Wang Zhewei, Email: wangzhewei99@163.com, Tel: +86-21-20261641

【Abstract】 Objective To study the influential factors on the relapse of anovulation of polycystic ovary syndrome (PCOS) patients who stop the treatment of combined oral contraceptive (COC). **Methods** In the prospective observational study from April 2018 to April 2020, 259 anovulatory PCOS patients who visited in Shanghai First Maternity and Infant Hospital, School of Medicine, Tongji University were followed up after their androgen lowering therapy via COC for 3 months finished and survival analysis was adopted to analyze the influencing factors of anovulation recurrence. **Results** COX multivariate regression showed that for super heavy patients before COC treatment, reducing weight not less than 5% ($HR=0.539$, $P=0.001$) could relay the relapse whereas glycometabolism and insulin metabolism abnormality at withdrawal time was promoting factor of relapse ($HR=1.829$, $P=0.008$); for non super heavy patients, hyperandrogenism at withdrawal time may promote relapse of anovulation. K-M test showed that for 50 super heavy patients before COC treatment who reduced weight not less than 5% during treatment, the weight gain after COC withdrawal indicated the shorter relapse time [1.0 (1.0, 2.0) cycle vs. 3.0 (2.0, 8.0) cycles, $P=0.001$]. Among 35 patients whose glucose and insulin metabolism had returned to normal at withdrawal time, those who used maintenance dosage of Metformin after withdrawal had later relapse of anovulation [2.0 (1.0, 4.0) cycles vs. 1.0 (0.0, 3.0) cycle, $P=0.022$] than those who did not. **Conclusion** To relay the relapse of anovulation after COC treatment, we suggest that super heavy patients reduce weight moderately and remedy glycometabolism abnormality, and non super heavy patients reduce androgen to normal before withdrawal. For the patients whose glucose metabolism return to normal at withdrawal time, it is better to continue using maintenance dosage of Metformin after withdrawal.

【Key words】 Polycystic ovary syndrome; Insulin resistance; Anovulation; Relapse

Fund program: Shanghai First Maternity and Infant Hospital, Tongji University Science Foundation (2017B11)

DOI: 10.3760/cma.j.cn101441-20200510-00272

收稿日期 2020-05-18 收稿日期 宋培培

引用本文: 张合龙, 崔趁趁, 李蕾, 等. 邻苯二甲酸二丁酯暴露对不孕女性助孕结局及小鼠早期胚胎发育影响的研究[J]. 中华生殖与避孕杂志, 2021, 41(9): 805-811. DOI: 10.3760/cma.j.cn101441-20200510-00272.

·实验研究·

邻苯二甲酸二丁酯暴露对不孕女性助孕结局及小鼠早期胚胎发育影响的研究

张合龙 崔趁趁 李蕾 陈欢欢 张磊 赵华

河南省人民医院生殖医学中心, 郑州 450003

通信作者: 赵华, Email: 417692121@qq.com, 电话: +86-371-

87160178

【摘要】 目的 探讨体内邻苯二甲酸二丁酯(di-n-butyl phthalate, DBP)暴露水平对不孕患者早期助孕结局的影响及其对小鼠早期胚胎发育的影响。方法 本研究选取2019年2月至10月期间在河南省人民医院生殖中心就诊的因输卵管因素行体外受精-胚胎移植(*in vitro* fertilization-embryo transfer, IVF-ET)治疗的患者, 根据病历号尾号抽取单号的112例不孕患者为研究对象, 应用高效液相色谱串联质谱检测尿液中DBP代谢产物邻苯二甲酸单丁酯(mono-n-butyl phthalate, MBP)的浓度, 采用多元回归模型分析尿液中MBP水平与不孕患者受精率、优质胚胎率及囊胚形成率等早期助孕结局的关系。同时将40只3周龄清洁级ICR雌性小鼠简单随机抽样分为对照(玉米油)组和低、中、高剂量DBP染毒组(300 mg/kg、600 mg/kg、1200 mg/kg)四组, 每组10只。将各组雌鼠促排卵与非染毒雄鼠合笼后, 取受精卵, 比较各组间胚胎卵裂率、囊胚形成率和着床位点的差异。结果 在控制了混杂因素后, 患者尿液中MBP浓度与受精率、优质胚胎数、囊胚形成数及囊胚形成率呈负相关($P=0.01$ 、 $P=0.04$ 、 $P=0.03$ 、 $P=0.05$)。DBP低剂量组、中剂量组、高剂量组的小鼠受精后胚胎卵裂率[58.38%(115/197)、43.42%(99/228)、36.60%(71/194)]、囊胚形成率[54.78%(63/115)、44.44%(44/99)、39.44%(28/71)]及胚胎着床位点数(12.20 ± 3.03 、 11.80 ± 2.68 、

11.60±2.41) 明显低于对照组小鼠 [87.12% (142/163), $P<0.001$; 86.62% (123/142), $P<0.001$; 16.80±0.84, $P<0.001$)。DBP 低剂量组卵裂率高于中剂量组、高剂量组, 差异有统计学意义 ($P=0.002$, $P<0.001$)。DBP 低剂量组囊胚形成率高于 DBP 高剂量组, 差异有统计学意义 ($P=0.042$)。DBP 染毒的三组小鼠之间胚胎着床位点数差异无统计学意义 ($P>0.05$)。结论 DBP 暴露与不孕女性临床结局存在相关性, 且 DBP 暴露对小鼠早期胚胎发育产生毒性损伤。

