

DOI: 10.3760/cma.j.cn101441-20250209-00053

收稿日期 2025-02-09 本文编辑 孙敏

引用本文: 郭雪江. 精子质量与子代健康[J]. 中华生殖与避孕杂志, 2025, 45(6): 541-544. DOI: 10.3760/cma.j.cn101441-20250209-00053.

精子质量与子代健康

郭雪江

南京医科大学生殖医学与子代健康全国重点实验室, 南京 211166

Email: guo_xuejiang@njmu.edu.cn

【摘要】 生殖与子代健康是民生大计, 目前男性不育大部分可归因于精子质量的下降, 而精子作为遗传信息的载体可从不同方面影响全生命周期和子代健康。本文重点关注精子质量与子代健康的关系及相应机制, 精子可从遗传或表观遗传等方面对子代健康产生深远的影响, 男性的身心健康状况引起的精子质量问题可导致染色体数目异常、代谢性疾病或者精神类疾病等后代健康问题。未来应更加重视父源遗传物质缺陷或表观遗传异常致精子质量下降引发的子代健康问题, 建立早期筛查与检测的体系及临床推广应用, 对提升生殖健康和促进优生优育具有重要意义。

【关键词】 遗传; 表观遗传; 精子质量; 子代健康; 精子微小 RNA
基金项目: 国家自然科学基金 (82221005、82371606)

Sperm quality and offspring health

Guo Xuejiang

Nanjing Medical University, State Key Laboratory of Reproductive Medicine and Offspring Health, Nanjing 211166, China

Email: guo_xuejiang@njmu.edu.cn

【Abstract】 Reproduction and offspring health are important for people's livelihood. Most of the male infertility can be attributed to the sperm quality decline. Sperm, the carrier of genetic information, can affect the whole life cycle and offspring health from different aspects. This article focused on the relationship between sperm quality and offspring health and the underlying mechanisms. Sperm can have a profound impact on the health of the offspring from genetic or epigenetic aspects. Sperm defects caused by the physical and mental health of the father can lead to offspring health problems such as chromosome numerical abnormalities, metabolic diseases or mental diseases. In the future, more attention

should be paid to the offspring health caused by the paternal genetic or epigenetic defects. The establishment of an early screening and detection system and its clinical application are of great significance to improve reproductive health and prenatal and postnatal care.

【Key words】 Genetics; Epigenetics; Sperm quality; Offspring health; Sperm small RNA

Fund program: National Natural Science Foundation of China (82221005, 82371606)

男性不育专栏

DOI: 10.3760/cma.j.cn101441-20250225-00090

收稿日期 2025-02-25 本文编辑 孙敏

引用本文: 房建正, 孙雪萍, 沈鉴东, 等. 常染色体显性多囊肾合并男性不育患者的遗传学诊断及其行 PGT-M 的助孕结局分析 [J]. 中华生殖与避孕杂志, 2025, 45(6): 545-550. DOI: 10.3760/cma.j.cn101441-20250225-00090.

常染色体显性多囊肾合并男性不育患者的遗传学诊断及其行 PGT-M 的助孕结局分析

房建正¹ 孙雪萍¹ 沈鉴东¹ 王增军² 杨晓玉¹

¹南京医科大学第一附属医院生殖医学科, 南京 210029; ²南京医科大学第一附属医院泌尿外科, 南京 210029

通信作者: 杨晓玉, Email: yxy1921@163.com

【摘要】 目的 探讨常染色体显性多囊肾 (autosomal dominant polycystic kidney disease, ADPKD) 合并男性不育患者的精液特征及 *PKD1* 突变对其行胚胎植入前单基因遗传病检测 (preimplantation genetic testing for monogenic, PGT-M) 助孕结局的影响。方法 采用回顾性队列研究方法, 对 2015 年 1 月至 2023 年 12 月于南京医科大学第一附属医院生殖医学科就诊的 20~45 岁 ADPKD 合并男性不育患者 (记为观察组, $n=78$) 和 *PKD1* 突变但精液参数正常的 ADPKD 患者 (记为对照组, $n=5$) 的临床资料进行分析。根据 *PKD1* 突变类型将研究对象分为截短突变组和非截短突变组, 比较两组患者的基本特征、促排卵结局及 PGT-M 临床结局的差异。采用二元 logistic 回归分析评估年龄、家族史、*PKD1* 突变类型和突变位置对精液参数及助孕活产率的影响。结果 观察组中弱精子症 28 例, 少弱精子症 38 例, 无精子症 12 例。观察组中弱精子症、少弱精子症和无精子症患者的精子总数和精子前向

运动比例与对照组相比, 差异有统计学意义 (均 $P < 0.001$)。遗传性诊断检测到 70 例有 *PKD1* 突变, 1 例有 *PKD2* 突变, 7 例未检测到已知致病突变。70 例 *PKD1* 突变 ADPKD 患者中的 52 对夫妇进行了 PGT-M 助孕, 非截短突变组囊胚形成率 [44.74% (51/114)] 低于截短突变组 [58.76% (161/274), $P = 0.011$], 两组间其他参数如男女双方年龄、精液参数、获卵数、双原核率、可利用胚胎数、优质胚胎率、临床妊娠率、流产率及活产率差异均无统计学意义 (均 $P > 0.05$)。二元 logistic 回归分析显示, ADPKD 患者的 *PKD1* 突变类型及突变部位均不是影响精液参数异常及活产率的独立影响因素 (均 $P > 0.05$)。结论 弱精子症和少弱精子症是 ADPKD 合并男性不育最常见的精液表型; *PKD1* 突变类型和突变位置与 ADPKD 合并不育患者精液参数异常未见相关性; 不同类型的 *PKD1* 突变不影响 ADPKD 合并不育患者行 PGT-M 的助孕结局。

【关键词】 多囊肾, 常染色体显性; 男性不育症; *PKD1*; 精液参数; 胚胎植入前单基因遗传病检测

基金项目: 国家自然科学基金面上项目 (82271638)

Genetic diagnosis in male infertility patients with autosomal dominant polycystic kidney disease and assisted reproductive outcomes after PGT-M

Fang Jianzheng¹, Sun Xueping¹, Shen Jiandong¹, Wang Zengjun², Yang Xiaoyu¹

¹ Clinical Center of Reproductive Medicine, the First Affiliated Hospital of Nanjing Medical University, Nanjing 210029, China; ² Department of Urology, the First Affiliated Hospital of Nanjing Medical University, Nanjing 210029, China

Corresponding author: Yang Xiaoyu, Email: yxy1921@163.com

【Abstract】 Objective To investigate the semen characteristics of male patients with autosomal dominant polycystic kidney disease (ADPKD) complicated by infertility and the impact of *PKD1* mutations on their reproductive outcomes following preimplantation genetic testing for monogenic diseases (PGT-M). **Methods** A retrospective cohort study was conducted to analyze the clinical data of ADPKD patients in the Clinical Center of Reproductive Medicine, the First Affiliated Hospital of Nanjing Medical University from January 2015 to December 2023. The study included two groups: observation group consisting of male infertility patients with ADPKD aged 20–45 years ($n=78$), and control group comprising ADPKD patients with *PKD1* mutations who demonstrated normal semen parameters ($n=5$). According to the type of mutation, the patients were further divided into the *PKD1* truncated mutation group and the non-truncated mutation group. Baseline data, ovulation induction outcomes and PGT-M clinical outcomes were compared between the two groups. Binary logistic regression analysis was used to assess the effects of age, family history, mutation type and mutation position on semen quality and live birth rates. **Results** In the observation group, there were 28 cases of asthenozoospermia, 38 cases of oligoasthenozoospermia, and 12 cases of azoospermia. The total sperm count and forward motility ratio of patients with asthenozoospermia, oligoasthenozoospermia, and azoospermia in the observation group were significantly different from those in control group (all $P < 0.001$). Genetic diagnosis revealed *PKD1* mutations in 70 cases, *PKD2* mutation in 1 case, and no known

pathogenic mutations were identified in 7 cases. Among the 70 ADPKD patients with *PKD1* mutations, 52 couples underwent PGT-M assisted reproduction. The blastocyst formation rate was significantly lower in the non-truncating mutation group [44.74% (51/114)] than in the truncating mutation group [58.76% (161/274), $P=0.011$]. No statistically significant differences were observed between the two groups in other parameters including age of both partners, semen parameters, number of oocytes retrieved, two pronuclei (2PN) rate, number of available embryos, high-quality embryo rate, clinical pregnancy rate, miscarriage rate, and live birth rate (all $P>0.05$). Binary logistic regression analysis showed that neither *PKD1* mutation type nor *PKD1* mutation site was an independent factor affecting semen parameters and live birth rate in ADPKD patients (all $P>0.05$).

