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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@sibpt.com
http://zhshzybyzz.yiigle.com

总编辑

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编辑部主任

王 健

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目 次

述 评

《WHO人类精液检查与处理实验室手册》(第6版)

修订内容的启示·····879
朱伟杰

临床研究

体质量指数与体质量对早卵泡期长效方案治疗后

卵巢反应性的影响·····887
夏雷震 田莉峰 伍琼芳

胚胎移植未孕史患者筛查慢性子宫内膜炎时机的探讨·····894

孙迪 杨硕 李蓉

体外受精中嵌合体胚胎发生率的相关因素分析·····902

刘景 周梦鸽 管一春 李真 王兴玲 张亚新 袁二凤 张琳琳
杨如镜

子宫瘢痕憩室及宫腔积液对体外受精-胚胎移植妊娠结局的影响·····909

王雪金 孔祥怡 李秋圆 胡秀玉 郑媛媛 张宏展 徐士儒 莫美兰

实验研究

缺氧对雌性小鼠生殖衰老及其子代健康的影响·····917

何桂元 高晓雨 金诺 李岩 韩文菊 魏晗 邵小光

流行病学研究

个体化避孕节育干预对产后妇女的影响·····924

奚卫 刘怡 简春宣 张杰 陈昊 宋春燕 张鹏兮

云南省育龄女性睡眠质量与抑郁的关联性研究·····933

邓星梅 杜敏 叶汉凤 刘继红 代树花 韩春花 荀丽琦 景文展
吴保 刘珏 刘民

临床报道

GnRH超短激动剂联合拮抗剂方案在POSEIDON低预后患者中的

应用效果分析·····942

刘源斌 杜晓果 陈立雪 杨蕊 王永清 王颖 李蓉 刘平 乔杰

个案报道

移植1枚第2日透明带部分消失的胚胎后活产的病例报道与

文献复习·····948

刘霜 王明勇 黄桂英 王芳 付莉 张俊 陈绍威

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Fax: 0086-21-64438975
Email: rande@sibpt.com
http://zhshzybyzz.yiigle.com

Editor-in-Chief

Qiao Jie

Managing Director

Wang Jian

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CONTENTS IN BRIEF

Editorial

- Enlightenment from the contents revised of the 6th edition of the WHO Laboratory Manual for the Examination and Processing of Human Semen**879
Zhu Weijie

Clinical Studies

- Effect of body mass index and body weight on ovarian response in *in vitro* fertilization-embryo transfer with early follicular phase long-acting long regimen**887
Xia Leizhen, Tian Lifeng, Wu Qiongfang
- Exploring the optimal time to screen for chronic endometritis in patients with previous unpregnant embryo transfer cycle**894
Sun Di, Yang Shuo, Li Rong
- Analysis of possible factors influencing mosaicism in *in vitro* fertilization**902
Liu Jing, Zhou Mengge, Guan Yichun, Li Zhen, Wang Xingling,
Zhang Yaxin, Yuan Erfeng, Zhang Linlin, Yang Rujing
- Effect of cesarean scar defect and endometrial cavity fluid on the pregnancy outcomes of *in vitro* fertilization embryo transfer**909
Wang Xuejin, Kong Xiangyi, Li Qiuyuan, Hu Xiuyu, Zheng Yuanyuan,
Zhang Hongzhan, Xu Shiru, Mo Meilan

Laboratory Studies

- Effects of hypoxia on reproductive aging and offspring health in female mice**917
He Guiyuan, Gao Xiaoyu, Jin Nuo, Li Yan, Han Wenju, Wei Han,
Shao Xiaoguang

Epidemiological Studies

- Influence of individual contraceptive intervention on postpartum women**924
Xi Wei, Liu Yi, Jian Chunxuan, Zhang Jie, Chen Hao, Song Chunyan,
Zhang Meixi
- Relationship between sleep quality and depression among fertile women in Yunnan Province**933
Deng Xingmei, Du Min, Ye Hanfeng, Liu Jihong, Dai Shuhua,
Han Chunhua, Xun Liqi, Jing Wenzhan, Wu Yu, Liu Jue, Liu Min

Clinical Reports

- Application of controlled ovarian hyperstimulation with agonist-antagonist protocol in POSEIDON group 3 and group 4 patients with low prognosis**942
Liu Yuanying, Du Xiaoguo, Chen Lixue, Yang Rui, Wang Yongqing,
Wang Ying, Li Rong, Liu Ping, Qiao Jie

Case Report

- Live birth following the transfer of an embryo with partial dissolution of zona pellucida on day 2: a case report and literature review**948
Liu Shuang, Wang Mingyong, Huang Guiying, Wang Fang, Fu Li, Zhang Jun, Chen Shaowei
- Fibrous encapsulated nodule with massive pyometra caused by intrauterine device: a case report**952
Song Xumin, Shan Ying, Jiang Cui, Li Yanyi, Geng Yuanyuan, Chen Li

Reviews

- Research progress on the damage of human reproductive function caused by common endocrine disruptors and its drug intervention**956
Zhou Ping, Wu Jianhui
- Research progress of progestins in endometriosis treatment**962
Huang Xin, Huang Wei
- Advances in ZP gene mutation causing abnormal oocyte and infertility**.....967
Yao Yejie, Sun Yun
- Research progress on epididymal epithelial cells regulate sperm maturation through the epididymosome**974
Zhang Huanan, Zhao Zhiwei, Wei Jinhua, Li Zhen

Interpretation of Guide

- Interpretation to European Society for Medical Oncology Clinical Practice Guideline 2020: Fertility Preservation and Post-treatment Pregnancies in Post-pubertal Cancer Patients**980
Wang Wei, Li Shunshuang, Liu Gang

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· 述评 ·

《WHO 人类精液检查与处理实验室手册》(第 6 版)修订内容的启示

朱伟杰

暨南大学生命科学技术学院生殖免疫研究所, 广州 510632

通信作者: Email: tzhuwj@jnu.edu.cn, 电话: +86-20-85225718

【摘要】 《WHO 人类精液检查与处理实验室手册》是人类精液检查与精子评估程序和方法的重要参考文献。在手册第 6 版, 精子活力采用 4 级分类系统评定, 精子形态使用结构化顺序分析, 不再表述精液参数参考值范围、限值和精液质量术语, 强调实验室的质量保证和质量控制, 删除了精子与宫颈黏液、卵透明带和卵母细胞相互作用试验, 以及去透明带仓鼠卵穿透试验; 新增加检测精子 DNA 损伤、精子染色质、精子非整倍体和精液白细胞介素的试验, 新介绍玻璃化冷冻精子、计算机辅助精子分析 (computer-aided sperm analysis, CASA) 系统评价精子超活化运动、磁激活细胞分选术制备精子和检查射精顺序的方法。手册第 6 版中保留、修订的内容, 在一定程度反映了国际上现今精液检查与精子评估的标准化、实用性和发展方向, 对我国男科学实验室的发展有指导和促进作用。

【关键词】 不育, 男性; 精液检查; 精子功能; 男科学实验室; WHO 实验室手册

Enlightenment from the contents revised of the 6th edition of the *WHO Laboratory Manual for the Examination and Processing of Human Semen*

Zhu Weijie

Institute of Reproductive Immunology, College of Life Science and Technology, Jinan University, Guangzhou 510632, China

corresponding author: Email: tzhuwj@jnu.edu.cn, Tel: +86-20-85225718

【Abstract】 The *WHO Laboratory Manual for the Examination and Processing of Human Semen* is an important reference document for procedures and methods for human semen examination and sperm evaluation. In the 6th edition of the manual, a four-category system for grading sperm motility is recommended, sperm morphology analysis using a systematic approach is described, and both quality

assurance and quality control are given more attention. Reference values of semen characteristics and nomenclature of semen are no longer used. Obsolete tests such as the human oocyte and human zona pellucida binding and the hamster oocyte penetration tests have been removed. On the other hand, assays to detect sperm DNA fragmentation, sperm chromatin, sperm aneuploidy and semen interleukin have been added. In addition, methods concerning vitrification of sperm freezing, computer-aided sperm analysis (CASA) evaluation of sperm hyperactivation, magnetic activated cell sorting for sperm selection, and assessment of ejaculation sequence have been described. The contents retained and revised in the 6th edition of the manual reflect, to a certain extent, the standardization, practicality and developmental direction of semen examination and sperm evaluation in the world, which will benefit the development of andrology laboratories in China.