【关键词】 酞酸酯类; 邻苯二甲酸二丁酯; 邻苯二甲酸单丁酯; 内暴露; 受精, 体外; 胚胎移植

基金项目: 国家自然科学基金 (81701444); 河南省科技攻关项目 (202102310065、182102310390); 河南卫健委科技创新杰出青年人才培养项目 (YXKC2020021)

Effects of exposure to di-n-butyl phthalate on pregnancy outcome in infertile women and early embryo development in mice

Zhang Helong, Cui Chenchen, Li Lei, Chen Huanhuan, Zhang Lei, Zhao Hua

Reproductive Medicine Center, Henan Province People's Hospital, Zhengzhou 450003, China

Corresponding author: Zhao Hua, Email: 417692121@qq.com, Tel: +86-371-87160178

【Abstract】 **Objective** To explore the influence of di-n-butyl phthalate (DBP) exposure levels on early reproductive outcomes *in vivo* in infertile women, and its influence on early embryonic development of DBP exposed mice. **Methods**

This study population sampling selected 112 patients according to the tail number of the medical record number who underwent *in vitro* fertilization-embryo transfer (IVF-ET) treatment for tubal factor infertility from February to October 2019 in Reproductive Medicine Center of Henan Province People's Hospital. The concentration of DBP metabolite mono-n-butyl phthalate (MBP) in patients' urine was determined by HPLC tandem mass spectrometry. Multiple regression model analysis was used to analyze the relationship between urine level of MBP and early reproductive outcomes in patients with infertility. At the same time, 40 3-week-old clean grade ICR infected female mice were randomly divided into control (corn oil) group and low-, middle- and high-dose DBP infected (300 mg/kg, 600 mg/kg, 1200 mg/kg) groups, with 10 mice in each group. Fertilized eggs were collected from female ovulation induction and non-infected male mice in each group, and the differences of embryo cleavage rate, blastocyst formation rate and landing point were compared. **Results** After controlling for the mixed factors, the concentration of MBP was negatively correlated with the fertilization rate, the number of good-quality embryos, the number of blastocyst formation and the rate of blastocyst formation as the urine level increased ($P=0.01$, $P=0.04$, $P=0.03$, $P=0.05$). There were statistically significant differences in cleavage rate between the low-dose group and the middle-dose group [58.38% (115/197) vs. 43.42% (99/228), $P=0.002$], between the low-dose group and the high-dose group [58.38% (115/197) vs. 36.60% (71/194), $P<0.001$], and no statistically significant difference was observed between the middle-dose group and the high-dose group ($P>0.05$). There was a statistical

difference in blastocyst formation rate between the low-dose group and the high-dose group [54.78% (63/115) vs. 39.44% (28/71), $P=0.042$], and no statistical difference was observed between the other two groups ($P>0.05$). There was no statistically significant difference in implantation sites among the three groups of mice exposed to DBP ($P>0.05$). **Conclusion** There was a correlation between DBP exposure and clinical outcomes in infertile women, and DBP exposure caused toxic damage to early embryonic development in mice.

【 Key words 】 Phthalate esters; Di-n-butyl phthalate; Mono-n-butyl phthalate; In exposure; Fertilization *in vitro*; Embryo transfer

Fund program: National Natural Science Foundation of China (81701444); Science and Technology Project of Henan Province (202102310065, 182102310390); Science and Technology Innovation Outstanding Young Talents Training Program of Henan Health Commission (YXKC2020021)

·实验研究·

DOI: 10.3760/cma.j.cn101441-20200825-00460

收稿日期 2020-08-26 本文编辑 孙敏

引用本文: 顾艳, 乔磊, 范卓然, 等. miR-3074-5p 及其靶基因 *p27* 在子痫前期胎盘组织中的异常表达[J]. 中华生殖与避孕杂志, 2021, 41(9): 812-821. DOI: 10.3760/cma.j.cn101441-20200825-00460.

miR-3074-5p 及其靶基因 *p27* 在子痫前期胎盘组织中的异常表达

顾艳¹ 乔磊¹ 范卓然¹ 顾文文² 盛红娜¹ 王建梅¹ 华绍芳¹

张璇²

¹天津医科大学第二医院 300221; ²上海市生物医药技术研究院, 国家卫生健康委员会计划生育药具重点实验室 200032

通信作者: 华绍芳, Email: hsf1974@126.com, 电话: +86-13920618612

【摘要】 目的 观察 miR-3074-5p 及其靶基因 *p27* 在子痫前期胎盘组织中的表达情况, 初步探讨 miR-3074-5p/*p27* 分子途径在子痫前期病理过程中的作用。方法 收集 2017 年 9 月至 2018 年 3 月期间在天津医科大学第二医院产科行