Conclusions Asthenospermia and oligoasthenospermia are the most common semen phenotypes in ADPKD-associated male infertility. The *PKD1* mutation type and location are not associated with abnormal semen parameters in ADPKD-associated infertility patients. *PKD1* mutation types do not affect the outcomes of PGT-M in infertile patients with ADPKD.

【Key words】 Polycystic kidney, autosomal dominant; Male infertility; *PKD1*; Semen parameters; Preimplantation genetic testing for monogenic

Fund program: General Program of National Natural Science Foundation of China (82271638)

·男性不育专栏·

DOI: 10.3760/cma.j.cn101441-20250228-00096

收稿日期 2025-02-28 本文编辑 王李艳

引用本文: 吴俊杰, 余怡, 汪凯, 等. 人参皂苷 Rg1 通过调控自噬改善糖尿病所致小鼠睾丸损伤[J]. 中华生殖与避孕杂志, 2025, 45(6): 551-557. DOI: 10.3760/cma.j.cn101441-20250228-00096.

人参皂苷 Rg1 通过调控自噬改善糖尿病所致小鼠睾丸损伤

吴俊杰¹ 余怡² 汪凯³ 刘朋飞⁴ 战明威⁴ 王磊⁵ 姚凡¹ 徐立奇⁶ 商学军¹

¹南京中医药大学金陵临床医学院, 南京 210002; ²宁波大学附属第

一医院生殖医学中心, 宁波 315010; ³中国人民解放军联勤保障部

队第九〇六医院病理科, 宁波 315040; ⁴ 南京大学医学院附属金陵

医院泌尿外科, 南京 210002; ⁵ 东南大学医学院, 南京 210009; ⁶

中国人民解放军联勤保障部队第九〇六医院生殖中心, 宁波 315040

余怡与吴俊杰对本文有同等贡献

通信作者: 商学军, Email: shangxj98@163.com

【摘要】 目的 探究人参皂苷 Rg1 对糖尿病所致小鼠生精功能障碍的影响及其作用机制。**方法** 将 18 只 C57BL/6 雄性小鼠通过完全随机法随机分为对照组、模型组、人参皂苷 Rg1 组, 每组 6 只。模型组和人参皂苷 Rg1 组通过高脂饮食联合腹腔注射链脲佐菌素建立 2 型糖尿病模型, 对照组注射等量生理盐水。建模成功后对照组给予常规饮食 8 周, 模型组和人参皂苷 Rg1 组给予高脂饮食 8 周, 人参皂苷 Rg1 组同时给予人参皂苷 Rg1 药物治疗。酶联免疫吸附实验检测试剂盒检测生殖激素水平, Western blotting 检测凋亡相关蛋白 (Bcl2 蛋白、Caspase-3 蛋白、Bax 蛋白)、自噬相关蛋白 (P62、LC3 I、LC3 II、Beclin1)、 β -Catenin 蛋白、mTOR 蛋白、LAMP1 蛋白和转录因子 EB 的表达, 比较各组小鼠体质量、血糖水平、睾丸指数及睾丸损伤状况。**结果** 模型组小鼠体质量 [(18.77 $\pm$ 1.14) g]、睾酮水平 [(141.07 $\pm$ 8.47) ng/L]、卵泡刺激素水平 [(9.19 $\pm$ 0.74) U/L]、黄体生成素水平 [(1497.91 $\pm$ 99.57) pg/L] 均显著低于对照组 [(31.57 $\pm$ 2.35) g, $P<0.001$; (171.50 $\pm$ 11.76) ng/L, $P<0.001$; (12.46 $\pm$ 1.54) U/L, $P<0.001$; (1807.29 $\pm$ 92.76) pg/L, $P<0.001$], 空腹血糖水平 [(20.82 $\pm$ 1.11) mmol/L]、糖化血红蛋白 (12.67% $\pm$ 1.03%)、睾丸指数 (0.65% $\pm$ 0.03%) 显著高于对照组 [(6.40 $\pm$ 1.34) mmol/L, $P<0.001$; 5.17% $\pm$ 1.17%, $P<0.001$; 0.48% $\pm$ 0.04%, $P<0.001$]。与模型组相比, 人参皂苷 Rg1 组小鼠体质量 [(22.62 $\pm$ 0.92) g, $P=0.023$]、睾酮水平 [(172.63 $\pm$ 9.20) ng/L, $P<0.001$]、卵泡刺激素水平 [(12.37 $\pm$ 1.15) U/L, $P<0.001$]、黄体生成素水平 [(1847.80 $\pm$ 108.80) pg/L, $P<0.001$] 显著升高, 空腹血糖水平 [(18.63 $\pm$ 1.14) mmol/L, $P=0.017$]、糖化血红蛋白 (8.50% $\pm$ 1.05%, $P<0.001$) 和睾丸指数 (0.54% $\pm$ 0.02%, $P<0.001$) 显著下降。与对照组相比, 模型组小鼠睾丸组织 P62 ($P=0.039$)、LC3 II/LC3 I ($P<0.001$)、Beclin1 ($P=0.002$)、mTOR ($P=0.036$) 表达均增加, β -Catenin ($P<0.001$)、LAMP1 ($P=0.005$)、转录因子 EB ($P<0.001$) 表达均降低。与模型组相比, 人参皂苷 Rg1 组自噬相关蛋白 P62 ($P=0.048$)、LC3 II/LC3 I ($P<0.001$)、Beclin1 ($P=0.023$)、mTOR ($P=0.005$) 表达均下降, β -Catenin ($P=0.001$)、LAMP1 ($P=0.011$)、转录因子 EB ($P=0.022$) 表达均增加。透射电子显微镜检测到模型组小鼠睾丸自噬溶酶体数量减少, 药物干预后有所好转。HE 染色显示模型组小鼠睾丸出现生精细胞脱落、排列紊乱等表型, 而人参皂苷 Rg1 能改善这些表型。**结论** 人参皂苷 Rg1 可通过调控自噬改善糖尿病所致的小鼠睾丸损伤。

【关键词】 糖尿病, 2 型; 自噬; 人参皂苷 Rg1; 睾丸损伤; 转录因子 EB

基金项目：浙江省医药卫生科技计划项目（2025KY1378）；宁波市自然科学基金（2023J364）

Ginsenoside Rg1 improves testicular injury induced by diabetes in mice by regulating autophagy

Wu Junjie¹, Yu Yi², Wang Kai³, Liu Pengfei⁴, Zhan Mingwei⁴, Wang Lei⁵, Yao Fan¹, Xu Liqi⁶, Shang Xuejun¹

¹ Jinling Clinical Medical College, Nanjing University of Chinese Medicine, Nanjing 210002, China; ² Center of Reproductive Medicine, the First Affiliated Hospital of Ningbo University, Ningbo 315010, China; ³ Department of Pathology, the 906th Hospital of the Joint Logistics Support Force of the People's Liberation Army of China, Ningbo 315040, China; ⁴ Department of Urology, Jinling Hospital Affiliated to Nanjing University School of Medicine, Nanjing 210002, China; ⁵ School of Medicine, Southeast University, Nanjing 210009, China; ⁶ Reproductive Center, the 906th Hospital of the Joint Logistics Support Force of the People's Liberation Army of China, Ningbo 315040, China