【Key words】 Infertility, male; Semen examination; Sperm function; Andrology laboratory; WHO laboratory manual

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·临床研究·

体质量指数与体质量对早卵泡期长效长方案治疗后卵巢反应性的影响

夏雷震 田莉峰 伍琼芳

江西省妇幼保健院辅助生殖中心, 南昌 330006

通信作者: 伍琼芳, Email: wuqiongfang898@sina.com, 电话: +86-13970017651

【摘要】 目的 探讨体质量指数 (body mass index, BMI) 与体质量对行体外受精/卵胞质内单精子注射-胚胎移植 (*in vitro* fertilization/intracytoplasmic sperm injection-embryo transfer, IVF/ICSI-ET) 患者早卵泡期长效长方案促排卵过程中卵巢反应性的影响, 指导生殖医生在确定个体化促性腺激素 (gonadotropin, Gn) 启动剂量时选择更准确的指标。方法 回顾性队列研究分析 2014 年 1 月至 2019 年 12 月期间于江西省妇幼保健院辅助生殖中心行 IVF/ICSI-ET 治疗时应用早卵泡期长效长方案且 Gn 启动剂量均为 112.5 U 的 5762 例患者临床资料。选择 BMI 中位 1/5 人群 (BMI 范围为 20.70~22.03 kg/m²), 按照体质量分为低体质量组 (<51 kg)、

正常体质量组 (51~56 kg)、高体质量组 (>56 kg), 分析三组的卵巢反应性。选择体质量中位 1/5 患者 (体质量范围为 52~55 kg), 按照 BMI 大小分为低 BMI 组 (<20.30 kg/m²)、正常 BMI 组 (20.30~22.19 kg/m²)、高 BMI 组 (>22.19 kg/m²), 分析三组的卵巢反应性。结果 BMI 中位人群按体质量大小分组时, 三组 Gn 总剂量 [1 612.50 (1 350.00, 1 950.00) U 比 1 687.50 (1 387.50, 2 100.00) U 比 1 793.75 (1 443.75, 2 250.00) U]、人绒毛膜促性腺激素 (human chorionic gonadotropin, hCG) 扳机日孕酮 [0.89 (0.60, 1.19) μg/L 比 0.78 (0.53, 1.05) μg/L 比 0.69 (0.50, 0.92) μg/L] 与雌激素水平 [2 569.00 (1 774.00, 3 681.00) ng/L 比 2 208.50 (1 614.00, 3 020.52) ng/L 比 2 018.00 (1 385.00, 2 787.00) ng/L]、IVF 正常受精率 [66.36% (1539/2319) 比 66.46% (5460/8216) 比 62.86% (1281/2038)]、ICSI 正常受精率 [74.77% (320/428) 比 78.31% (1368/1747) 比 71.34% (224/314)] 差异均有统计学意义 ($P=0.006$, $P<0.001$, $P<0.001$, $P=0.008$, $P=0.014$)。通过协方差分析平衡 BMI、年龄、窦卵泡计数 (antral follicle count, AFC) 显示, 三组获卵数差异有统计学意义 ($P=0.022$)。体质量中位人群按 BMI 大小分组时, 三组年龄 [28 (26, 31) 岁比 29 (27, 32) 岁比 29 (27, 32) 岁]、Gn 使用总量 [1 725.00 (1 368.75, 2 100.00) U 比 1 725.00 (1 387.50, 2 100.00) U 比 1 875.00 (1 425.00, 2 300.00) U]、IVF 正常受精率 [66.06% (1775/2687) 比 65.88% (5689/8635) 比 62.91% (1589/2526)]、ICSI 正常受精率 [74.73% (482/645) 比 77.93% (1511/1939) 比 67.97% (418/615)] 与可利用胚胎数 [3.0 (2.0, 5.0) 枚比 3.0 (2.0, 5.0) 枚比 3.0 (2.0, 4.0) 枚] 差异均有统计学意义 ($P=0.015$, $P=0.042$, $P=0.015$, $P<0.001$, $P<0.001$)。通过协方差分析平衡体质量、年龄、AFC 显示, 三组获卵数差异无统计学意义 ($P=0.443$)。结论 体质量较 BMI 对卵巢反应性更具有预测价值, 建议生殖医生根据体质量而非 BMI 确定 Gn 启动剂量。

【关键词】 体质量指数; 受精, 体外; 体质量; 卵巢反应性; 早卵泡期长效方案

Effect of body mass index and body weight on ovarian response in *in vitro* fertilization-embryo transfer with early follicular phase long-acting long regimen

Xia Leizhen, Tian Lifeng, Wu Qiongfang

The Assisted Reproductive Center, Jiangxi Maternal and Child Health Hospital, Nanchang 330006, China

Corresponding author: Wu Qiongfang, Email: wuqiongfang898@sina.com, Tel: +86-13970017651

【Abstract】 **Objective** To explore the effect of body mass index (BMI) and body weight on the ovarian responsiveness of patients undergoing *in vitro* fertilization/intracytoplasmic sperm injection-embryo transfer (IVF/ICSI-ET) treatment with early follicular phase long-acting long regimen, and to instruct reproductive doctors to choose the most accurate indicators when formulating individualized starting dosage of gonadotropin (Gn). **Methods** A retrospective cohort study analysis of the clinical data of 5762 patients who applied the early follicular phase long-acting long regimen and the Gn starting dosage was 112.5 U during IVF/ICSI-ET treatment at the Assisted Reproductive Center of Jiangxi

Maternal and Child Health Hospital from January 2014 to December 2019. Totally 1/5 patients in the middle of BMI (BMI range: 20.70–22.03 kg/m²) were selected and divided into low weight group (<51 kg), normal weight group (51–56 kg), and high weight group (>56 kg). According to body weight, the ovarian reactivity was analyzed among the three groups. In the same way, 1/5 patients in the middle of weight (weight range: 52 kg to 55 kg) were divided into low BMI group (<20.30 kg/m²), normal BMI group (20.30–22.19 kg/m²), high BMI group (>22.19 kg/m²) and the ovarian reactivity of the three groups was analyzed. **Results** There were significant differences in total Gn used dosage [1 612.50(1 350.00, 1 950.00) U vs. 1 687.50(1 387.50, 2 100.00) U vs. 1 793.75(1 443.75, 2 250.00) U], progesterone level [0.89(0.60, 1.19) μg/L vs. 0.78(0.53, 1.05) μg/L vs. 0.69(0.50, 0.92) μg/L] and estradiol level [2 569.00(1 774.00, 3 681.00) ng/L vs. 2 208.50(1 614.00, 3 020.52) ng/L vs. 2 018.00(1 385.00, 2 787.00) ng/L] on the day of human chorionic gonadotropin (hCG) injection, IVF normal fertilization rate [66.36% (1539/2319) vs. 66.46% (5460/8216) vs. 62.86% (1281/2038)] and ICSI normal fertilization rate [74.77% (320/428) vs. 78.31% (1368/1747) vs. 71.34% (224/314)] among the 1/5 patients in the middle of BMI grouped by body weight ($P=0.006$, $P<0.001$, $P<0.001$, $P=0.008$, $P=0.014$). Covariance analysis was used to balance BMI, age and antral follicle count (AFC), and it is found that the number of oocytes retrieved in the three groups was significantly different ($P=0.022$). However, for the 1/5 patients in the middle of body weight grouped by BMI, there were significant differences in age [28(26, 31) years vs. 29(27, 32) years vs. 29(27, 32) years], total Gn used dosage [1 725.00(1 368.75, 2 100.00) U vs. 1 725.00(1 387.50, 2 100.00) U vs. 1 875.00(1 425.00, 2 300.00) U], IVF normal fertilization rate [66.06% (1775/2687) vs. 65.88% (5689/8635) vs. 62.91% (1589/2526)], ICSI normal fertilization rate [74.73% (482/645) vs. 77.93% (1511/1939) vs. 67.97% (418/615)] and the number of available embryos [3.0(2.0, 5.0) vs. 3.0(2.0, 5.0) vs. 3.0(2.0, 4.0)] among the three groups ($P=0.015$, $P=0.042$, $P=0.015$, $P<0.001$, $P<0.001$). The results of covariance analysis showed that there was no difference in the number of oocytes retrieved among the three groups after balancing BMI, age and AFC ($P=0.443$). **Conclusion** Body weight is more predictive of ovarian responsiveness than BMI. It is recommended that reproductive doctors determine the starting dosage of Gn based on body weight rather than BMI.

【Key words】 Body mass index; Fertilization *in vitro*; Body weight; Ovarian response; Early follicular phase long-acting long regimen

·临床研究·

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胚胎移植未孕史患者筛查慢性子宫内膜炎时机的探讨

孙迪 杨硕 李蓉

北京大学第三医院妇产科生殖医学中心, 北京 100191

通信作者: 李蓉, Email: roseli001@sina.com, 电话/传真: +86-10-82266849

【摘要】 目的 探讨既往有移植未孕史患者宫腔镜检查及子宫内膜活检筛查慢性子宫内膜炎的时机。方法 回顾性队列研究分析 2015 年 1 月至 2018 年 12 月期间在北京大学第三医院妇产科生殖医学中心既往有胚胎移植未孕史患者, 在下次冻融胚胎移植助孕前行或未行门诊宫腔镜检查同时子宫内膜活检检查患者的临床资料, 共 10 218 例。根据是否行宫腔镜检查及子宫内膜活检分为宫腔镜组 (1848 例) 与对照组 (8370 例), 并根据既往胚胎移植未孕次数进行组间比较。以活产率为主要终点指标, 并对相关因素进行回归分析。结果 既往有 2 次或 3 次胚胎移植未孕史患者慢性子宫内膜炎发生率较既往仅有 1 次胚胎移植未孕的患者高 [47.3% (490/1035)、44.5% (182/409) 比 34.7% (140/404), $P=0.002$]; 既往不同移植未孕次数宫腔镜异常表现比例组间差异无统计学意义 ($P>0.05$); 既往胚胎移植未孕 1 次或 2 次患者, 在下次冻融胚胎移植前是否行宫腔镜检查及子宫内膜活检对活产无明显影响 ($OR=1.158$, 95% $CI=0.870\sim1.542$, $P>0.05$; $OR=0.950$, 95% $CI=0.729\sim1.238$, $P>0.05$), 但既往胚胎移植未孕 3 次患者, 在下次冻融胚胎移植前行宫腔镜检查及子宫内膜活检是活产的保护因素 ($OR=1.703$, 95% $CI=1.008\sim2.876$, $P=0.047$)。结论 在 B 超未提示子宫内膜或宫腔形态异常情况下, 有 2 次或以上移植未孕史患者可考虑通过宫腔镜检查及子宫内膜活检筛查慢性子宫内膜炎以改善妊娠结局。