剖宫产手术的子痫前期患者（子痫前期组，16 例）和相同孕周非子痫前期的剖宫产产妇（对照组，9 例）的胎盘组织，通过实时定量 PCR、免疫组织化学（immunohistochemistry, IHC）和 Western blotting 检测，比较两组胎盘组织中 miR-3074-5p 以及 p27、细胞周期蛋白 D1（cyclin D1, CCND1）和细胞周期蛋白依赖性激酶 2（cyclin dependent kinase 2, CDK2）等蛋白的表达水平。应用双荧光素酶报告系统，验证 miR-3074-5p 对 p27 mRNA 的靶向抑制作用；通过 RNA 干扰技术，敲低人绒毛外滋养细胞系 HTR-8/SVneo 中 p27 蛋白的表达水平，观察 p27 表达下调对细胞生理活性的影响。结果 与对照组相比，子痫前期组胎盘组织中 miR-3074-5p（ $P=0.034$ ）与 CCND1 蛋白的表达量都显著下调（ $P=0.031$ ），而 p27 蛋白的表达量则显著上调（ $P=0.010$ ）；IHC 结果显示，p27 和 CCND1 蛋白主要表达于合体滋养层细胞中。双荧光素酶报告系统检测结果证实，miR-3074-5p 能与 p27 mRNA 的 3' UTR 序列结合而抑制其表达；敲低 HTR-8/SVneo 细胞中 p27 的表达水平后，细胞的增殖（ $P=0.014$ ）和侵袭（ $P=0.045$ ）活性都显著增强。结论 miR-3074-5p 可能通过直接靶向抑制 p27 的表达而参与调控人绒毛外滋养层细胞的生理活性，进而影响胎盘发育及功能；胎盘组织中 miR-3074-5p 的异常低表达可能通过诱导 p27 的表达而参与子痫前期的病理过程。

【关键词】 miR-3074-5p; p27; 子痫前期; 胎盘; 滋养层细胞

基金项目：国家自然科学基金（81701445）；天津市自然科学基金（17JCYBJC26400）

Dysregulated expressions of miR-3074-5p and its target gene p27 in placenta of pre-eclampsia patients

Gu Yan¹, Qiao Lei¹, Fan Zhuoran¹, Gu Wenwen², Sheng Hongna¹, Wang Jianmei¹, Hua Shaofang¹, Zhang Xuan²

¹ The Second Hospital of Tianjin Medical University, Tianjin 300221, China; ²NHC Key Lab of Reproduction Regulation (Shanghai Institute for Biomedical and Pharmaceutical Technologies), Fudan University, Shanghai 200032, China

Corresponding author: Hua Shaofang, Email: hsf1974@126.com, Tel: +86-13920618612

【Abstract】 Objective To detect the expression levels of miR-3074-5p and its target gene p27 in the placental tissues of pre-eclampsia (PE) patients, and to preliminarily explore the association of miR-3074-5p/p27 pathway in the pathogenesis of PE. **Methods** From September 2017 to March 2018, 16 pregnant women with PE (PE group) and 9 normal pregnant women (control group) were enrolled in Obstetrics Department in the Second Hospital of Tianjin Medical University. The placental expression levels of miR-3074-5p, p27, cyclin D1 (CCND1) and cyclin dependent kinase 2 (CDK2) were determined by quantitative PCR (qPCR), Western blotting and immunohistochemistry (IHC) analyses. The dual-luciferase reporter assay was applied to authenticate the directly targeted effect of miR-3074-5p on expression of p27 mRNA. The expression of p27 in the human extravillous trophoblast cell line HTR-8/SVneo was down-regulated by its specific shRNA, and the effects of down-regulated p27 expression on physiological activities of HTR-8/SVneo cells were detected. **Results** Compared with control group, the expression levels of miR-3074-5p ($P=0.034$) and CCND1 ($P=0.031$) protein in the

placenta of PE patients were significantly decreased, whereas the placental p27 ($P=0.010$) protein expression was significantly increased in PE group. IHC analysis showed that, the signals of p27 and CCND1 proteins were dominantly detected in syncytiotrophoblast. The results of dual-luciferase reporter assay confirmed that miR-3074-5p could inhibit the expression of p27 by directly bound to the 3'UTR of p27 mRNA. After the p27 expression was down-regulated, the proliferative and invasive activities of HTR-8/SVneo cells were significantly enhanced ($P=0.014$, $P=0.045$). **Conclusion** miR-3074-5p might participate in the regulation of physiological activities of extravillous trophoblast cells by its targeted inhibition on p27 expression, and the abnormally decreased miR-3074-5p in trophoblast cells might be associated with the pathogenesis of PE by promoting the expression of p27.

【Key words】 miR-3074-5p; p27; Preeclampsia; Placenta; Trophoblast cell

Fund program: National Natural Science Foundation of China (81701445); The Municipal Natural Science Foundation of Tianjin (17JCYBJC26400)

DOI: 10.3760/cma.j.cn101441-20200720-00404

收稿日期 2020-09-10 本文编辑 王李艳

引用本文: 杨慧敏, 傅赞星, 王飞苗, 等. LncRNA AC000061.1 调控 *CFTR* 在非梗阻性无精子症发病机制中的作用[J]. 中华生殖与避孕杂志, 2021, 41(9): 822-831. DOI: 10.3760/cma.j.cn101441-20200720-00404.