Yu Yi and Wu Junjie contributed equally to the article

Corresponding author: Shang Xuejun, Email: shangxj98@163.com

【Abstract】 Objective To explore the effect of ginsenoside Rg1 on spermatogenic dysfunction in mice caused by diabetes and its mechanism of action. **Methods** Eighteen male C57BL mice were randomly divided into control group, the model group and the ginsenoside Rg1 group by completely random method, with 6 mice in each group. Type 2 diabetes models were established in the model group and the ginsenoside Rg1 group by a high-fat diet combined with intraperitoneal injection of streptozotocin, while control group was injected with the same amount of normal saline. After successful modeling, control group was given a regular diet for 8 weeks, while the model group and ginsenoside Rg1 group were given a high-fat diet for 8 weeks. The ginsenoside Rg1 group was also treated with ginsenoside Rg1 medication. Reproductive hormone levels were detected by enzyme-linked immunosorbent assay test kits, and Western blotting was used to detect the expressions of apoptosis-related proteins (Bcl2 protein, Caspase-3 protein, Bax protein), autophagy-related proteins (P62, LC3 I, LC3 II, Beclin1), β -Catenin protein, mTOR protein, LAMP1 protein and transcription factor EB. The body weight, blood glucose levels, testicular index of mice in each group were compared, as well as the testicular injury status. **Results** The body weight [(18.77 $\pm$ 1.14) g], testosterone level [(141.07 $\pm$ 8.47) ng/L], follicle-stimulating hormone level [(9.19 $\pm$ 0.74) U/L], and luteinizing hormone level [(1 497.91 $\pm$ 99.57) pg/L] of mice in the model group were significantly lower than those in the control [(31.57 $\pm$ 2.35) g, P <0.001; (171.50 $\pm$ 11.76) ng/L, P <0.001; (12.46 $\pm$ 1.54) U/L, P <0.001; (1 807.29 $\pm$ 92.76) pg/L, P <0.001]; fasting blood glucose level [(20.82 $\pm$ 1.11) mmol/L], glycosylated hemoglobin (12.67% $\pm$ 1.03%), the testis index (0.65% $\pm$ 0.03%) were significantly higher than those in the control [(6.40 $\pm$ 1.34) mmol/L, P <0.001; 5.17% $\pm$ 1.17%, P <0.001; 0.48% $\pm$ 0.04%, P <0.001]. Compared

with the model group, the body weight $[(22.62\pm0.92) \text{ g}, P=0.023]$, testosterone level $[(172.63\pm9.20) \text{ ng/L}, P<0.001]$, follicle-stimulating hormone level $[(12.37\pm1.15) \text{ U/L}, P<0.001]$, and luteinizing hormone level $[(1\ 847.80\pm108.80) \text{ pg/L}, P<0.001]$ of mice in the ginsenoside Rg1 group increased significantly, fasting blood glucose level $[(18.63\pm1.14) \text{ mmol/L}, P=0.017]$, glycosylated hemoglobin $(8.50\%\pm1.05\%, P<0.001)$ and testicular index $(0.54\%\pm0.02\%, P<0.001)$ decreased significantly. Compared with the control, the expressions of P62 ($P=0.039$), LC3 II /LC3 I ($P<0.001$), Beclin1 ($P=0.002$) and mTOR ($P=0.036$) in the testicular tissue of mice in the model group all increased, the expression of β -Catenin ($P<0.001$), LAMP1 ($P=0.005$), transcription factor EB ($P<0.001$) all decreased. Compared with the model group, the expressions of autophagy-related proteins P62 ($P=0.048$), LC3 II /LC3 I ($P<0.001$), Beclin1 ($P=0.023$) and mTOR ($P=0.005$) in the ginsenoside Rg1 group all decreased, while the expression of β -Catenin ($P=0.001$), LAMP1 ($P=0.011$) and transcription factor EB ($P=0.022$) all increased. Transmission electron microscopy detected a decrease in the number of autophagosomes in the testicles of mice in the model group, and it improved after drug intervention. The HE staining showed that the testes of mice in the model group exhibited phenotypes such as the shedding and disorganization of spermatogenic cells, while ginsenoside Rg1 was able to improve these phenotypes.

Conclusion Ginsenoside Rg1 can improve testicular injury caused by diabetes in mice by regulating autophagy.

【Key words】 Type 2 diabetes mellitus; Autophagy; Ginsenoside Rg1; Testicular injury; Transcription factor EB

Fund program: Zhejiang Medicine and Health Science and Technology Project (2025KY1378); Ningbo Natural Science Foundation (2023J364)

·男性不育专栏·

DOI: 10.3760/cma.j.cn101441-20250216-00068

收稿日期 2025-02-16 本文编辑 李天琦

引用本文: 战明威, 吴俊杰, 周慕华, 等. 慢性附睾炎对男性生殖功能的影响及相关机制研究进展[J]. 中华生殖与避孕杂志, 2025, 45(6): 558-563. DOI: 10.3760/cma.j.cn101441-20250216-00068.

慢性附睾炎对男性生殖功能的影响及相关机制研究进展

战明威¹ 吴俊杰² 周慕华³ 赵彬彬³ 刘朋飞¹ 余怡⁴ 商学军

¹南京大学医学院附属金陵医院泌尿外科, 南京 210002; ²南京中医药大学金陵临床医学院泌尿外科, 南京 210002; ³浙江中医药大学附属杭州市中医院泌尿外科, 杭州 310007; ⁴宁波大学附属第一医院生殖医学中心, 宁波 315010

通信作者: 商学军, Email: shangxj98@163.com

【摘要】 慢性附睾炎 (chronic epididymitis, CE) 是一种由急性感染后未彻底治愈、慢性感染或药物等因素引起的附睾长期炎症性疾病, 临床主要表现为单侧或双侧阴囊持续性钝痛或坠胀感, 病程通常超过 3 个月且具有隐匿性与反复发作的特点。现有研究表明, CE 可能通过引发局部炎症反应、氧化应激、纤维化重塑、细胞自噬等多重病理过程, 破坏附睾微环境, 影响精子成熟、运输及获能, 进而导致男性生殖功能障碍和不育。本文对 CE 的主要病因、病理生理学特征及其对男性生殖功能的影响进行综述, 重点解析了炎症因子及相关信号通路、氧化应激机制、纤维化进程在 CE 发病中的作用, 并探讨了基于这些机制的靶向治疗策略, 旨在为 CE 引起男性生殖功能损伤的关键分子靶点和信号通路提供一定的理论依据。

【关键词】 附睾炎; 不育, 男性; 信号通路; 氧化应激; 纤维化
基金项目: 浙江省医药卫生科技计划项目 (2025KY1378)

Research progress on the impact of chronic epididymitis on male reproductive function and its related mechanisms

Zhan Mingwei¹, Wu Junjie², Zhou Muhua³, Zhao Binbin³, Liu Pengfei¹, Yu Yi⁴, Shang Xuejun¹

¹ Department of Urology, Nanjing Jinling Hospital, Affiliated Hospital of Medical School, Nanjing University, Nanjing 210002, China; ² Department of Urology, Jinling Clinical Medical College, Affiliated Hospital of Medical School, Nanjing University of Chinese Medicine, Nanjing 210002, China; ³ Department of Urology, Hangzhou Hospital of Traditional Chinese Medicine, Zhejiang Chinese Medical University, Hangzhou 310007, China; ⁴ Center of Reproductive Medicine, the First Affiliated Hospital of Ningbo University, Ningbo 315010, China

Corresponding author: Shang Xuejun, Email: shangxj98@163.com

【Abstract】 Chronic epididymitis (CE) is a long-standing inflammatory condition of the epididymis caused by unresolved acute infections, chronic infections, medication use, or other factors. Clinically, it is characterized by persistent dull pain or a dragging sensation in one or both sides of the scrotum. The disease course typically exceeds three months and is marked by insidious onset and recurrent episodes. Current studies suggest that CE may disrupt the epididymal microenvironment through multiple pathological processes, including local inflammatory responses, oxidative stress, fibrotic remodeling, and autophagy. These alterations impair sperm maturation, transport, and capacitation, thereby

contributing to male reproductive dysfunction and infertility. This review summarizes the major etiologies and pathophysiological characteristics of CE and its impact on male reproductive function. It focuses on the roles of inflammatory cytokines and related signaling pathways, oxidative stress mechanisms, and fibrotic progression in the pathogenesis of CE. Moreover, it explores targeted therapeutic strategies based on these mechanisms, aiming to provide a theoretical basis for identifying key molecular targets and signaling pathways involved in CE-induced male reproductive impairment.