【关键词】 慢性子宫内膜炎; 反复着床失败; 冻融胚胎移植

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Exploring the optimal time to screen for chronic endometritis in patients with previous unpregnant embryo transfer cycle

Sun Di, Yang Shuo, Li Rong

Reproductive Medical Center, Obstetrics and Gynecology Department, Peking University Third Hospital, Beijing 100191, China

Corresponding author: Li Rong, Email: roseli001@sina.com, Tel/Fax: +86-10-82266849

【Abstract】 Objective To explore the optimal time to screen for chronic endometritis by hysteroscopy and endometrial biopsy in patients with previous unpregnant embryo transfer cycle. **Methods** A retrospective cohort analysis of

patients with unpregnant embryo transfer cycle whether perform hysteroscopy and endometrial biopsy or not before next frozen-thawed embryo transfer cycle was performed in the Reproductive Medical Center of the Peking University Third Hospital from January 2015 to December 2019, including 10 218 patients. Patients were divided into hysteroscopy group (1848 cases) and control group (8370 cases) according to whether hysteroscopy was performed or not and subgroup analysis was performed according to the number of pregnancies in previous embryo transfer. The primary endpoint was live birth rate and the influencing factors were analyzed by regression analysis. **Results** The incidence of chronic endometritis was higher in patients with two or three previous unpregnant embryo transfer cycles than that in patients with only one unpregnant embryo transfer cycle [47.3% (490/1035), 44.5%(182/409) vs. 34.7% (140/404), $P=0.002$]; there was no significant difference in the proportion of abnormal hysteroscopic findings among groups ($P>0.05$). For patients with one or two previous unpregnant embryo transfer cycles, whether perform hysteroscopy and endometrial biopsy or not before next frozen-thawed embryo transfer did not affect live birth ($OR=1.158$, 95% $CI=0.870-1.542$, $P>0.05$; $OR=0.950$, 95% $CI=0.729-1.238$, $P>0.05$), but hysteroscopy and endometrial biopsy was the protective factor for patients with 3 previous unpregnant ET cycles ($OR=1.703$, 95% $CI=1.008-2.876$, $P=0.047$). **Conclusion** For patients with two or more previous unpregnant embryo transfer cycles and without positive findings in ultrasound, hysteroscopy and endometrial biopsy can be considered to screen for endometrial abnormalities.

【Key words】 Chronic endometritis; Recurrent implantation failure; Frozen-thawed embryo transfer

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·临床研究·

体外受精中嵌合体胚胎发生率的相关因素分析

刘景¹ 周梦鸽¹ 管一春¹ 李真¹ 王兴玲¹ 张亚新¹ 袁二凤²

张琳琳² 杨如镜¹

¹郑州大学第三附属医院生殖医学中心, 郑州 450052; ²郑州大学第三附属医院科研中心, 郑州 450052

通信作者: 杨如镜, Email: rujingy@hotmail.com, 电话: +86-17803860099

【摘要】 目的 初步探讨体外受精 (*in vitro* fertilization, IVF) 治疗中影响嵌合体胚胎发生的相关因素。方法 采用病例对照研究回顾性分析了郑州大学第三附属医院生殖医学中心 2017 年 1 月至 2020 年 12 月期间的 579 个胚胎植入前遗传学检测 (preimplantation genetic testing, PGT) 周期的 2252 个囊胚移植患者的临床资料。使用二代测序 (next generation sequencing, NGS) 技术进行活检细胞的分析, 根据分析结果将所有的胚胎分为嵌合体组及非嵌合体组。嵌合类型包括整倍体-非整倍体嵌合, 非整倍体-非整倍体嵌合和复杂嵌合。比较两组胚胎来源的人群特征及实验室相关参数, 对嵌合体发生率做单因素及多因素分析以评价影响嵌合体胚胎发生的相关因素。结果 905 个胚胎为整倍体 (40.2%), 923 个为非整倍体 (41.0%), 424 个为嵌合体 (18.8%)。共有 228 个胚胎为整倍体-非整倍体嵌合 (10.1%), 59 个 (2.6%) 为非整倍体-非整倍体嵌合, 137 个 (6.1%) 为复杂嵌合。共有 4 个遗传检测机构进行 NGS 技术的测序, 嵌合体率波动在 7.6%~26.2%。调整男女方年龄、男方精子质量、促排卵方案、试剂类型、PGT 的适应证、不同的活检操作者及囊胚发育时期后显示, 囊胚滋养外胚层细胞评分 (C 级比 A 级, $P=0.014$) 及遗传检测机构 (机构 2 比机构 1 前期, $P<0.001$; 机构 1 后期比机构 1 前期, $P<0.001$) 对嵌合体的发生有显著影响。与滋养层细胞 (trophectoderm, TE) 评分为 A 级相比, C 级发生嵌合体的概率升高 66% ($aOR=1.66$, 95% $CI=1.11\sim2.50$, $P=0.014$), 与机构 1 前期相比, 机构 2 的嵌合体发生率是前者的 2.28 倍 ($aOR=2.28$, 95% $CI=1.71\sim3.04$, $P<0.001$), 机构 1 后期是机构 1 前期的 2.17 倍 ($aOR=2.17$, 95% $CI=1.41\sim3.34$, $P<0.001$)。结论 IVF 技术中的嵌合体胚胎的发生率与 NGS 检测机构及滋养外胚层细胞质量相关。

【关键词】 嵌合; 二代测序; 胚胎植入前遗传学检测

Analysis of possible factors influencing mosaicism in *in vitro* fertilization

Liu Jing¹, Zhou Mengge¹, Guan Yichun¹, Li Zhen¹, Wang Xingling¹, Zhang Yaxin¹, Yuan Erfeng², Zhang Linlin², Yang Rujing¹

¹Reproductive Medicine Center, the Third Affiliated Hospital of Zhengzhou University, Zhengzhou 450052, China; ²Research Center, the Third Affiliated Hospital of Zhengzhou University, Zhengzhou 450052, China

Corresponding author: Yang Rujing, Email: rujingy@hotmail.com, Tel: +86-17803860099

【Abstract】 **Objective** To preliminarily explore the related factors that affect chimera mosaicism in *in vitro* fertilization (IVF) treatment. **Methods** A case-control study was conducted to retrospectively analyze the clinical data of 2252 blastocysts in 579 preimplantation genetic testing (PGT) cycles in the Reproductive

Medicine Center of the Third Affiliated Hospital of Zhengzhou University from January 2017 to December 2020. Biopsy cells were analyzed by next generation sequencing (NGS). According to the analysis results, all embryos were divided into mosaicism group and non-mosaicism group. Mosaicism types included euploid-aneuploid mosaicism, aneuploid-aneuploid mosaicism and complex mosaicism. The population characteristics and laboratory-related parameters of the two groups of embryos were compared, and single-factor and multi-factor analysis of the incidence of mosaicism were performed to evaluate the related factors that affect the development of mosaic embryos. **Results** A total of 2252 blastocysts in 579 cycles were included in this study, 905 embryos (40.2%) were euploid, 923 (41.0%) were aneuploid, and 424 (18.8%) were mosaicism. Among them, 228 (10.1%) were euploid-aneuploidy mosaicism, 59 (2.6%) were aneuploidy-aneuploidy mosaicism, and 137 (6.1%) were complex mosaicism. NGS technology was performed in 4 institutions, and the mosaicism rate fluctuated between 7.6% and 26.2%. After adjusting the confounding factors (the age of the male and female partners, the quality of the male partner's sperm, the ovarian stimulation protocols, the type of culture medium, the indications of PGT, the different biopsy operators and the developmental stage of the blastocyst), it was found that the blastocyst trophectoderm cell (TE) score (grade C vs. grade A, $P=0.014$) and the genetic testing institutions (institution 2 vs. early stage of institution 1, $P<0.001$; late stage of institution 1 vs. early stage of institution 1, $P<0.001$) had a significant effect on the occurrence of mosaicism. Compared with the TE score of grade A, the chance of mosaicism in grade C increased by 66% ($aOR=1.66$, 95% $CI=1.11-2.50$, $P=0.014$). Compared with the early stage of institution 1, the incidence of mosaicism in institution 2 and late stage of institution 1 was 2.28 times ($aOR=2.28$, 95% $CI=1.71-3.04$, $P<0.001$), and late stage of institution 1 was 2.17 times that of the early stage ($aOR=2.17$, 95% $CI=1.41-3.34$, $P<0.001$). **Conclusion** The incidence of mosaicism during IVF treatment is related to NGS genetic testing institutions and the quality of trophectoderm cells

【Key words】 Mosaicism; Next generation sequencing; Preimplantation genetic testing