·实验研究·

LncRNA AC000061.1 调控 *CFTR* 在非梗阻性无精子症发病机制中的作用

杨慧敏¹ 傅赞星¹ 王飞苗² 王亚飞¹ 季静¹ 李嘉玲¹ 胡蓉²

¹宁夏医科大学, 银川 750000; ²宁夏医科大学总医院生殖医学中心,

银川 750000

通信作者: 胡蓉, Email: Hr7424@126.com, 电话: +86-13895078588

【摘要】 目的 探讨长链非编码 RNA(long non-coding RNA, LncRNA) AC000061.1 调节 *CFTR* 基因表达在非梗阻性无精子症(nonobstructive azoospermia, NOA)发病机制中的作用。方法 基因芯片检测梗阻性无精子症

(obstructive azoospermia, OA) 组 (50 例)、NOA 组 (50 例) 及对照组 (50 例) 患者的睾丸组织中差异表达的 LncRNA 并对其对应的靶向 mRNA 进行生物信息学分析, 用 qRT-PCR 和 Western blotting 法检测三组患者的睾丸组织凋亡基因 *Bcl-2* 表达差异。qRT-PCR 验证三组患者睾丸组织、血清、精浆中 LncRNA AC000061.1 和 *CFTR* mRNA 表达水平。酶联免疫吸附法 (enzyme-linked immunosorbent assay, ELISA) 检测血清和精浆中 CFTR 蛋白浓度。构建 LncRNA AC000061.1 过表达 (H-LncRNA 组)、沉默 (Si-LncRNA 组) 及空载对照组载体转染至睾丸癌细胞系 (NTERA-2), qRT-PCR 验证 LncRNA AC000061.1 及 *CFTR* mRNA 的表达, Western blotting 检测 CFTR 蛋白水平, CCK-8 检测细胞增殖能力, 流式细胞术及 TUNEL 凋亡试剂盒检测细胞凋亡率。结果 芯片检测和 qRT-PCR 显示, 与对照组相比, NOA 组睾丸组织 LncRNA AC000061.1 和 *CFTR* 表达降低 ($P=0.033$, $P=0.042$), OA 组 LncRNA AC000061.1 表达无差异, *CFTR* 低表达 ($P=0.039$); OA 组和 NOA 组凋亡基因 *Bcl-2* 表达水平依次增高 ($P=0.031$, $P=0.008$)。三组血清中 LncRNA AC000061.1 mRNA 和 *CFTR* mRNA 及蛋白表达水平差异均无统计学意义 (P 均 >0.05)。在精浆中, 与对照组相比, NOA 组和 OA 组 LncRNA AC000061.1 和 *CFTR* mRNA 及蛋白含量依次降低 ($P=0.002$, $P=0.038$ 和 $P=0.006$, $P=0.026$), 且 LncRNA AC000061.1 与 *CFTR* mRNA 呈正相关 ($r=0.169$, $P=0.039$)。质粒转染 NTERA-2 细胞后, 沉默 Si-LncRNA 组 LncRNA AC000061.1 mRNA 及 *CFTR* mRNA 和蛋白表达均降低 ($P=0.005$, $P=0.003$), 过表达 H-LncRNA 组 LncRNA AC000061.1 mRNA 及 *CFTR* mRNA 和蛋白表达均显著增高 ($P=0.002$, $P=0.009$)。沉默 Si-LncRNA 组细胞增殖能力显著下降 ($P=0.003$), 细胞凋亡率明显增高 ($P=0.001$); 过表达 H-LncRNA 组细胞增殖能力增加 ($P=0.017$), 细胞凋亡率降低 ($P=0.017$)。结论 NOA 睾丸组织中 LncRNA AC000061.1 通过调控 *CFTR* 基因表达引发细胞增殖与凋亡的异常, 可能参与 NOA 的发病机制。

【关键词】 长链非编码 RNA; *CFTR* 基因; 非梗阻性无精子症; 增殖; 凋亡

基金项目: 国家自然科学基金 (8196277、81660257); 宁夏自然科学基金 (2020AAC03381); 宁夏回族自治区重点研究开发计划重大 (重点) 项目 (2019BFG02005); 2016 领军人才 (宁夏); 宁夏医科大学校级项目 (XY201807)

LncRNA AC000061.1 regulates *CFTR* in the pathogenesis of nonobstructive azoospermia

Yang Huimin¹, Fu Yunxing¹, Wang Feimiao², Wang Yafei¹, Ji Jing¹, Li Jialing¹, Hu Rong²
¹Ningxia Medical University, Yinchuan 750000, China; ²Reproductive Medicine Center of General Hospital of Ningxia Medical University, Yinchuan 750000, China

Corresponding author: Hu Rong, Email: Hr7424@126.com, Tel: +86-13895078588

【Abstract】 **Objective** To explore the role of long non-coding RNA (LncRNA) AC000061.1 involved in the pathogenesis of nonobstructive azoospermia (NOA) by regulating the *CFTR* gene expression. **Methods** Bioinformatics analysis was conducted with the use of gene microarray to screen the differentially expressed LncRNAs and corresponding mRNAs in the testicular tissue of patients in three groups including obstructive azoospermia (OA) group ($n=50$), NOA group ($n=50$), and control group ($n=50$). The expression of apoptosis-related gene *Bcl-2* in the