【Key words】 Epididymitis; Infertility, male; Signaling pathways; Oxidative stress; Fibrosis

Fund program: Zhejiang Provincial Health and Medicine Science and Technology Program(2025KY1378)

男性不育专栏

DOI: 10.3760/cma.j.cn101441-20250307-00112

收稿日期 2025-03-07 本文编辑 宋培培

引用本文: 夏思怡, 石玉琴, 张玲. 肠道菌群失调与男性生育力: 机制和调节策略的研究进展[J]. 中华生殖与避孕杂志, 2025, 45(6): 564-570. DOI: 10.3760/cma.j.cn101441-20250307-00112.

肠道菌群失调与男性生育力: 机制和调节策略的研究进展

夏思怡 石玉琴 张玲

武汉科技大学医学部公共卫生学院 湖北省职业危害识别与控制重

点实验室, 武汉 430065

通信作者: 张玲, Email: zhangling@wust.edu.cn

【摘要】 近年来, 肠道菌群与全身各系统疾病的关系逐渐被揭示, 其在男性生殖系统中发挥的作用也被广泛研究。肠道菌群是栖息在人体肠道内复杂且庞大的微生物群落, 可通过影响性激素水平、炎症反应、代谢产物、免疫调节、内分泌途径等诸多机制参与调节男性生育力。同时, 地中海饮食调节、生活方式及医学干预可以通过调节肠道菌群平衡从而改善男性生育力。深入研究肠道菌群与男性生育力的关系具有重要的科学意义和临床价值。本文就肠道菌群失调与男性生育力之间作用机制的研究进展作一综述, 并探讨针对肠道菌群失调进行干预作为改善生育结局潜在新策略的可行性。

【关键词】 炎症； 免疫； 膳食； 生活方式； 激素； 肠道菌群； 男性生育力

Gut microbiota dysbiosis and male fertility: research progress on mechanisms and modulation strategies

Xia Siyi, Shi Yuqin, Zhang Ling

School of Public Health, Faculty of Medicine, Wuhan University of Science and Technology; Hubei Provincial Key Laboratory of Occupational Hazard Identification and Control, Wuhan 430065, China

Corresponding author: Zhang Ling, Email: zhangling@wust.edu.cn

【Abstract】 In recent years, the relationship between gut microbiota and various systemic diseases has been increasingly elucidated, and its role in the male reproductive system has attracted growing attention. The gut microbiota, a complex and vast microbial community residing in the human intestine, is involved in the regulation of male fertility through multiple mechanisms, including modulation of sex hormone levels, inflammatory responses, microbial metabolites, immune regulation, and endocrine signaling pathways. Furthermore, dietary interventions, lifestyle modifications, and medical therapies can improve male fertility by restoring gut microbial balance. Exploring the intricate relationship between gut microbiota and male fertility holds significant scientific and clinical value. This review summarizes the current research progress on the mechanisms underlying the relationship between gut microbiota dysbiosis and male fertility, and discusses the potential of interventions targeting gut microbiota dysbiosis as a novel strategy to improve reproductive outcomes.

【Key words】 Inflammation; Immunity; Diet; Lifestyle; Hormones; Gut microbiota; Male fertility

·临床研究·

DOI: 10.3760/cma.j.cn101441-20250114-00016

收稿日期 2025-01-14 本文编辑 王李艳

引用本文: 张园, 刘文, 王菁, 等. 不同卵巢反应患者 COS 过程中 FSH 固定剂量和调整剂量的累积活产率和 FSH 成本效益比较: 一项单中心 5 年真实世界研究[J]. 中华生殖与避孕杂志, 2025, 45(6): 571-581. DOI: 10.3760/cma.j.cn101441-20250114-00016.

不同卵巢反应患者 COS 过程中 FSH 固定剂量和调整剂量的累积活产率和

FSH 成本效益比较:一项单中心 5 年真实世界研究

张园¹ 刘文² 王菁¹ 甘世林² 黄清浩² 钱易¹ 徐慧¹ 丁小芹

¹ 邓波¹ 刘金勇¹ 刘嘉茵¹ 柏建岭² 马翔¹

¹南京医科大学第一附属医院 江苏省人民医院生殖医学科, 南京

210029; ²南京医科大学公共卫生学院统计教研室, 南京 210029

通信作者: 马翔, Email: sxmaxiang@126.com

【摘要】 目的 评估卵泡刺激素 (follicle-stimulating hormone, FSH) 固定剂量与调整剂量对不同卵巢反应不孕女性在首个辅助生殖技术 (assisted reproductive technology, ART) 周期后的累积活产率 (cumulative live birth rate, CLBR) 及 FSH 成本效益的影响。**方法** 采用回顾性真实世界队列研究, 分析 2013 年 1 月至 2017 年 12 月于南京医科大学第一附属医院生殖医学科首次行 ART 治疗的 5 419 例不孕女性的临床资料, 均采用个体化促性腺激素启动剂量, 根据控制性卵巢刺激 (controlled ovarian stimulation, COS) 过程中是否调整 FSH 剂量分为固定剂量组 ($n=2\ 061$) 和调整剂量组 ($n=3\ 358$)。分析不同卵巢反应人群中两组临床助孕结局和 FSH 成本效益, 主要观察指标为 CLBR。利用倾向性评分匹配 (propensity score matching, PSM) 和多因素 logistic 回归以调整潜在的混杂因素。**结果** COS 期间 FSH 剂量调整的周期占 62.0% (3 358/5 419), PSM 后组间基线资料差异均无统计学意义 (均 $P>0.05$)。多因素 logistic 回归分析调整混杂因素后, 调整剂量与否与 CLBR 无显著相关性 ($OR=1.06$, 95% CI : 0.94~1.20, $P=0.332$)。和调整剂量组相比, 固定剂量组的 CLBR 在各卵巢反应组别差异均无统计学意义 (均 $P>0.05$)。两组卵巢过度刺激综合征 (ovarian hyperstimulation syndrome, OHSS) 发生率差异无统计学意义 ($P>0.05$)。固定剂量组的 FSH 总剂量在低反应人群、正常反应人群及高反应人群中分别为 1 350 (375, 1 825) U、1 200 (375, 1 500) U 和 525 (375, 1 128) U, 显著低于调整剂量组 [1 875 (1 425, 2 294) U, $P=0.001$; 1 425 (450, 1 875) U, $P<0.001$; 600 (375, 1 425) U, $P=0.020$] ; 固定剂量组的平均 FSH 费用在低反应人群、正常反应人群及高反应人群中分别为 4 725.0 (1 312.5, 6 387.5) 元、4 200.0 (1 312.5, 5 250.0) 元和 1 837.5 (1 312.5, 3 947.3) 元, 显著低于调整剂量组 [6 562.5 (4 987.5, 8 028.1) 元, $P=0.001$; 4 987.5 (1 575.0, 6 562.5) 元, $P<0.001$; 2 100.0 (1 312.5, 4 987.5) 元, $P=0.020$]。对于正常反应人群来说, FSH 固定剂量组获得每优质胚胎 FSH 费用为 1 365.0 (875.0, 2 537.5) 元, 显著低于调整剂量组 [2 056.3 (1 268.8, 3 412.5)