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·临床研究·

子宫瘢痕憩室及宫腔积液对体外受精-胚胎移植妊娠结局的影响

王雪金 孔祥怡 李秋圆 胡秀玉 郑媛媛 张宏展 徐士儒 莫美兰

深圳中山泌尿外科医院生殖科, 深圳 518000

通信作者: 莫美兰, Email: dearalan@126.com, 电话: +86-755-82220030

【摘要】 目的 探讨剖宫产后瘢痕憩室及宫腔积液对体外受精-胚胎移植术临床妊娠结局的影响。方法 本研究为回顾性队列研究, 选取 2019 年 1 月至 2020 年 3 月期间在深圳中山泌尿外科医院生殖科行冻融胚胎移植 (frozen-thawed embryo transfer, FET) 周期合并剖宫产史的瘢痕子宫的 732 例患者作为研究对象, 并根据是否合并瘢痕憩室和 (或) 宫腔积液将其分为四组: 有瘢痕憩室+无宫腔积液 (A 组, $n=39$); 有瘢痕憩室+有宫腔积液 (B 组, $n=82$); 无瘢痕憩室+无宫腔积液 (C 组, $n=495$); 无瘢痕憩室+有宫腔积液 (D 组, $n=116$), 比较各组的一般情况和妊娠结局, 并通过 logistics 回归分析校正混杂因素后分析各组的妊娠结局。结果 A 组的移植年龄高于 B 组 [(38.33 ± 3.55) 岁比 (36.93 ± 3.59) 岁, $P=0.045$], C 组的黄体转化日内膜厚度及移植优质胚胎率均高于 D 组 [(9.40 ± 1.56) mm 比 (9.03 ± 1.59) mm, $P=0.025$; 75.76% ($375/495$) 比 65.52% ($76/116$), $P=0.024$], A 组的取卵年龄高于 C 组 [(37.72 ± 3.55) 岁比 (36.25 ± 4.52) 岁, $P=0.049$], 但黄体转化日内膜厚度较薄 [(8.74 ± 1.58) mm 比 (9.40 ± 1.56) mm, $P=0.012$], 且差异均有统计学意义; C 组的种植率、生化妊娠率、临床妊娠率均高于 D 组 [34.23% ($230/672$) 比 22.58% ($35/155$), $P=0.007$; 48.28% ($239/495$) 比 37.93% ($44/116$), $P=0.044$; 42.83% ($212/495$) 比 30.17% ($35/116$), $P=0.012$]; D 组的早期流产率高于 B 组 [40.00% ($14/35$) 比 17.24% ($5/29$), $P=0.047$], 差异有统计学意义, 在校正移植年龄、取卵年龄、抗苗勒管激素 (anti-Müllerian hormone, AMH)、窦卵泡计数 (antral follicle count, AFC)、基础卵泡刺激素 (follicle-stimulating hormone, FSH)、内膜 CD138 检测结果、FET 方案、移植胚胎属性、移植胚胎数、移植是否含有优质胚胎、黄体转化日内膜厚度、黄体转化日孕酮值、不孕因素可能影响妊娠结局的混杂因素后, 多因素 logistics 回归分析显示 D 组的种植率 [22.58% ($35/155$)]、生化妊娠率 [37.93% ($44/116$)]、临床妊娠率 [30.17% ($35/116$)] 均明显低于 C 组 [34.23% ($230/672$), $P=0.006$; 48.28% ($239/495$), $P=0.047$; 42.83% ($212/495$), $P=0.022$], B 组种植率 [29.52% ($31/105$)]、生化妊娠率 [48.78% ($40/82$)]、临床妊娠率 [35.37% ($29/82$)] 均高于 D 组 [22.58% ($35/155$), $P=0.049$; 37.93% ($44/116$), $P=0.012$; 30.17% ($35/116$), $P=0.030$], 差异均有统计学意义。结论 对于曾有剖宫产史的不孕症患者, 宫腔积液较瘢痕憩室是明显影响 FET 妊娠结局的主要因素。

【关键词】 受精, 体外; 胚胎移植; 瘢痕子宫; 瘢痕憩室; 宫腔积液; 妊娠结局

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Effect of cesarean scar defect and endometrial cavity fluid on the pregnancy outcomes of *in vitro* fertilization embryo transfer

Wang Xuejin, Kong Xiangyi, Li Qiuyuan, Hu Xiuyu, Zheng Yuanyuan, Zhang Hongzhan, Xu Shiru, Mo Meilan

Fertility Center, Shenzhen Zhongshan Urology Hospital, Shenzhen 518000, China

Corresponding author: Mo Meilan, Email: dearalan@126.com, Tel: +86-755-82220030

【Abstract】 Objective To investigate the effect of cesarean scar defect and endometrial cavity fluid on the pregnancy outcomes of infertility patients with previous cesarean scar uterus undergoing *in vitro* fertilization-embryo transfer (IVF-

ET). **Methods** This was a retrospective cohort study. Totally 732 cases of patients

with previous cesarean scar uterus were selected from frozen-thawed embryo

transfer (FET) cycles in the Fertility Center, Shenzhen Zhongshan Urology Hospital

from January 2019 to March 2020. They were divided into four groups: group A

($n=39$) including patients with previous cesarean scar defect and without endometrial cavity fluid; group B ($n=82$) including patients with previous cesarean

scar defect and with endometrial cavity fluid; group C ($n=495$) including patients without previous cesarean scar defect and without endometrial cavity fluid; group D

($n=116$) including patients without previous cesarean scar defect and with endometrial cavity fluid. The general data and pregnancy outcomes were compared among these groups. Multivariate logistics regression analysis of pregnancy outcome

indexes was performed. **Results** The transplantation age of group A was higher than that of group B [(38.33 \pm 3.55) years vs. (36.93 \pm 3.59) years, $P=0.045$], the

endometrial thickness of luteal transformation day and the rate of good-quality embryo transplantation of group C were higher than those of group D [(9.40 \pm 1.56)

mm vs. (9.03 \pm 1.59) mm, $P=0.025$; 75.76% (375/495) vs. 65.52% (76/116), $P=0.024$].

The egg retrieval age of group A was higher than that of group C [(37.72 \pm 3.55) years vs. (36.25 \pm 4.52) years, $P=0.049$], but the endometrial thickness of luteal

transformation day was thinner [(8.74 \pm 1.58) mm vs. (9.40 \pm 1.56) mm, $P=0.012$], and the differences were statistically significant. The implantation rate, the biochemical

pregnancy rate and the clinical pregnancy rate of group C were higher than those of group D [34.23% (230/672) vs. 22.58% (35/155), $P=0.007$; 48.28% (239/495) vs.

37.93% (44/116), $P=0.044$; 42.83% (212/495) vs. 30.17% (35/116), $P=0.012$]. The early abortion rate in group D was higher than that in group B [40.00% (14/35) vs.

17.24 % (5/29), $P=0.047$], the difference was statistically significant. Multivariate logistics regression analyses were used with adjustment for possible confounders:

the maternal age at embryo transfer, the maternal age at egg retrieval, anti-Müllerian hormone (AMH), antral follicle count (AFC), basic follicle-stimulating hormone (FSH),

endometrial CD138 results, FET protocol, and embryo attributes, the number of embryos transferred, embryo quality, the endometrial thickness and the

progesterone value on the day of luteal transformation, the result showed that the implantation rate, the biochemical pregnancy rate and the clinical pregnancy rate of

group D were lower than those of group C [22.58% (35/155) vs. 34.23% (230/672), $P=0.006$; 37.93% (44/116) vs. 48.28% (239/495), $P=0.047$; 30.17% (35/116) vs.

42.83% (212/495), $P=0.022$] and the differences were statistically significant. The implantation rate, the biochemical pregnancy rate and the clinical pregnancy rate of group B were higher than those of group D [29.52% (31/105) vs. 22.58% (35/155), $P=0.049$; 48.78% (40/82) vs. 37.93% (44/116), $P=0.012$; 35.37% (29/82) vs. 30.17% (35/116), $P=0.030$] and the differences were statistically significant. **Conclusion** Endometrial cavity fluid is the main factor that obviously affects the pregnancy outcome of infertility patients with previous cesarean scar uterus undergoing FET cycles.

【Key words】 Fertilization *in vitro*; Embryo transfer; Cesarean scar uterus; Cesarean scar defect; Endometrial cavity fluid; Pregnancy outcome

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·实验研究·

缺氧对雌性小鼠生殖衰老及其子代健康的影响

何桂元¹ 高晓雨² 金诺¹ 李岩¹ 韩文菊¹ 魏晗¹ 邵小光¹

¹ 辽宁省大连市妇女儿童医疗中心(集团), 大连市生殖生命与母子遗传重点实验室, 大连 116037; ² 大连医科大学, 大连 116044

通信作者: 何桂元, Email: he_guiyuan@hotmail.com

【摘要】 目的 探索缺氧与雌性小鼠生育力之间的关系。方法 选择 21 只清洁级 14 周昆明雌鼠, 分成缺氧组(11 只)和常氧组(10 只), 分别在低氧气浓度(10%~20.5%)及常氧气浓度(20.5%)下饲养, 4 周后低氧小鼠恢复常氧环境。两组 21 只雌鼠分别与雄鼠进行交配, 记录后代的数量和体质量。这些雌鼠饲养至 43 周, 重复上述缺氧交配实验。二次缺氧并交配产仔后 2 周, 对雌鼠进行麻醉下内眦采血, 采用罗氏生化分析仪对雌鼠血雌二醇和孕酮水平进行检测。小鼠过量麻醉致死获取卵子、卵巢和子宫组织, 对卵子活性氧进行检测, 对卵巢和子宫进行 HE 染色。结果 年轻缺氧组产仔数为 13.64 ± 3.35 , 稍高于年轻常氧组(13.22 ± 1.92), 但差异无统计学意义($P=0.734$)。年轻缺氧组子代出生体质量 [(1.73 ± 0.20) g] 明显低于年轻常氧组 [(1.82 ± 0.22) g, $P<0.001$]。年老缺氧组的后代数量(5.11 ± 3.58) 明显高于年老常氧组 (1.38 ± 2.56 , $P=0.022$)。与 23 周龄的常氧雌鼠相比, 年老