testicular tissue of patients in these three groups was detected by qRT-PCR and Western blotting. Additionally, qRT-PCR was performed to determine the expression of LncRNA AC000061.1 and *CFTR* mRNA in the testicular tissue, serum, and seminal plasma of patients in the three groups, and enzyme-linked immunosorbent assay (ELISA) was conducted to detect the CFTR protein level in the serum and seminal plasma. LncRNA AC000061.1 overexpression (H-LncRNA group) and silencing vectors (Si-LncRNA group) and empty vectors were constructed and transfected into the testicular cancer cell line NTERA-2. Subsequently, the expression of LncRNA AC000061.1 and *CFTR* mRNA was determined by qRT-PCR, and CFTR protein expression was measured by Western blotting assay. Cell proliferation was assessed using CCK-8 and cell apoptosis was evaluated by flow cytometry and TUNEL. **Results** Microarray analysis and qRT-PCR showed that the expression of LncRNA AC000061.1 and *CFTR* decreased in NOA group compared with control group ($P=0.033$ and $P=0.042$). But there was no difference in the expression of LncRNA AC000061.1 between OA group and control group, while *CFTR* in OA group was lowly expressed compared with that in control group ($P=0.039$). Bcl-2 expression was sequentially upregulated in OA and NOA groups relative to normal control group ($P=0.031$ and $P=0.008$). No significant difference was noted in the serum levels of LncRNA AC000061.1 and *CFTR* mRNA and protein among the three groups ($P>0.05$). The results also showed sequentially decreased levels of LncRNA AC000061.1 and *CFTR* mRNA and protein in seminal plasma in NOA and OA groups when compared with control group ($P=0.002$, $P=0.038$ and $P=0.006$, $P=0.026$) and a positive correlation of LncRNA AC000061.1 expression with *CFTR* mRNA expression ($r=0.169$, $P=0.039$). LncRNA AC000061.1 and *CFTR* mRNA and protein expression decreased in Si-LncRNA group ($P=0.005$, $P=0.003$), but significantly increased in H-LncRNA group ($P=0.002$, $P=0.009$). Furthermore, cell proliferation was significantly repressed while apoptosis rate was elevated in Si-LncRNA group ($P=0.003$ and $P=0.001$). On the contrary, enhanced cell proliferation and inhibited apoptosis were observed in H-LncRNA group ($P=0.017$ and $P=0.017$). **Conclusion** LncRNA AC000061.1 in the testicular tissue of NOA patients induced abnormal cell proliferation and apoptosis via mediating *CFTR* gene expression, thereby participating in the pathogenesis of NOA.

【Key words】 Long non-coding RNA; *CFTR*; Nonobstructive azoospermia; Proliferation; Apoptosis

Fund program: National Natural Science Foundation of China (8196277, 81660257); Ningxia Natural Science Foundation (2020AAC03381); Major (Key) Project of the Key Research and Development Plan of Ningxia Hui Autonomous Region (2019BFG02005); 2016 Leading Talent (Ningxia); School-level Project of Ningxia Medical University (XY201807)

·临床报道·

收稿日期 2020-04-23 本文编辑 王李艳

引用本文: 周梁, 王盛兴, 周党侠, 等. 青春期启动前后行睾丸下降固定术对同周期 ICSI-microTESE 临床结局的比较分析[J]. 中华生殖与避孕杂志, 2021, 41(9): 832-838. DOI: 10.3760/cma.j.cn101441-20200421-00235.

青春期启动前后行睾丸下降固定术 对同周期 ICSI-microTESE 临床结 局的比较分析

周梁¹ 王盛兴² 周党侠³ 季兴哲¹ 孙建华¹ 王磊¹ 张洲¹ 吕
茉琦³ 杨杰¹ 施文浩¹

¹西北妇女儿童医院生殖中心, 西安 710003; ²西安市儿童医院泌尿外科 710003; ³西安交通大学医学部病理系 710061

通信作者: 周梁, Email: worldfish@163.com, 电话: +86-29-87219120

【摘要】 目的 探讨青春期启动前、后行睾丸下降固定术对隐睾后非梗阻性无精子症 (nonobstructive azoospermia, NOA) 患者行同周期显微睾丸取精 (microdissection testicular sperm extraction, microTESE) 结合卵胞质内单精子显微注射 (intracytoplasmic sperm injection, ICSI) 临床结局的影响。方法 回顾性队列研究分析 2013 年 12 月至 2019 年 8 月期间在西北妇女儿童医院生殖中心接受同周期 microTESE 结合 ICSI 治疗的 NOA 患者, 比较隐睾后 NOA 与非隐睾后 NOA 的精子获得率 (sperm retrieval rate, SRR), 同时将隐睾后 NOA 患者, 按既往接受睾丸下降固定术的时间, 分为青春期前手术组和青春期启动后手术组, 比较两组患者在实施同周期 microTESE 结合 ICSI 治疗后的 SRR 和妊娠结局。结果 34 例隐睾后 NOA 患者和 604 例非隐睾后 NOA 患者接受了 microTESE 手术, 其中隐睾后 NOA 患者的 SRR 为 85.3% (29/34), 非隐睾后 NOA 患者的 SRR 为 40.2% (243/604), 两组间 SRR 差异有统计学意义 ($P < 0.001$)。34 例隐睾后 NOA 患者中, 青春期前组 17 例, 有 17 例检出精子; 青春期启动后组 17 例, 有 12 例检出精子, 两组间 SRR 差异有统计学意义 ($P = 0.044$)。隐睾后 NOA 患者接受 ICSI 治疗的总临床妊娠率为 65.4% (17/26); 其中青春期前组的临床妊娠率为 62.5% (10/16), 青春期启动后组临床妊娠率为 70.0% (7/10), 两组间临床妊娠率、孕早期流产率、双原核率及优质胚胎率差异均无统计学意义