元, $P<0.001$]。结论 COS 期间 FSH 剂量调整与 CLBR 和 OHSS 发生率无关,但在不同卵巢反应人群中 FSH 固定剂量组 FSH 总剂量更低、费用更低。在辅助生殖进展医保大环境下, FSH 固定剂量可能是一种成本效益更高的促排卵方案。

【关键词】 女性不孕症; 卵泡刺激素; 控制性卵巢刺激; 累积活产率; 成本效益

基金项目: 国家重点研发计划 (2024YFC2706704、2021YFC2700404); 江苏省科技厅计划 (BE2021743、M2020097); 国家自然科学基金 (81401267)

Comparison of cumulative live birth rates and cost-effectiveness of FSH between gonadotrophin fixed protocol and adjusted protocol in patients with different ovarian responses during COS: a single-center 5-year real-world study

Zhang Yuan¹, Liu Wen², Wang Jing¹, Gan Shilin², Huang Qinghao², Qian Yi¹, Xu Hui¹, Ding Xiaoqin¹, Deng Bo¹, Liu Jinyong¹, Liu Jiayin¹, Bai Jianling², Ma Xiang¹

¹ Department of Reproductive Medicine, the First Affiliated Hospital of Nanjing Medical University; Jiangsu Province Hospital, Nanjing 210029, China; ² Department of Biostatistics, School of Public Health, Nanjing Medical University, Nanjing 210029, China

Corresponding author: Ma Xiang, Email: sxmaxiang@126.com

【Abstract】 Objective To evaluate the cumulative live birth rate (CLBR) and cost-effectiveness of fixed versus adjusted follicle-stimulation hormone (FSH) dosages in infertile women with different ovarian responses during their first assisted reproductive technology (ART) cycle. **Methods** A retrospective real-world cohort study was conducted on 5 419 infertile women who underwent their first ART treatment at the Department of Reproductive Medicine of the First Affiliated Hospital of Nanjing Medical University between January 2013 and December 2017. All patients received an individualized starting dosage of gonadotropin. Based on whether FSH dosages were adjusted during controlled ovarian stimulation (COS), patients were divided into fixed-dosage group ($n=2\ 061$) and adjusted-dosage group ($n=3\ 358$). Clinical outcomes and FSH cost-effectiveness were compared between the two groups across different ovarian response groups, with CLBR as the primary outcome. Propensity score matching (PSM) and multivariable logistic regression were used to adjust for potential confounders. **Results** FSH dosage adjustments were found in 62.0% ($3\ 358/5\ 419$) of cycles during COS. After PSM, baseline characteristics were comparable between the two groups (all $P>0.05$). After adjusting for confounders using multivariable logistic regression, FSH dosage adjustment was not significantly associated with CLBR ($OR=1.06$, 95% CI : $0.94-1.20$, $P=0.332$). Compared with the adjusted-dosage group, the fixed-dosage group showed no significant differences in CLBR in poor-, normal-, and high-responder groups (all $P>0.05$). The incidence of ovarian hyperstimulation syndrome (OHSS) did not differ significantly between the two groups ($P>0.05$). In poor-, normal-, and high-responder groups, the total FSH dosages in the fixed-dose group [$1\ 350$ ($375, 1\ 825$) U, $1\ 200$ ($375, 1\ 500$) U and 525 ($375, 1\ 128$) U, respectively] were significantly lower than those in the adjusted-dose group [$1\ 875$

(1 425, 2 294) U, $P=0.001$; 1 425 (450, 1 875) U, $P<0.001$; 600 (375, 1 425) U, $P=0.020$]. Similarly, average FSH costs in different ovarian response groups in the fixed-dosage group [4 725.0 (1 312.5, 6 387.5) yuan, 4 200.0 (1 312.5, 5 250.0) yuan and 1 837.5 (1 312.5, 3 947.3) yuan, respectively] were significantly lower than those in the adjusted-dosage group [6 562.5 (4 987.5, 8 028.1) yuan, $P=0.001$; 4 987.5 (1 575.0, 6 562.5) yuan, $P<0.001$; 2 100.0 (1 312.5, 4 987.5) yuan, $P=0.020$]. For normal-responders, the FSH cost per high-quality embryo in the fixed-dosage group [1 365.0 (875.0, 2 537.5) yuan] was significantly lower than that in the adjusted-dosage group [2 056.3 (1 268.8, 3 412.5) yuan, $P<0.001$]. **Conclusion** FSH dosage adjustment during COS is not associated with CLBR or the incidence of OHSS. However, the fixed-dose group exhibited lower total FSH dosages and costs across different ovarian response populations. In the context of ART being covered by medical insurance, fixed FSH dosage may represent a more cost-effective ovarian stimulation protocol.

【Key words】 Female infertility; Follicle-stimulating hormone; Controlled ovarian stimulation; Cumulate live birth rate; Cost-effectiveness

Fund program: National Key Research and Development Program of China (2024YFC2706704, 2021YFC2700404); Jiangsu Provincial Department of Science and Technology Project (BE2021743, M2020097); National Natural and Science Foundation of China (81401267)

临床研究

DOI: 10.3760/cma.j.cn101441-20250213-00063

收稿日期 2025-02-13 本文编辑 李天琦

引用本文: 李培鑫, 俎若雯, 任炳楠, 等. 冻融周期单囊胚移植中血清 β -hCG 水平对囊胚质量与妊娠结局关系的中介作用研究 [J]. 中华生殖与避孕杂志, 2025, 45(6): 582-590. DOI: 10.3760/cma.j.cn101441-20250213-00063.