缺氧组和常氧组的雌二醇水平都有下降, 差异均有统计学意义($P=0.019$; $P=0.035$); 但年老缺氧组与年老常氧组之间的雌二醇水平差异无统计学意义($P=0.913$)。年老常氧组与年老缺氧组小鼠卵子活性氧水平差异无统计学意义($P>0.05$)。组织 HE 染色显示, 年老常氧组小鼠的子宫有明显的充血, 年老缺氧组子宫外观正常。年老缺氧组比常氧组小鼠卵巢中含有更多的窦卵泡数量, 且大小均一。结论 缺氧小鼠的后代数量更多, 但后代的出生体质量显著低于常氧小鼠。缺氧年老鼠比常氧年老鼠的卵巢中含有更多的卵泡。

【关键词】 缺氧; 卵巢; 衰老; 出生体质量

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Effects of hypoxia on reproductive aging and offspring health in female mice

He Guiyuan¹, Gao Xiaoyu², Jin Nuo¹, Li Yan¹, Han Wenju¹, Wei Han¹, Shao Xiaoguang¹

¹Dalian Municipal Women and Children's Medical Center (Group), Key Laboratory of Reproductive Life and Mother-Child Genetics in Dalian, Dalian 116037, China; ²Dalian Medical University, Dalian 116044, China

Corresponding author: He Guiyuan, Email: he_guiyuan@hotmail.com

【Abstract】 Objective To explore the relationship between hypoxia and fertility in female mice. **Methods** Twenty-one clean-grade 14-week Kunming female mice were selected and divided into hypoxia groups ($n=11$) and normoxia groups ($n=10$), and raised under low oxygen concentration (10%-20.5%) and normal oxygen concentration (20.5%) respectively. Four weeks later, hypoxic mice were returned to normoxia environment. Two groups of 21 females were mated with males, the quantity of the litters and body mass at birth were recorded. These females were maintained until 43 weeks to repeat the hypoxic and mating experiments described above. Two weeks after the secondary hypoxia, mating and delivery, these female mice were sampled under anesthesia for inner canthus blood, and the blood estradiol and progesterone were measured by a Roche biochemical analyzer. The mice were put to death by giving over dosage of anesthesia drug; oocytes, ovaries and uterus tissues were obtained, for detection of reactive oxygen species of the oocytes, and HE staining of the ovaries and uterus. **Results** The number of litters produced in the young hypoxia group was 13.64 ± 3.35 , which was slightly higher than that in the young normoxia group (13.22 ± 1.92), but the difference was not significant ($P=0.734$). The birth body mass of the litters in the young hypoxic group [(1.73 ± 0.20) g] was significantly lower than that in the young normoxic group [(1.82 ± 0.22) g, $P<0.001$]. The mean number of litters in the old hypoxic group (5.11 ± 3.58) was significantly higher than that in the old normoxic group (1.38 ± 2.56 , $P=0.022$). Compared with 23 weeks female normoxia mice, estradiol levels decreased in both the old hypoxia and old normoxic groups ($P=0.019$; $P=0.035$), but there was no significant difference in estradiol level between old hypoxia and old normoxic groups ($P=0.913$). There was no significant difference in reactive oxygen species of the oocytes between old normoxic and old hypoxic mice ($P>0.05$). Tissue HE staining showed that the old normoxic mice had obvious uterine hyperemia, and the outlook of the uterus of the old hypoxic mice was normal. The

old hypoxia mice had more antral follicles than the normoxic group and the size of the follicles was more even. **Conclusion** The hypoxia mice produced more offspring than the normoxia mice, however, the birth body mass of the offspring was significantly lower than that in normoxic mice. The ovaries of the old hypoxic mice contained more follicles than the old normoxic mice.

【Key words】 Hypoxia; Ovarian; Aging; Birth body mass

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·流行病学研究·

个体化避孕节育干预对产后妇女的影响

奚卫¹ 刘怡¹ 简春宣¹ 张杰¹ 陈昊¹ 宋春燕¹ 张鹏兮²

¹重庆市人口和计划生育科学技术研究院, 重庆 400020; ²重庆医科大学, 重庆 400020

通信作者: 刘怡, Email: 26435180@qq.com, 电话: +86-15978907788

【摘要】 目的 探讨个体化避孕节育干预对产后妇女所产生的影响, 为今后广泛开展产后避孕提供依据。方法 采用前瞻性研究于 2019 年 7 月至 2020 年 6 月期间在重庆市人口和计划生育科学技术研究院附属医院和另外 7 家医院住院分娩女性 4200 例为研究对象, 采用随机数字表法随机分为观察组和对照组各 2100 例。观察组予住院分娩及产后 42 d 返诊时严格宣教避孕, 个体化落实避孕措施, 发放避孕宣传手册及安全套, 加入避孕咨询与交流平台。对照组按个体化避孕常规宣教及监测。分别于产后 3、6、9、12 个月对研究对象进行电话随访, 获得研究对象的产后性生活恢复时间、月经复潮时间、避孕方式及使用情况、母乳喂养时间、1 年内非意愿妊娠及结局等情况。结果 观察组和对照组的产后避孕知识知晓率 [62.96% (1314/2087) 比 29.35% (606/2065)]、产后 1 年内规范避孕率 [91.71% (1914/2087) 比 44.94% (928/2065)]、高效长效避孕率 [28.08% (586/2087) 比 10.02% (207/2065)]、产后 1 年内非意愿妊娠率 [2.06% (43/2087) 比 8.04% (166/2065)]、人工流产率 [1.29% (27/2087) 比 7.36% (152/2065)] 比较, 差异均有统计学意义 (均 $P < 0.001$)。结论 产后尽早个体化避孕节育干预更有利

于产后妇女掌握避孕相关知识，提升有效避孕率，避免非意愿妊娠，适时保持妊娠间隔，保护生育力，保障生殖健康。

【关键词】 产后避孕； 个体化干预； 非意愿妊娠； 人工流产

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Influence of individual contraceptive intervention on postpartum women

Xi Wei¹, Liu Yi¹, Jian Chunxuan¹, Zhang Jie¹, Chen Hao¹, Song Chunyan¹, Zhang Meixi²

¹ Chongqing Institute of Population and Family Planning Science and Technology, Chongqing 400020, China; ² Chongqing Medical University, Chongqing 400020, China

Corresponding author: Liu Yi, Email: 26435180@qq.com, Tel: +86-15978907788

【 Abstract 】 Objective To explore the influence of individual contraceptive intervention on postpartum women, and to provide basis for widely developing postpartum contraception in the future. **Methods** A prospective study was adopted from July 2019 to June 2020 in the Affiliated Hospital of Chongqing Population and Family Planning Science and Technology Research Institute and other seven hospitals, a total of 4200 cases hospitalized delivery female were randomly divided into observation group and control group using random number table, each group included 2100 cases. The observation group was given the following intervention measures: strict education on contraception during delivery in hospital and 42 d after delivery; individualized implementation of contraceptive measures; distribution of contraceptive brochures and condoms; join the contraceptive consultation and communication platform. The control was given routine education and monitoring. After 3, 6, 9 and 12 months of postpartum, the patients were followed up by telephone. All of the information about their postpartum sexual life recovery time, menstruation time, contraceptive methods and use, breastfeeding time, one year of accidental pregnancy and outcomes were obtained. **Results** Between observation group and control group, there were significant differences in the awareness rate of postpartum contraceptive knowledge [62.96% (1314/2087) vs. 29.35% (606/2065), $P<0.001$], the rates of standard contraception [91.71% (1914/2087) vs. 44.94% (928/2065), $P<0.001$], high-effect and long-effect contraception [28.08% (586/2087) vs. 10.02% (207/2065), $P<0.001$], accidental pregnancy rate [2.06% (43/2087) vs. 8.04% (166/2065), $P<0.001$] and induced abortion rate within one year after delivery [1.29% (27/2087) vs. 7.36% (152/2065), $P<0.001$]. **Conclusion** Individualized contraceptive intervention as early as possible after delivery is more conducive to these women to grasp the knowledge of contraception, improve the effective contraceptive rate, avoid unwanted pregnancy, timely maintain the pregnancy interval, protect fertility and ensure reproductive health.