($P>0.05$)。隐睾后 NOA 患者中, 未检见精子者的睾丸病理类型均为唯支持细胞综合征 (Sertoli cell only syndrome, SCOS), 青春期启动后组的 SCOS 占比 [76.5% (13/17)] 要高于青春期前组的 SCOS 占比 [35.3% (6/17)], 差异有统计学意义 ($P=0.016$)。此外, 睾丸体积、卵泡刺激素、睾酮与 SRR 均无显著相关性。结论 隐睾后 NOA 患者的 SRR 较高, 通过同周期 ICSI-microTESE 治疗的临床效果满意, 睾丸下降固定术的手术时间对 ICSI 的妊娠结局可能影响不大。尽早实施睾丸下降固定术对于 microTESE 的精子获取可能更有利。

【关键词】 非梗阻性无精子症; 隐睾; 睾丸显微取精术; 卵胞质内单精子显微注射

基金项目: 国家自然科学基金 (81673224); 陕西省自然科学基金 (2019JM-029)

Effects of orchidopexy operations in different pubertal status on the clinical outcomes of ICSI-micro TESE: a comparative analysis

Zhou Liang¹, Wang Shengxing², Zhou Dangxia³, Ji Xingzhe¹, Sun Jianhua¹, Wang Lei¹, Zhang Zhou¹, Lyu Moqi³, Yang Jie¹, Shi Wenhao¹

¹ Assisted Reproduction Center, Northwest Women and Children's Hospital, Xi'an 710003, China; ² Department of Urology, Xi'an Children's Hospital, Xi'an 710003, China; ³ Department of Pathology, Medical School, Xi'an Jiaotong University, Xi'an 710061, China

Corresponding author: Zhou Liang, Email: worldfish@163.com, Tel: +86-29-87219120

【Abstract】 **Objective** To investigate the effect of treatment with orchidopexy at different ages on the clinical outcomes of nonobstructive azoospermia (NOA) patients with a history of cryptorchidism who underwent microdissection testicular sperm extraction (microTESE) combined with intracytoplasmic sperm injection (ICSI). **Methods** NOA patients undergoing microTESE combined with ICSI from December 2013 to August 2019 in the ICSI treatment cycle in Assisted Reproduction Center of Northwest Women and Children's Hospital were collected in this retrospective cohort study. According to the history of cryptorchidism, the patients were divided into cryptorchidism group and non-cryptorchidism group. The sperm retrieval rates (SRRs) were assessed between these two groups. Then, based on the timing of treatment with orchidopexy, the NOA patients with orchidopexy were subdivided into prepubertal group and pubertal-postpubertal group. The SRRs and the pregnancy outcomes were also assessed. **Results** There were 34 NOA patients with cryptorchidism and 604 NOA patients without cryptorchidism underwent microTESE. The SRRs in NOA patients with or without cryptorchidism were 85.3% (29/34) and 40.2% (243/604), respectively. The differences were statistically significant ($P<0.001$). In the prepubertal surgery group, sperm was detected in 17 cases, while in the pubertal-postpubertal surgery group, the sperm was detected in 12 cases. The differences were statistically significant ($P=0.044$). The total clinical pregnancy rate of cryptorchidism NOA patients treated with ICSI was 65.4% (17/26). Among these individuals, the clinical pregnancy rate of the prepubertal group was 62.5% (10/16) and the pubertal-postpubertal group was 70.0% (7/10). There were no statistical differences in clinical pregnancy rate.

Some other clinical pregnancy outcomes, including miscarriage rate in early pregnancy, the rate of cycle with 2PN and the rate of cycle with top-quality embryo, also showed no differences between the two groups. In pathology analysis, all the cryptorchidism NOA patients with failure sperm retrieval were Sertoli cell only syndrome (SCOS). The pubertal-postpubertal group had a significant higher morbidity of SCOS [76.5% (13/17)] compared with the prepubertal group [35.3% (6/17)] ($P=0.016$). In addition, the volume of testis, the level of follicle-stimulating hormone and testosterone were not statistically associated with SRR. **Conclusion** The SRR of NOA patients with cryptorchidism was higher than those without cryptorchidism. The age at orchidopexy operation may have little effect on the pregnancy outcome of ICSI. It may be more beneficial for microTESE to obtain sperm by undergoing orchidopexy as early as possible.

【 Key words 】 Nonobstructive azoospermia; Cryptorchidism; Microdissection testicular sperm extraction; Intracytoplasmic sperm injection

Fund program: National Natural Science Foundation of China (81673224); Natural Science Foundation of Shaanxi Province (2019JM-029)

·综述·

DOI: 10.3760/cma.j.cn101441-20200408-00203

收稿日期 2020-04-14 本文编辑 宋培培

引用本文: 李京哲, 高敏芝. 双刺激方案在卵巢低反应患者中的应用研究进展[J]. 中华生殖与避孕杂志, 2021, 41(9): 839-842. DOI: 10.3760/cma.j.cn101441-20200408-00203.