冻融周期单囊胚移植中血清 β -hCG 水平对囊胚质量与妊娠结局关系的 中介作用研究

李培鑫 俎若雯 任炳楠 韩静宜 郑威 杨宸 管一春

郑州大学第三附属医院生殖健康医院, 郑州 450052

通信作者: 管一春, Email: lisamayguan@126.com

【摘要】 目的 探讨在冻融周期单囊胚移植后 14 d 血清 β -人绒毛膜促性腺激素 (human chorionic gonadotropin, hCG) 水平在囊胚质量与妊娠结局之间的中介作用。**方法** 本研究为回顾性队列研究, 收集 2017 年 8 月至 2021 年 6 月在郑州大学第三附属医院生殖健康医院接受体外受精/卵胞质内单精子注射冻融周期单囊胚移植治疗的患者资料。根据囊胚质量对患者进行分组, 分为优质囊胚组 ($n=3191$) 和可利用囊胚组 ($n=2027$), 比较两组移植后 14 d 的血清 β -hCG 水平及妊娠结局的差异, 采用中介效应分析和受试者工作特征 (receiver operating characteristic, ROC) 曲线分析, 进一步探讨 β -hCG 水平在囊胚质量与妊娠结局之间的中介作用, 并评估两组的胎盘源性疾病发生率有无差异。**结果** 优质囊胚组患者移植后 14 d 血清 β -hCG 水平 [$1177.0 (1.8, 2278.5)$ U/L]、临床妊娠率 [65.62% (2094/3191)] 和活产率 [52.55% (1667/3191)] 显著高于可利用囊胚组 [54.4 (0.1, 1453.5) U/L, $P<0.001$; 46.13% (935/2027), $P<0.001$; 34.19% (693/2027), $P<0.001$], 优质囊胚组的早期流产率 [13.47% (282/2094)] 低于可利用囊胚组 [19.14% (179/935), $P<0.001$]。移植后 14 d 血清 β -hCG 水平在两组的临床妊娠率 ($r=-0.126$)、活产率 ($r=-0.122$) 和早期流产率 ($r=0.028$) 之间均存在显著的中介效应 (均 $P<0.001$)。可利用囊胚组和优质囊胚组预测活产的 β -hCG 截断值分别为 366.9 U/L 和 485.5 U/L, 阳性预测值分别为 76.28% (672/881) 和 82.84% (1628/1965), 阴性预测值分别为 98.15% (1114/1135) 和 96.14% (1170/1217), 预测临床妊娠的截断值为 118.8 U/L 和 226.5 U/L, 阳性预测值分别为 95.43% (919/963) 和 98.45% (2037/2069), 阴性预测值分别为 99.72% (1050/1053) 和 94.89% (1059/1116), 预测早期流产的截断值分别为 1337.0 U/L 和 1162.6 U/L, 阳性预测值分别为 32.75% (130/397) 和 30.18% (150/497), 阴性预测值分别为 90.89% (489/538) 和 91.73% (1465/1597), 但两组的胎盘源性疾病发生率差异均无统计学意义 (均 $P>0.05$)。**结论** 囊胚质量和移植后 14 d 血清 β -hCG 水平显著影响妊娠结局, 且 β -hCG 水平在囊胚质量与妊娠结局间起重要中介作用。ROC 分析验证了血清 β -hCG 水平在妊娠结局预测中的良好效能, 为优化囊胚选择提供了科学依据。

【关键词】 妊娠结局; 中介效应; β -人绒毛膜促性腺激素; 单囊胚移植; 冻融周期

基金项目: 国家重点研发计划 (2022YFC2703500); 国家自然科学基金面上项目 (82471712); 河南省重点研发专项 (241111310300)

Mediating role of serum β -hCG levels in the relationship between blastocyst quality and pregnancy outcomes in frozen-thawed single blastocyst transfer

Li Peixin, Zu Ruowen, Ren Bingnan, Han Jingyi, Zheng Wei, Yang Chen, Guan Yichun
Reproductive Health Hospital, Third Affiliated Hospital of Zhengzhou University,
Zhengzhou 450052, China

Corresponding author: Guan Yichun, Email: lisamayguan@126.com

【Abstract】 Objective To investigate the mediating role of serum β -human chorionic gonadotropin (hCG) levels on the relationship between embryo quality and pregnancy outcomes following single frozen-thawed blastocyst transfer 14 d post-transfer. **Methods** This retrospective cohort study collected data from patients who underwent *in vitro* fertilization/intracytoplasmic sperm injection (IVF/ICSI) frozen-thawed single blastocyst transfer at the Reproductive Health Hospital of the Third Affiliated Hospital of Zhengzhou University between August 2017 and June 2021. Patients were grouped according to embryo quality into good-quality blastocyst group ($n=3\ 191$) and available blastocyst group ($n=2\ 027$). Differences in serum β -hCG levels and pregnancy outcomes at 14 d post-transfer were compared between the two groups. Mediation analysis and receiver operating characteristic (ROC) analysis were used to explore the mediating effect of β -hCG levels on the relationship between embryo quality and pregnancy outcomes and to evaluate the differences in the incidence of placental-related diseases between the two groups. **Results** The good-quality blastocyst group had significantly higher serum β -hCG levels [1 177.0 (1.8, 2 278.5) U/L], clinical pregnancy rate [65.62% (2 094/3 191)], and live birth rate [52.55% (1 667/3 191)] compared with the available blastocyst group [54.4 (0.1, 1 453.5) U/L, $P<0.001$; 46.13% (935/2 027), $P<0.001$; 34.19% (693/2 027), $P<0.001$]. The early miscarriage rate in the good-quality group [13.47% (282/2 094)] was lower than that in the available blastocyst group [19.14% (179/935), $P<0.001$]. Serum β -hCG levels at 14 d post-transfer showed significant mediating effects on clinical pregnancy rate ($r=-0.126$), live birth rate ($r=-0.122$), and early miscarriage rate ($r=0.028$) in both groups (all $P<0.001$). The cut-off values for β -hCG to predict live birth in the available and good-quality blastocyst groups were 366.9 U/L and 485.5 U/L, with positive predictive values of 76.28% (672/881) and 82.84% (1 628/1 965), respectively, and negative predictive values of 98.15% (1 114/1 135) and 96.14% (1 170/1 217). The cut-off values for predicting clinical pregnancy were 118.8 U/L and 226.5 U/L, with positive predictive values of 95.43% (919/963) and 98.45% (2 037/2 069), and negative predictive values of 99.72% (1 050/1 053) and 94.89% (1 059/1 116). The cut-off values for predicting early miscarriage were 1 337.0 U/L and 1 162.6 U/L, with positive predictive values of 32.75% (130/397) and 30.18% (150/497), and negative predictive values of 90.89% (489/538) and 91.73% (1 465/1 597). No differences were found in the incidence of placental-related diseases between the two groups (all $P>0.05$). **Conclusion** This study indicates that both embryo quality and serum β -hCG levels at 14 d post-transfer significantly affect pregnancy outcomes. β -hCG levels play an important mediating role between embryo quality and pregnancy outcomes. ROC analysis demonstrates the good predictive efficacy of serum β -hCG levels for pregnancy outcomes, providing scientific evidence for optimizing embryo selection.

【Key words】 Pregnancy outcome; Mediation analysis; β -human chorionic gonadotropin; Single blastocyst transfer; Frozen-thawed cycle

Fund program: National Key Research and Development Program of China (2022YFC2703500); General Program of National Natural Science Foundation of

DOI: 10.3760/cma.j.cn101441-20241219-00481

收稿日期 2024-12-19 本文编辑 孙敏

引用本文: 邢晶晶, 王峥, 李蓉, 等. 新鲜和冻融胚胎移植对高龄 DOR 患者助孕结局的影响[J]. 中华生殖与避孕杂志, 2025, 45(6): 591-599. DOI: 10.3760/cma.j.cn101441-20241219-00481.

新鲜和冻融胚胎移植对高龄 DOR 患者助孕结局的影响

邢晶晶^{1,2} 王峥¹ 李蓉¹ 李莉¹

¹北京大学第三医院妇产科生殖医学中心, 北京 100191; ²郑州市妇

幼保健院生殖遗传科, 郑州 450052

通信作者: 李蓉, Email: roseli001@sina.com

【摘要】 目的 探究新鲜和冻融胚胎移植对高龄卵巢储备功能减退 (diminished ovarian reserve, DOR) 患者助孕结局的影响。方法 通过回顾性队列研究, 选取 2018 年 1 月至 2022 年 12 月于北京大学第三医院妇产科生殖医学中心首次接受体外受精-胚胎移植 (*in vitro* fertilization and embryo transfer, IVF-ET) 治疗的高龄 DOR 患者, 根据其首次胚胎移植的周期类型进行分组, 纳入新鲜胚胎移植组 563 例 (记为 A 组), 冻融胚胎移植组 234 例 (记为 B 组), 采用 1:1 倾向性评分对两组患者的基本资料和胚胎移植情况进行匹配, 匹配到 A 组和 B 组患者各 184 例。分析新鲜和冻融胚胎移植对高龄 DOR 患者助孕结局的影响。结果 ①匹配后两组间一般资料、促排卵及胚胎实验室参数差异均无统计学意义 (均 $P>0.05$)。②匹配后 A 组的临床妊娠率 [23.91% (44/184)]、胚胎着床率 [16.55% (48/290)]、持续妊娠率 [16.85% (31/184)]、活产率 [16.30% (30/184)] 显著高于 B 组 [14.67% (27/184)、10.27% (30/292)、9.78% (18/184)、9.24% (17/184)], 差异均具有统计学意义 ($P=0.025$ 、 $P=0.026$ 、 $P=0.046$ 、 $P=0.042$)。两组间流产率、多胎妊娠率、早产率、分娩孕周及新生儿出生体质量差异均无统计学意义 (均 $P>0.05$)。③控制混杂因素后, 冻融胚胎移植、女方年龄和移植优质胚胎数是临床妊娠 ($OR=0.486$, 95% CI : 0.275~0.858, $P=0.013$; $OR=0.761$, 95% CI : 0.686~0.844,