【 Key words 】 Postpartum contraception; Individualized intervention; Unwanted pregnancy; Induced abortion

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·流行病学研究·

云南省育龄女性睡眠质量与抑郁的关联性研究

邓星梅¹ 杜敏² 叶汉风³ 刘继红⁴ 代树花⁴ 韩春花¹ 荀丽琦¹

景文展² 吴昊² 刘珏² 刘民²

¹云南省曲靖市妇幼保健院, 曲靖 655000; ²北京大学公共卫生学院流

行病与卫生统计学系, 北京 100191; ³云南省人口和计划生育科学技术

研究所, 昆明 650021; ⁴昆明医科大学第二附属医院, 昆明 650101

邓星梅和杜敏对本文有同等贡献

通信作者: 刘民, Email: liumin@bjmu.edu.cn, 电话: +86-13381081707

【摘要】 目的 探讨育龄女性睡眠质量与抑郁的关系, 为促进育龄女性心理健康提供科学依据。方法 本项横断面研究纳入 2019 年 1 月至 2019 年 11 月期间于云南省昆明医科大学第二附属医院和曲靖市妇幼保健院门诊就诊的 12 518 例 15~49 岁育龄女性, 通过自设问卷收集睡眠质量信息, 采用爱丁堡产后抑郁量表收集抑郁信息, 利用 logistic 回归分析控制其他因素影响后, 分析睡眠质量与抑郁的关系。结果 被调查的 12 518 名女性中, 睡眠质量不佳者 3197 人, 占 25.54% (95% CI=24.77%~26.30%)。抑郁状态检出率为 55.59% (6959/12 518; 95% CI=54.72%~56.46%)。睡眠质量不佳组的抑郁状态检出率 [75.40% (2410/3197)] 显著高于睡眠质量良好组的抑郁状态检出率 [48.80% (4549/9321)], 差异具有统计学意义 ($P<0.001$)。多因素 logistic 回归分析显示, 在控制了基本人口学特征、健康状况及生活方式等因素的影响后, 抑郁仍与睡眠质量不佳有关 ($aOR=3.28$, 95% CI=2.99~3.60; $P<0.001$)。结论 育龄女性的睡眠及抑郁问题不容忽视, 且女性睡眠质量与抑郁相关, 提示应当注意保持良好的生活方式, 改善睡眠质量, 促进心理健康。

【关键词】 睡眠; 抑郁; 育龄女性; 云南

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Relationship between sleep quality and depression among fertile women in Yunnan Province

Deng Xingmei¹, Du Min², Ye Hanfeng³, Liu Jihong⁴, Dai Shuhua⁴, Han Chunhua¹, Xun Liqi¹, Jing Wenzhan², Wu Yu², Liu Jue², Liu Min²

¹ Yunnan Maternal and Child Health Hospital of Qujing, Qujing 655000, China; ² Department of Epidemiology and Biostatistics, School of Public Health, Peking University, Beijing 100191, China; ³ Yunnan Institute of Population and Family Planning Science and Technology, Kunming 650021, China; ⁴ The Second Affiliated Hospital of Kunming Medical University, Kunming 650101, China

Deng Xingmei and Du Min contributed equally to the article

Corresponding author: Liu Min, Email: liumin@bjmu.edu.cn, Tel: +86-13381081707

【Abstract】 Objective To explore the relationship between sleep quality and depression among fertile women, and provide a scientific reference for protecting the mental health of fertile women. **Methods** The study included 12 518 fertile women who were 15 to 49 years old from the Second Affiliated Hospital of Kunming Medical University and Maternal and Child Health Hospital of Qujing in Yunnan Province from January 2019 to November 2019. Sleep quality was collected by using self-reported questionnaires, and depression was evaluated by using the Edinburgh Postpartum Depression Scale. We used logistic regression to analyze the relationship between sleep quality and depression after controlling for other factors. **Results** Among 12 518 fertile women, 3197 had poor sleep quality which accounted for 25.54% (95% CI=24.77%-26.30%). The detection rate of depression was 55.59% (6959/12 518; 95% CI=54.72%-56.46%). The detection rate of depression of the poor sleep quality group [75.40% (2410/3197)] was significantly higher than that of the good sleep quality group [48.80% (4549/9321), $P<0.001$]. Multivariate logistic regression analysis showed that after controlling for basic demographic characteristics, health status, lifestyle habits and other factors, depression was still associated with poor sleep quality (aOR=3.28, 95% CI=2.99-3.60; $P<0.001$). **Conclusion** The problem of depression and sleep quality on fertile women cannot be ignored, and sleep quality was associated with depression significantly which suggested that it was necessary to keep good life style, improve sleep quality and promote mental health.

【Key words】 Sleep; Depression; Fertile women; Yunnan province

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·临床报道·

GnRH 超短激动剂联合拮抗剂方案在 POSEIDON 低预后患者中的应用效果分析

刘源瀛 杜晓果 陈立雪 杨蕊 王永清 王颖 李蓉 刘平 乔杰
北京大学第三医院妇产科生殖医学中心，国家妇产疾病临床研究中心
（北京大学第三医院），辅助生殖教育部重点实验室（北京大学），北
京市生殖内分泌与辅助生殖技术重点实验室，北京 100191

通信作者：杨蕊，Email: yrjeff@126.com，电话：+86-10-82266625

【摘要】 目的 探讨促性腺激素释放激素(gonadotropin-releasing hormone, GnRH)超短激动剂联合拮抗剂(agonist-antagonist protocol, AAP)方案与标准拮抗剂方案相比，是否可以改善波塞冬(Patient-Oriented Strategies Encompassing Individualized Oocyte Number, POSEIDON)分类标准低预后患者的临床结局。方法 采用病例对照研究，回顾性分析 2016 年 1 月至 2018 年 5 月期间就诊于北京大学第三医院妇产科生殖医学中心，接受体外受精-胚胎移植(*in vitro* fertilization-embryo transfer, IVF-ET)的低预后患者(POSEIDON 3 组、4 组)646 个周期的临床资料。使用 AAP 方案的，记为 AAP 组(323 个周期)，对照组按照 1:1 选择同时期年龄匹配、应用标准拮抗剂方案患者，比较两组患者的一般资料、促排卵周期指标及临床结局。结果 AAP 组窦卵泡计数(antral follicle count, AFC)偏少[3.00(2.00, 4.00)比 4.00(2.00, 5.00), $P<0.001$]，抗苗勒管激素(anti-Müllerian hormone, AMH)水平两组相似[0.51(0.25, 0.83) $\mu\text{g/L}$ 比 0.53(0.31, 0.81) $\mu\text{g/L}$, $P>0.05$]，AAP 组促性腺激素(gonadotropin, Gn)使用时间更短[10.00(8.00, 11.00) d 比 10.00(9.00, 11.00) d, $P=0.020$]，Gn 用量更低[2 675.00(2 100.00, 3 300.00) U 比 3 075.00(2 550.00, 3 750.00) U, $P<0.001$]，两组获卵数相当[3.00(2.00, 5.00)枚比 4.00(2.00, 6.00)枚, $P>0.05$]。在受精方案比例(常规受精/卵胞质内单精子注射受精)相当的情况下，AAP 组有更高的受精率[74.15%(955/1288)比 69.13%(918/1328), $P=0.004$]和优质胚胎率[62.57%(585/935)比 56.94%(509/894), $P=0.014$]，且最终有更高的胚胎着床率[22.31%(87/390)比 15.84%(64/404), $P=0.020$]、累积临床妊娠率[32.50%(78/240)比 22.86%(56/245), $P=0.018$]和累积活产率[25.83%(62/240)比 17.96%(44/245), $P=0.036$]。结论 对于 POSEIDON 低预后 3 组、4 组患者，AAP 方案较常规拮抗剂方案有更佳的临床结局。

【关键词】 促性腺激素释放激素； 促性腺激素释放激素超短激动剂； 促性腺激素释放激素拮抗剂； 卵巢低反应

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Application of controlled ovarian hyperstimulation with agonist-antagonist protocol in POSEIDON group 3 and group 4 patients with low prognosis

Liu Yuanying, Du Xiaoguo, Chen Lixue, Yang Rui, Wang Yongqing, Wang Ying, Li Rong, Liu Ping, Qiao Jie

Department of Obstetrics and Gynecology, Reproductive Medical Center, Peking University Third Hospital, National Clinical Research Center for Obstetrics and Gynecology (Peking University Third Hospital), Key Laboratory of Assisted Reproduction (Peking University), Ministry of Education, Beijing Key Laboratory of Reproductive Endocrinology and Assisted Reproductive Technology, Beijing 100191, China

Corresponding author: Yang Rui, Email: yrjeff@126.com, Tel: +86-10-82266625

【Abstract】 Objective By comparing standard gonadotropin-releasing hormone antagonist regimen and gonadotropin-releasing hormone agonist-antagonist protocol (AAP regimen) in Patient-Oriented Strategies Encompassing Individualized Oocyte Number (POSEIDON) group 3 and group 4 patients with low prognosis, to study if AAP regimen could improve the clinical outcomes in low prognosis patients. **Methods** A case-control study was performed, the clinical data of 646 cycles of prospective poor ovarian response (POR) patients (POSEIDON group 3 and 4) who received *in vitro* fertilization and embryo transfer (IVF-ET) in Peking University Third Hospital Department of Obstetrics and Gynecology, Reproductive Medical Center from January 2016 to May 2018 were retrospectively analyzed. The total number of AAP cycle was 323, and control group was selected from the database with 1:1 matching of contemporaneous prospective POR patients (POSEIDON group 3 and group 4) with similar age and approaching date of oocyte retrieval. Patients' general information, ovarian stimulation indexes and clinical outcomes were compared. **Results** AAP group had fewer antral follicle count (AFC) [3.00(2.00,4.00) vs. 4.00(2.00,5.00), $P<0.001$] and similar anti-Müllerian hormone (AMH) level [0.51(0.25,0.83) $\mu\text{g/L}$ vs. 0.53(0.31,0.81) $\mu\text{g/L}$, $P>0.05$] compared with control group. AAP group had shorter duration of gonadotropin (Gn) used [10.00(8.00,11.00) d vs. 10.00(9.00,11.00) d, $P=0.020$] and lower dosage of Gn used [2 675.00(2 100.00,3 300.00) U vs. 3 075.00(2 550.00,3 750.00) U, $P<0.001$] than control group. AAP group had similar number of oocytes obtained [3.00(2.00,5.00) vs. 4.00(2.00,6.00), $P>0.05$] compared with control group. Under the same proportion of fertilization schemes (routine or intracytoplasmic sperm injection methods), AAP group had higher fertilization rate [74.15% (955/1288) vs. 69.13% (918/1328), $P=0.004$] and good-quality embryo rate [62.57% (585/935) vs. 56.94% (509/894), $P=0.014$], and ultimately had higher embryo implantation rate [22.31% (87/390) vs. 15.84% (64/404), $P=0.020$], cumulative clinical pregnancy rate [32.50% (78/240) vs. 22.86% (56/245), $P=0.018$] and cumulative live birth rate [25.83% (62/240) vs. 17.96% (44/245), $P=0.036$]. **Conclusion** For POSEIDON patients with low prognosis and POR, controlled ovarian hyperstimulation with AAP regimen had better clinical outcomes compared with conventional antagonist regimen.