双刺激方案在卵巢低反应患者中的应用研究进展

李京哲 高敏芝

上海交通大学医学院附属仁济医院生殖中心 上海市辅助生殖与优生重点实验室 200135

通信作者: 高敏芝, Email: 328gao@sina.com, 电话: +86-21-20284570

【摘要】 卵巢低反应 (poor ovarian response, POR) 是一种生殖内分泌疾病, 患者行体外受精促排卵后的获卵数往往较低, 严重影响妊娠成功率。双刺激方案利用黄体期卵巢刺激的原理, 通过在一个月经周期内二次取卵, 短时间内可以获取更多数量的卵子。因此, 进一步探索这种新的促排卵方案可能有助于为 POR

患者提供更好的治疗策略。本文从 POR 定义、双刺激方案的作用机制和发展历史，以及在 POR 患者中的应用进行综述。

【关键词】 卵巢低反应； 黄体期刺激； 冷冻胚胎移植； 双刺激方案
基金项目：中华医学会临床医学科研专项资金（18010370766）

Recent advances of double stimulation protocols in poor ovarian responders

Li Jingzhe, Gao Minzhi

Center for Reproductive Medicine, Renji Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai Key Laboratory for Assisted Reproduction and Reproductive Genetics, Shanghai 200135, China

Corresponding author: Gao Minzhi, Email: 328gao@sina.com, Tel: +86-21-20284570

【Abstract】 Poor ovarian response (POR) is a reproductive endocrinology disease that seriously affects the number of oocytes retrieved and reduces the success rate of *in vitro* fertilization (IVF). The double stimulation protocol utilizes the principle of ovarian stimulation in both the follicular and luteal phase. By retrieving oocytes within one menstrual cycle, more oocytes can be obtained in a fairly short period of time. Therefore, to further explore this new ovarian stimulation protocol may help to provide better treatment strategies for POR patients. This paper reviews the definition of POR, the mechanism and developments of double stimulation, and its application in POR patients.

【Key words】 Poor ovarian response; Luteal phase stimulation; Frozen embryo transfer; Double stimulation

Fund program: Special Fund for Clinical Medical Research of Chinese Medical Association (18010370766)

·综述·

DOI: 10.3760/cmaj.cn101441-20200401-00178

收稿日期 2020-04-30 本文编辑 李天琦

引用本文：刘旭东，李彦锋. 精子鞭毛多发形态异常的相关基因研究进展[J]. 中华生殖与避孕杂志, 2021, 41(9): 843-849. DOI: 10.3760/cmaj.cn101441-20200401-00178.

精子鞭毛多发形态异常的相关基因研究进展

刘旭东 李彦锋

陆军军医大学大坪医院泌尿外科，重庆 400042

通信作者：李彦锋，Email: 1738401063@qq.com，电话：+86-

13883402349

【摘要】 精子具有高度特异性的结构特征,这是其所具有的独特受精功能所必需的。其中,精子鞭毛是精子产生运动所必需的一种特定细胞器。鞭毛的完整性对正常精子功能的维持至关重要,鞭毛缺陷常导致精子的运动能力减弱或缺失,从而引起男性不育。鞭毛多发形态异常(multiple morphological abnormalities of the sperm flagellum, MMAF)是导致男性不育的最严重的精子鞭毛缺陷之一,其特征是精子鞭毛存在变短、卷曲、缺失和不规则的现象。人类精子鞭毛中存在1000种以上的蛋白,因而形成MMAF的病因具有明显遗传异质性。近年来,对MMAF表型的基因组学研究已经鉴定出20余种导致MMAF和不育的突变基因。本文总结了导致MMAF的相关基因编码的蛋白信息、定位特征及其潜在的功能。

【关键词】 精子; 鞭毛; 不育; 基因突变; 形态异常

基金项目: 国家自然科学基金(81571491)

Progress in the study of the related genes of multiple morphological abnormalities of the sperm flagellum

Liu Xudong, Li Yanfeng

Department of Urology, Daping Hospital, Army Medical University, Chongqing 400042, China

Corresponding author: Li Yanfeng, Email: 1738401063@qq.com, Tel: +86-13883402349

【Abstract】 Spermatozoa have highly specific structural characteristics, which are necessary for their unique function of fertilization. Among them, sperm flagellum is a specific organelle which is necessary for sperm movement. The integrity of the flagellum is crucial to the maintenance of normal sperm function. Flagellum defects often lead to the reduction or loss of sperm motility, which lead to male infertility. Multiple morphological abnormalities of the sperm flagellum (MMAF) is one of the most serious defects of sperm flagella leading to male infertility, which is characterized by the short, curly, missing and irregular caliber of sperm flagellum. Recent studies have shown that there are more than 1000 kinds of proteins in human sperm flagella, so the etiology of MMAF has obvious genetic heterogeneity. In recent years, genomics studies of the MMAF phenotype have identified over 20 mutated genes leading to MMAF and infertility. In this paper, we summarized the information of the related genes causing MMAF, including their coding protein characteristics, specific localization and potential functions.

【Key words】 Sperm; Flagellum; Infertility; Gene mutation; Morphological abnormality

Fund program: National Natural Science Foundation of China (81571491)

·综述·

DOI: 10.3760/cmaj.cn101441-20200413-00211

收稿日期 2020-04-21 本文编辑 宋培培

引用本文: 谢来娣, 刘爱霞. 环状 RNA 在滋养细胞功能障碍相关疾病中的研究进展[J]. 中华生殖与避孕杂志, 2021, 41(9): 850-856. DOI: 10.3760/cmaj.cn101441-20200413-00211.