$P<0.001$; 移植 1 枚优质胚胎 $OR=5.213$, 95% CI : 1.501~18.105, $P=0.009$; 移植 2 枚优质胚胎 $OR=8.144$, 95% CI : 2.072~32.009, $P=0.003$) 和活产 ($OR=0.468$, 95% CI : 0.240~0.916, $P=0.027$; $OR=0.733$, 95% CI : 0.645~0.834, $P<0.001$; 移植 1 枚优质胚胎 $OR=5.457$, 95% CI : 1.218~24.448, $P=0.027$; 移植 2 枚优质胚胎 $OR=5.900$, 95% CI : 1.132~30.754, $P=0.035$) 的独立影响因素。④控制混杂因素后, 在年龄 >40 岁患者的移植周期中, A 组临床妊娠率 [14.46% (12/83)] 显著高于 B 组 [4.88% (4/82)], 差异有统计学意义 ($OR=0.285$, 95% CI : 0.086~0.946, $P=0.040$); 在单卵裂期胚胎移植周期中, A 组临床妊娠率 [21.79% (17/78)] 和活产率 [16.67% (13/78)] 均显著高于 B 组 [9.21% (7/76)], $OR=0.311$, 95% CI : 0.113~0.857, $P=0.024$; 6.58% (5/76), $OR=0.468$, 95% CI : 0.240~0.916, $P=0.027$], 差异均有统计学意义; 在移植 1 枚优质胚胎的周期中, A 组临床妊娠率 [27.66% (26/94)] 和活产率 [20.21% (19/94)] 均显著高于 B 组 [13.54% (13/96)], $OR=0.347$, 95% CI : 0.157~0.765, $P=0.009$; 10.42% (10/96), $OR=0.407$, 95% CI : 0.171~0.968, $P=0.042$], 差异均有统计学意义。结论 高龄 DOR 女性新鲜周期胚胎移植能获得更好的助孕结局, 尤其在年龄 >40 岁、单卵裂期胚胎移植周期或仅有 1 枚优质胚胎的情况下, 建议优先考虑行新鲜周期胚胎移植。

【关键词】 高龄; 卵巢储备功能减退; 新鲜胚胎移植; 冻融胚胎移植
基金项目: 国家自然科学基金 (82288102)

Impact of fresh and frozen-thawed embryo transfer on pregnancy outcomes in elderly women with DOR

Xing Jingjing^{1,2}, Wang Zheng¹, Li Rong¹, Li Li¹

¹Center for Reproductive Medicine, Department of Obstetrics and Gynecology, Peking University Third Hospital, Beijing 100191, China; ²Department of Reproductive Genetics, Zhengzhou Women's and Children's Health Hospital, Zhengzhou 450052, China

Corresponding author: Li Rong, Email: roseli001@sina.com

【Abstract】 **Objective** To investigate the impact of fresh and frozen-thawed embryo transfer on pregnancy outcomes in patients with diminished ovarian reserve (DOR) at an advanced age. **Methods** Using a retrospective cohort study design, we enrolled elderly women with DOR who underwent their first *in vitro* fertilization and embryo transfer (IVF-ET) treatment at Center for Reproductive Medicine, Department of Obstetrics and Gynecology, Peking University Third Hospital between January 2018 and December 2022. Patients were grouped according to the cycle type of their first embryo transfer: a fresh cycle transfer group (group A, $n=563$) and a frozen-thawed cycle transfer group (group B, $n=234$). Propensity score matching (PSM, 1 : 1) was used to match the baseline characteristics and embryo transfer information of the two groups, resulting in 184 patients in each group. The impact of fresh versus frozen-thawed embryo transfer on reproductive outcomes in elderly DOR patients was analyzed. **Results** 1) There were no statistically significant differences in general data, ovarian stimulation, and laboratory parameters of embryos between the two groups after PSM (all $P>0.05$). 2) The clinical pregnancy rate [23.91% (44/184)], the implantation rate [16.55% (48/290)], the ongoing pregnancy rate [16.85%

(31/184)], and the live birth rate [16.30% (30/184)] in group A were significantly higher than those in group B [14.67% (27/184), $P=0.025$; 10.27% (30/292), $P=0.026$; 9.78% (18/184), $P=0.046$; 9.24% (17/184), $P=0.042$], with statistically significant differences. There were no statistically significant differences in miscarriage rate, multiple pregnancy rate, preterm birth rate, gestational age at delivery, and neonatal birth weight between the two groups (all $P>0.05$). 3) After controlling for confounding factors, frozen-thawed embryo transfer, female age, and the number of transferred quality embryos were independent factors influencing clinical pregnancy ($OR=0.486$, 95% CI : 0.275–0.858, $P=0.013$; $OR=0.761$, 95% CI : 0.686–0.844, $P<0.001$; transferring one high-quality embryo $OR=5.213$, 95% CI : 1.501–18.105, $P=0.009$; transferring two high-quality embryos $OR=8.144$, 95% CI : 2.072–32.009, $P=0.003$) and live birth ($OR=0.468$, 95% CI : 0.240–0.916, $P=0.027$; $OR=0.733$, 95% CI : 0.645–0.834, $P<0.001$; transferring one high-quality embryo $OR=5.457$, 95% CI : 1.218–24.448, $P=0.027$; transferring two high-quality embryos $OR=5.900$, 95% CI : 1.132–30.754, $P=0.035$). 4) After controlling for confounding factors, in transfer cycles of patients older than 40 years, the clinical pregnancy rate in group A [14.46% (12/83)] was significantly higher than that in group B [4.88% (4/82)], with a statistically significant difference ($OR=0.285$, 95% CI : 0.086–0.946, $P=0.040$). In single cleavage-stage embryo transfer cycles, the clinical pregnancy rate [21.79% (17/78)] and the live birth rate [16.67% (13/78)] in group A were significantly higher than those in group B [9.21% (7/76), $OR=0.311$, 95% CI : 0.113–0.857, $P=0.024$; 6.58% (5/76), $OR=0.468$, 95% CI : 0.24–0.916, $P=0.027$], with both statistically significant differences. In cycles with transfer of only one high-quality embryo, the clinical pregnancy rate [27.66% (26/94)] and the live birth rate [20.21% (19/94)] in group A were significantly higher than those in group B [13.54% (13/96), $OR=0.347$, 95% CI : 0.157–0.765, $P=0.009$; 10.42% (10/96), $OR=0.407$, 95% CI : 0.171–0.968, $P=0.042$], with both statistically significant differences. **Conclusion** Fresh cycle embryo transfer can achieve better reproductive outcomes in elderly women with DOR, especially in patients older than 40 years, in single cleavage-stage embryo transfer cycles, or when only one high-quality embryo is available. Fresh cycle embryo transfer should be prioritized in these situations.

【Key words】 Advanced age; Diminished ovarian reserve; Fresh embryo transfer; Frozen-thawed embryo transfer

Fund program: National Natural Science Foundation of China (82288102)

临床研究

DOI: 10.3760/cma.j.cn101441-20250216-00069

收稿日期 2025-02-16 本文编辑 李天琦

引用本文：韩静宜，杨宸，俎若雯，等. 男性体质量指数对精液参数及夫精人工授精结局的影响：一项单中心回顾性队列研究[J]. 中华生殖与避孕杂志，2025，45(6)：600-606. DOI: 10.3760/cma.j.cn101441-20250216-00069.