【Key words】 Gonadotropin-releasing hormone; Ultrashort gonadotropin-releasing hormone agonist; Gonadotropin-releasing hormone antagonist; Poor ovarian response

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·个案报道·

移植 1 枚第 2 日透明带部分消失的胚胎后活产的病例报道与文献复习

刘霜¹ 王明勇¹ 黄桂英¹ 王芳¹ 付莉¹ 张俊² 陈绍威¹

¹西南医科大学附属医院生殖中心, 泸州 646000; ²西南医科大学心血管医学研究所, 泸州 646000

通信作者: 陈绍威, Email: csw1030@swmu.edu.cn, 电话: +86-15984021860

【摘要】 目的 探讨 1 枚第 2 日透明带部分消失的胚胎的处理方法及总结在培养过程中无透明带胚胎的鉴别和处理方法。方法 报道移植 1 枚第 2 日透明带部分消失的胚胎后成功活产的病例并文献复习。结果 经过减少移植清洗过程, 患者孕 39⁺₃ 周成功分娩 1 名女活婴。结论 透明带消失可能影响胚胎的致密化过程, 但经过对胚胎进行慎重筛选以及减少移植清洗过程, 仍可获得良好结局。

【关键词】 胚胎发育; 活产; 透明带消失

基金项目: 四川省科技厅应用基础研究(22YYJC3041); 西南医科大学校级课题(01/00030670)

Live birth following the transfer of an embryo with partial dissolution of zona pellucida on day 2: a case report and literature review

Liu Shuang¹, Wang Mingyong¹, Huang Guiying¹, Wang Fang¹, Fu Li¹, Zhang Jun², Chen Shaowei¹

¹ Reproductive Medical Center, Affiliated Hospital of Southwest Medical University, Luzhou 646000, China; ² Institute of Cardiovascular Medicine, Southwest Medical University, Luzhou 646000, China

Corresponding author: Chen Shaowei, Email: csw1030@swmu.edu.cn, Tel: +86-15984021860

【Abstract】 Objective To investigate the treatment of an embryo with the partial dissolution of zona pellucida on day 2 and summarize the identification and treatment of embryos without zona pellucida during culture. **Methods** A case of one live baby from an embryo with the partial dissolution of zona pellucida transferred on day 2 was retrospectively analyzed. **Results** Through reducing the transplant cleaning process, the patient got pregnant and delivered a live girl baby at 39⁺³ weeks of gestation. **Conclusion** The early dissolution of zona pellucida may affect the compaction process of embryos, but a good outcome can still be obtained by carefully selecting embryos and reducing the washing process of embryo transfer.

【Key words】 Embryonic development; Live birth; Dissolution of zona pellucida

Fund program: Science & Technology Department of Sichuan Province (22YYJC3041); Project of Southwest Medical University (01/00030670)

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·个案报道·

宫内节育器致纤维包裹结节伴大量宫腔积脓 1 例报道

宋旭敏¹ 单莺¹ 蒋翠¹ 李焱焱¹ 耿源源² 陈丽¹

¹上海市浦东医院妇产科, 上海 201399; ²上海市浦东医院病理科, 上海 201399

通信作者: 陈丽, Email: chenli8369@163.com, 电话: +86-13817458823

【摘要】 目的 探讨宫内节育器致纤维包裹结节伴大量宫腔积脓的诊断、治疗及预防。方法 对 1 例宫内节育器致纤维包裹结节伴大量宫腔积脓患者的诊治过程进行分析报道, 并复习相关文献, 分析病因及诊疗措施。结果 患者行全子宫+双附件切除术, 术后病理提示子宫腔局部内膜组织缺失, 见大量急慢性炎细胞浸润、淋巴滤泡形成伴炎性渗出及坏死, 包裹节育器结节为纤维素性坏死物。患者术后恢

复良好。结论 宫内节育器致纤维包裹结节伴大量宫腔积脓较为罕见，月经停止后6~12个月内建议取出宫内节育器以预防该疾病发生。

【关键词】 宫内节育器； 纤维包裹结节； 宫腔积脓

基金项目：上海市浦东医院院级人才培养“浦菁人才”资助（PJ201902）

Fibrous encapsulated nodule with massive pyometra caused by intrauterine device: a case report

Song Xumin¹, Shan Ying¹, Jiang Cui¹, Li Yanyi¹, Geng Yuanyuan², Chen Li¹

¹ Department of Obstetrics and Gynecology, Shanghai Pudong Hospital, Shanghai 2013992, China; ² Department of Pathology, Shanghai Pudong Hospital, Shanghai 201399, China

Corresponding author: Chen Li, Email: chenli8369@163.com, Tel: +86-13817458823

【 Abstract 】 Objective To explore the diagnosis, treatment and prevention of fibrous encapsulated nodules with massive pyometra caused by intrauterine device (IUD). **Methods** The diagnosis and treatment of a patient with fibrous encapsulated nodule and massive pyometra caused by IUD is reported and analyzed. **Results** The patient underwent panhysterectomy+bilateral adnexectomy. Postoperative pathology showed local endometrial tissue loss in the uterine cavity, a large number of acute and chronic inflammatory cell infiltration, inflammatory exudation and necrosis of lymphatic follicles. The encapsulated contraceptive nodule was fibrinous necrosis with an IUD in it. The patient recovered well after surgery. **Conclusion** Fibrous encapsulated nodules with massive pyometra caused by IUD are rare, and removal of IUD within 6–12 months after cessation of menstruation is suggested to prevent the occurrence of this disease.

【 Key words 】 Intrauterine device; Fibrous encapsulated nodule; Pyometra

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·综述·

常见内分泌干扰物对人类生殖功能损伤及其药物干预的研究进展

周萍 吴建辉

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，上海 200032

通信作者: 吴建辉, Email: wujh_731@163.com, 电话: +86-13764523712

【摘要】 内分泌干扰物 (endocrine disrupting chemicals, EDCs) 是一种新型持久性的有机污染物, 人们通过皮肤、消化道、呼吸道等途径不可避免地暴露于 EDCs, 大量研究表明 EDCs 可损害生殖系统、中枢神经系统、心血管系统、免疫系统以及内分泌系统, 因此亟待开展干预 EDCs 毒性的药物研究。双酚 A、邻苯二甲酸二 (2-乙基己基) 酯、重金属、丙烯酰胺是常见的 EDCs, 本文将对这些常见 EDCs 诱发的生殖损伤及现今相关药物干预研究进行总结概述, 以期开发更多干预 EDCs 的药物提供理论依据。

【关键词】 双酚 A; 邻苯二甲酸二 (2-乙基己基) 酯; 丙烯酰胺; 生殖损伤; 干预

基金项目: 上海市自然科学基金项目 (19ZR1444400)

Research progress on the damage of human reproductive function caused by common endocrine disruptors and its drug intervention

Zhou Ping, Wu Jianhui

NHC Key Lab. of Reproduction Regulation (Shanghai Institute for Biomedical and Pharmaceutical Technologies), Shanghai 200032, China

Corresponding author: Wu Jianhui, Email: wujh_731@163.com, Tel: +86-13764523712

【Abstract】 Endocrine disrupting chemicals (EDCs) are a new type of persistent organic pollutant. Humans are inevitably exposed to EDCs through multiple routes of skin, digestive tract, and respiratory tract. Several studies indicate that EDCs impair the reproductive system, central nervous system, cardiovascular system, immune system, and endocrine system. Therefore, it is urgent to carry out drug research to interfere with the toxicity of EDCs. Bisphenol A, di-(2-ethylhexyl) phthalate, heavy metals, and acrylamide are common endocrine disruptors. This article will summarize these common endocrine disruptors-induced reproductive damage and the current drug intervention studies, expecting to provide some theoretical support for the development of more drugs to interfere with EDCs.

【Key words】 Bisphenol A; Bis(2-ethylhexyl) phthalate; Acrylamide; Reproductive damage; Intervention

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·综述·

孕激素治疗子宫内膜异位症的研究进展

黄新 黄薇

四川大学华西第二医院生殖医学科 出生缺陷与相关妇儿疾病教育部重点实验室, 成都 610041

通信作者: 黄薇, Email: weihuang64@163.com, 电话: +86-13881858999

【摘要】 孕激素受体是配体激活的核转录调节因子, 其配体包含天然孕激素、孕激素衍生物及合成孕激素等。子宫内膜异位症是雌激素依赖的炎症性疾病, 孕激素类药物作用于异位病灶可以起到拮抗雌激素、抗炎、抗血管神经生成及促凋亡的作用。然而, 子宫内膜异位症存在孕激素抵抗等病因学因素, 孕激素类药物并不能对所有子宫内膜异位症患者起到令人满意的治疗效果。本文将对孕激素受体配体治疗子宫内膜异位症的机制、影响疗效的因素及改善疗效的策略进行综述, 为子宫内膜异位症的药物治疗提供新的思路。

【关键词】 孕激素受体; 子宫内膜异位症; 药物治疗; 孕激素抵抗

基金项目: 国家重大研发计划 (2017YFC1001202-2); 国家自然科学基金面上项目 (82071625); 四川省科学技术厅重点研发项目 (2021YFS0028)

Research progress of progestins in endometriosis treatment

Huang Xin, Huang Wei

Division of Reproductive Medicine, West China Second University Hospital of Sichuan University, Key Laboratory of Birth Defects and Related Diseases of Women and Children of Ministry of Education, Chengdu 610041, China

Corresponding author: Huang Wei, Email: weihuang64@163.com, Tel: +86-13881858999

【Abstract】 Progesterone receptor is ligands-activated nuclear transcription regulator, the ligands including natural progesterone, progesterone derivatives and synthetic progesterone. Endometriosis is estrogen-dependent inflammatory disease, progestins can induce anti-estrogenic, anti-inflammatory, anti-neuroangiogenesis and pro-apoptotic effects to endometriotic lesions. However, owing progesterone resistance and other etiological factors of endometriosis, progestins sometimes cannot achieve satisfactory therapeutic effects. This review focused on the mechanism of progesterone receptor ligands influencing endometriosis medical therapeutic effects, which may help to give novel clues to endometriosis drug therapy.