环状 RNA 在滋养细胞功能障碍相关疾病中的研究进展

谢来娣 刘爱霞

浙江大学医学院附属妇产科医院, 杭州 310006

通信作者: 刘爱霞, Email: liuaixia@zju.edu.cn, 电话: +86-571-87061501

【摘要】 环状 RNA (circular RNA, circRNA) 是一类具有稳定共价闭环结构的非编码 RNA。该类 RNA 不仅在肿瘤的发生发展中起着重要作用, 还是多种疾病诊断和治疗的新型生物标志物。滋养细胞功能障碍可导致胚胎着床失败、胎盘发育异常及母-胎界面血管重塑不足, 进而造成早期妊娠丢失、子痫前期、早产及胎儿生长受限 (fetal growth restriction, FGR)。本文主要从子痫前期、复发性流产 (recurrent spontaneous abortion, RSA)、FGR 等方面阐述 circRNA 近年来在滋养细胞功能障碍相关疾病的研究进展, 以便更好地理解妊娠相关疾病的发病机制, 进而为疾病的诊治提供新思路。

【关键词】 环状 RNA; 子痫前期; 复发性流产; 胎儿生长受限; 子宫内膜容受性

基金项目: 国家重点研发计划项目 (2018YFC1004403)

Research progress of circular RNA in diseases related to trophoblast dysfunction

Xie Laidi, Liu Aixia

Women's Hospital, School of Medicine, Zhejiang University, Hangzhou 310006, China

Corresponding author: Liu Aixia, Email: liuaixia@zju.edu.cn, Tel: +86-571-87061501

【Abstract】 Circular RNAs (circRNAs), non-coding RNA with stable circular covalently closed structures, provide new biomarkers for the diagnosis and treatment of various diseases and play an important role in the development of tumors. Trophoblast dysfunction can cause embryo implantation failure, placental dysplasia, and insufficient vascular remodeling at the maternal-fetal interface, leading to early pregnancy loss, preeclampsia (PE), premature delivery, and fetal growth restriction (FTR). Here, we review recent research progress in circRNAs in diseases related to trophoblast dysfunction such as PE, recurrent spontaneous abortion (RSA) and FGR. In this way, we can better understand the pathogenesis of pregnancy-related diseases and come up with new ideas for their future diagnosis and treatment.

【Key words】 Circular RNA; Preeclampsia; Recurrent spontaneous abortion; Fetal growth restriction; Endometrial receptivity

Fund program: National Key R&D Program of China (2018YFC1004403)

DOI: 10.3760/cma.j.cn101441-20200713-00393

收稿日期 2020-07-17 本文编辑 宋培培

引用本文: 郭佳妮, 孙青原. Cyclin B 家族在哺乳动物卵母细胞减数分裂成熟过程中的作用[J]. 中华生殖与避孕杂志, 2021, 41(9): 857-859. DOI: 10.3760/cma.j.cn101441-20200713-00393.

·综述·

Cyclin B 家族在哺乳动物卵母细胞减数分裂成熟过程中的作用

郭佳妮¹ 孙青原²

¹ 中国科学院动物研究所干细胞与生殖生物学国家重点实验室, 北京

100101; ² 广东省第二人民医院生殖医学中心, 广州 510317

通信作者: 孙青原, Email: sunqy@gd2h.org.cn, 电话: +86-

13661288044

【摘要】 哺乳动物卵母细胞在减数分裂过程中经历两次停滞与恢复, 而对细胞周期停滞与恢复的调控直接影响单倍体卵子的形成。在卵母细胞减数分裂中, 由细胞周期蛋白 B (Cyclin B) 与细胞周期蛋白依赖性激酶 (cyclin-dependent kinases, CDK) 组成的复合物可以激活或抑制下游相关分子, Cyclin B 的含量周期性变化可控制卵母细胞维持在该时期或进入下一时期, 调控减数分裂的进程。传统观念认为, Cyclin B1 是调控卵母细胞减数分裂进程的核心细胞周期蛋白, 但近来的多项实验结果证明, Cyclin B2 和 Cyclin B3 在卵母细胞减数分裂成熟调控中也发挥着不可或缺的作用。本文将围绕 Cyclin B 蛋白家族成员在哺乳动物卵母细胞减数分裂过程中的作用展开综述。

【关键词】 细胞周期蛋白 B; 卵母细胞; 减数分裂

The functions of Cyclin B family in mammalian oocyte meiotic maturation

Guo Jiani¹, Sun Qingyuan²

¹State Key Laboratory of Stem Cell and Reproductive Biology, Institute of Zoology, Chinese Academy of Sciences, Beijing 100101, China; ²Reproductive Medicine Center, Guangdong Second Provincial General Hospital, Guangzhou 510317, China

Corresponding author: Sun Qingyuan, Email: sunqy@gd2h.org.cn, Tel: +86-13661288044

【Abstract】 There are two rounds of meiotic arrest and resumption in mammalian oocyte, leading to the formation of haploid maternal genome. During the

oocyte maturation, Cyclin B and cyclin-dependent kinases (CDK) complex can active or inhibit downstream molecules to regulate meiotic progression. The periodic changes of Cyclin B controls meiotic cell cycle arrest or exit of oocyte. Traditionally, Cyclin B1 is believed to be the critical cyclin that regulates the progression of oocyte meiosis, however, recent studies have demonstrated that Cyclin B2 and Cyclin B3 also play indispensable roles in oocyte meiotic maturation. This review focuses on the roles of members of the Cyclin B protein family in meiosis of mammalian oocyte.

【Key words】 Cyclin B; Oocyte; Meiosis