【Key words】 Progesterone receptor; Endometriosis; Drug therapy; Progesterone resistance

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·综述·

人 *ZP* 基因突变导致卵子异常和不孕的研究进展

姚叶洁 孙贇

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

通信作者：孙贇, Email: syun163@163.com, 电话: +86-21-20284500

【摘要】 透明带 (zona pellucida, ZP) 基因属于卵细胞特异性表达基因, 编码 ZP 蛋白。人类的 ZP 蛋白包括 ZP1、ZP2、ZP3 和 ZP4 四个成员, 参与组成了围绕在卵子质膜周围的 ZP。ZP 能参与精卵识别、诱导顶体反应, 防止多精受精同时能保护早期胚胎发育。敲除小鼠相关 *ZP* 基因会导致卵子形态异常和 (或) 生育障碍。部分原发性不孕的患者存在 *ZP* 基因的突变, 主要表现为卵子 ZP 变薄、ZP 缺失或者空卵泡综合征。本文将对 *ZP* 基因及蛋白的结构和功能、人不同 *ZP* 基因突变与卵子异常的关联作一系统阐述。

【关键词】 透明带; 透明带基因突变; 卵子异常; 空卵泡综合征; 不孕

基金项目: 上海交通大学医学院高水平地方高校创新团队 (SSMU-ZLCX20180401); 上海市教育委员会高峰高原学科建设计划 (20161413)

Advances in *ZP* gene mutation causing abnormal oocyte and infertility

Yao Yejie, Sun Yun

Centre for Reproductive Medicine, Renji Hospital, Shanghai Jiao Tong University

School of Medicine, Shanghai Key Laboratory for Assisted Reproduction and Reproductive Genetics, Shanghai 200135, China

Corresponding author: Sun Yun, Email: syun163@163.com, Tel: +86-21-20284500

【Abstract】 Zona pellucida (ZP) genes, which code for the ZP glycoproteins, are expressed exclusively in oocytes. The ZP glycoproteins of human, consisting of ZP1, ZP2, ZP3 and ZP4, form ZP surrounding the oocytes' plasma membrane. ZP plays a critical role in sperm-egg binding and induction of acrosome reaction, prevents polyspermy and protects early embryo growth. The mice which knockout *ZP* gene have abnormal oocyte morphology and/or fertility disorders. Sequencing of the *ZP* gene has been detected in sporadic patients with repeated cycles of oocyte maturation arrest or morphologic defects, manifesting as ZP-thin oocytes, ZP-free oocytes and empty follicle syndrome. In this paper, the structure and function of *ZP*

gene and protein, the relationship between different ZP gene mutations and ovum abnormalities were systematically described.

【Key words】 Zona pellucida; Zona pellucida gene mutation; Abnormal oocyte; Empty follicle syndrome; Infertility

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·综述·

附睾上皮细胞通过附睾小体调节精子成熟的研究进展

张华楠 赵芝威 魏金花 李臻

空军军医大学人体解剖与组织胚胎学教研室, 西安 710032

通信作者: 魏金花, Email: xiaofang-720@163.com, 电话: +86-29-

84774511

【摘要】 哺乳动物睾丸中产生的精子缺乏运动性, 而且不具备受精能力, 因此在功能上尚不成熟。附睾是男性生殖道中一段非常特别、高度盘绕折叠的小管, 附睾各段通过上皮细胞分泌和吸收活动的共同协作用, 实现高度区域化, 保证不同区段精确的功能划分。精子在附睾近端完成功能上的成熟, 在远端以静息状态储存以备射精, 这一过程依赖于附睾管腔特殊的微环境。附睾管腔的微环境极为复杂, 目前已证实其中含有多无机离子、蛋白质和胞外囊泡(附睾小体)。附睾小体中包含多种蛋白和 sncRNA, 可直接或间接促进精子成熟。本文综述了附睾管腔微环境的特点, 特别关注了附睾上皮细胞产生的附睾小体对精子成熟的影响。

【关键词】 附睾; 精子成熟; 细胞内通讯; 蛋白运输; 附睾小体
基金项目: 国家自然科学基金(31871515); 陕西省重点研发计划(2021SF-055)

Research progress on epididymal epithelial cells regulate sperm maturation through the epididymosome

Zhang Huanan, Zhao Zhiwei, Wei Jinhua, Li Zhen

Department of Anatomy, Histology and Embryology, the Air Force Medical University, Xi'an 710032, China

Corresponding author: Wei Jinhua, Email: xiaofang-720@163.com, Tel: +86-29-84774511

【Abstract】 The spermatozoa produced in mammalian testis are functionally immature for lack of fertilizing ability and forward motility properties. Epididymis is a highly specialized and extremely coiled ductal system of the male reproductive tract. The precise division of the function in each segment is achieved by the combined secretory and absorptive activity of the epithelial cells lining each segment. Thus, spermatozoa acquire functional maturity in the proximal segments before being stored in a resting state in the distal segment preparing for ejaculation. Sperm maturation during epididymal transit is reliant on the highly specialized intraluminal microenvironment of the epididymis. The microenvironment of epididymal lumen is extremely complex, and the fluid contains a variety of inorganic ions, proteins and extracellular vesicles (epididymosome). Various components in epididymosome including kinds of proteins and sncRNA play an important role in regulating sperm maturation directly or indirectly. Here, we review the characteristics of microenvironment in the epididymal lumen, with a particular focus on the effects of epididymosome secreted by epididymal epithelial cells on sperm maturation.

【Key words】 Epididymis; Sperm maturation; Intracellular communication; Protein trafficking; Epididymosome

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·指南解读·

2020 年 ESMO 青春期后恶性肿瘤患者生育力保存和治疗后妊娠临床实践指南解读

王巍¹ 李顺双² 刘刚¹

¹ 河南省人民医院, 郑州大学人民医院妇产科, 临床医学研究中心, 郑

州 450003; ² 郑州大学第一附属医院妇产科, 郑州 450052

通信作者: 刘刚, Email: zdxliugang@126.com, 电话: +86-19837101990

【摘要】 全球范围内恶性肿瘤发病率呈上升趋势, 发病年龄呈年轻化趋势, 肿瘤患者的生育力保护和保存日益受到重视。2020 年欧洲肿瘤内科学会(European Society for Medical Oncology, ESMO) 发布了最新的青春期后恶性肿瘤患者生育力保存和治疗后妊娠的临床实践指南, 对生育力保护和保存策略的实施, 抗肿瘤治疗性腺毒性的风险评估, 遗传性肿瘤综合征患者生育力保存, 抗肿瘤治疗后妊娠等给出了基于循证医学证据的指导意义。指南提出在临床实践过程中应遵循个体化原则, 在不影响抗肿瘤治疗的情况下, 对青春期后肿瘤患者选择合适的生育力保存方案。

【关键词】 肿瘤; 生育力保护; 不育; 妊娠; 指南; 解读

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Interpretation to European Society for Medical Oncology Clinical Practice Guideline 2020: Fertility Preservation and Post-treatment Pregnancies in Post-pubertal Cancer Patients

Wang Wei¹, Li Shunshuang², Liu Gang¹

¹ Department of Gynecology and Obstetrics, Department of Clinical Research Center, Henan Provincial People's Hospital, People's Hospital of Zhengzhou University, Zhengzhou 450003, China; ² Department of Gynecology and Obstetrics, the First Affiliated Hospital of Zhengzhou University, Zhengzhou 450052, China

Corresponding author: Liu Gang, Email: zdxliugang@126.com, Tel: +86-19837101990

【Abstract】 With the increasing incidence of malignancy on a global scale and tendency of younger onset age, more attention being paid for the protection and conservation of fertility in cancer patients. In 2020, the European Society for Medical Oncology (ESMO) formulated the latest clinical practice guidelines for fertility preservation and post-treatment pregnancies in post-pubertal cancer patients. The guidance for implementation of fertility protection and preservation strategy, risk assessment of gonadal toxicity of anti-tumor treatment, intervention measures of gonadal damage caused by risk reduction surgery, fertility preservation of patients with hereditary cancer syndrome and pregnancy after anti-tumor treatment were given. The clinical practice guidelines suggest that the principle of individualization should be followed, and the appropriate fertility preservation scheme should be selected for cancer patients after puberty without affecting the anti-tumor treatment.

【Key words】 Tumor; Fertility preservation; Sterility; Pregnancy; Guideline; Interpretation

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