男性体质量指数对精液参数及夫精人工授精结局的影响：一项单中心回顾性队列研究

韩静宜 杨宸 俎若雯 李培鑫 申冉 郑威 刘汝升 任炳楠

管一春

郑州大学第三附属医院生殖健康医院，郑州 450052

通信作者：管一春，Email: lisamayguan@126.com

【摘要】 目的 探讨男性体质量指数 (body mass index, BMI) 对精液参数及夫精人工授精 (artificial insemination by husband, AIH) 助孕结局的影响。方法 采用回顾性队列研究，分析 2017 年 1 月至 2024 年 2 月因男方精液参数异常、男方性功能障碍、女方宫颈因素或生殖道畸形所致不孕以及不明原因不孕等因素于郑州大学第三附属医院生殖健康医院就诊并首次进行 AIH 助孕的 5 053 例患者的临床资料。根据男性 BMI 将患者分为 3 组，正常组：18.5~23.9 kg/m² (n=1 673)，超重组：24.0~27.9 kg/m² (n=2 078)，肥胖组：BMI≥28.0 kg/m² (n=1 302)，主要评估组间精液参数和围产期结局的差异，应用多因素 logistic 回归与线性回归分析调整可能影响精液参数及围产期结局的混杂因素。结果 正常组和超重组的精液体积 [4.00 (3.00, 5.50) mL, 4.00 (3.00, 5.50) mL] 均高于肥胖组 [4.00 (3.00, 5.00) mL]，3 组间比较差异具有统计学意义 ($P<0.001$, $aP<0.001$)。正常组和超重组的精子总数 [207.60 (121.90, 341.75) × 10⁶, 211.80 (119.88, 334.83) × 10⁶] 均高于肥胖组 [188.40 (110.96, 323.41) × 10⁶]，3 组间比较差异具有统计学意义 ($P=0.007$, $aP<0.001$)。正常组的前向运动精子总数 [88.18 (43.63, 163.80) × 10⁶] 高于肥胖组 [75.30 (40.29, 147.86) × 10⁶]，3 组间比较差异具有统计学意义 ($P=0.001$, $aP<0.001$)。正常组的前向运动精子百分比 [(45.37±17.16) %] 高于超重组 [(44.03±17.36) %] 和肥胖组 [(43.80±17.21) %]，3 组间比较差异具有统计学意义 ($P=0.020$, $aP=0.016$)。超重组和肥胖组的新生儿出生体质量 [(3 389.53±472.65) g, (3 408.57±507.90) g] 均高于正常组 [(3 271.32±532.02) g]，3 组间比较差异具有统计学意义 ($P=0.010$,

a P =0.009)。结论 男性高 BMI 导致精液质量下降, 并可能增加 AIH 助孕治疗后新生儿出生体质量。

【关键词】 体质量指数; 夫精人工授精; 精液参数; 围产期结局

基金项目: 国家自然科学基金面上项目 (82471712); 河南省医学科技研究与联合建设项目 (LHGJ20230380、LHGJ20230376); 河南省重点研发专项 (241111310300); 河南省中青年卫生健康科技创新领军人才培养项目 (YXKC2021020)

Impact of male body mass index on semen parameters and outcomes of artificial insemination by husband: a single-center retrospective cohort study

Han Jingyi, Yang Chen, Zu Ruowen, Li Peixin, Shen Ran, Zheng Wei, Liu Rusheng, Ren Bingnan, Guan Yichun

Reproductive Health Hospital, Third Affiliated Hospital of Zhengzhou University, Zhengzhou 450052, China

Corresponding author: Guan Yichun, Email: lisamayguan@126.com

【Abstract】 Objective To investigate the effects of male body mass index (BMI) on semen parameters and perinatal outcomes following artificial insemination by husband (AIH) treatment. **Methods** A retrospective cohort study was conducted to analyze the clinical data of 5 053 patients underwent AIH treatment at the Reproductive Health Hospital of the Third Affiliated Hospital of Zhengzhou University, from January 2017 to February 2024. The study focused on factors such as male semen parameter abnormalities, male sexual dysfunction, female cervical factors, reproductive tract malformations, and unexplained infertility. Patients were classified into three groups based on male BMI: normal weight group (18.5–23.9 kg/m², n =1 673), overweight group (24.0–27.9 kg/m², n =2 078), and obese group (BMI $\geq$ 28.0 kg/m², n =1 302). The primary objective was to assess the differences in semen parameters and perinatal outcomes among the three groups. Multivariable logistic regression and linear regression analyses were applied to adjust for potential confounders that could influence semen parameters and perinatal outcomes. **Results** Semen volume in the normal weight group and overweight group [4.00 (3.00, 5.50) mL, 4.00 (3.00, 5.50) mL] was higher than that in the obese group [4.00 (3.00, 5.00) mL], with a significant difference among the three groups (P <0.001, a P <0.001). The total sperm count in the normal group and overweight group [207.60 (121.90, 341.75) $\times$ 10⁶, 211.80 (119.88, 334.83) $\times$ 10⁶] was higher than that in the obese group [188.40 (110.96, 323.41) $\times$ 10⁶], with a significant difference among the three groups (P =0.007, a P <0.001). The total progressive sperm motility count in the normal group [88.18 (43.63, 163.80) $\times$ 10⁶] was higher than that in the obese group [75.30 (40.29, 147.86) $\times$ 10⁶], with a significant difference among the three groups (P =0.001, a P <0.001). The percentage of forward motile sperm in the normal group [(45.37 $\pm$ 17.16)%] was higher than that in the overweight group [(44.03 $\pm$ 17.36)%] and the obese group [(43.80 $\pm$ 17.21)%], with a significant difference compared among the three groups (P =0.020, a P =0.016). In terms of perinatal outcomes, after multivariate logistic regression analysis, only the overweight and obese groups had

higher newborn birth weights [(3 389.53±472.65) g, (3 408.57±507.90) g] compared with the normal group [(3 271.32±532.02) g], with a significant difference among the three groups ($P=0.010$, $aP=0.009$). **Conclusion** Higher male BMI is associated with decreased semen quality and may increase newborn birth weight following AIH treatment.

【Key words】 Body mass index; Artificial insemination by husband; Semen parameters; Perinatal outcome

Fund program: General Program of National Natural Science Foundation of China (82471712); Henan Province Medical Science and Technology Research and Joint Construction Program (LHGJ20230380, LHGJ20230376); Henan Provincial Key R&D Program (24111310300); Henan Provincial Middle-aged and Young Health Science and Technology Innovation Leading Talent Training Program (YXKC2021020)

·临床报道·

DOI: 10.3760/cma.j.cn101441-20241113-00416

收稿日期 2024-11-13 本文编辑 王李艳

引用本文: 王亚丛, 柯雪, 谢瑞华, 等. 超声探测内膜血流预测冻融胚胎移植妊娠结局的临床应用价值分析[J]. 中华生殖与避孕杂志, 2025, 45(6): 607-611. DOI: 10.3760/cma.j.cn101441-20241113-00416.

超声探测内膜血流预测冻融胚胎移植妊娠结局 的临床应用价值分析

王亚丛 柯雪 谢瑞华 杨晓曦 罗雯 王芳

电子科技大学医学院附属妇女儿童医院 成都市妇女儿童中心医院

生殖中心, 成都 611731

通信作者: 王芳, Email: wangfcd2022@163.com

【摘要】 目的 探讨超声探测子宫内膜血流灌注对评估冻融胚胎移植 (frozen-thawed embryo transfer, FET) 周期妊娠结局的临床应用价值。方法 纳入 2021 年 12 月至 2024 年 8 月在成都市妇女儿童中心医院生殖中心行胚胎植入前遗传学检测 (preimplantation genetic testing, PGT) -FET 患者进行病例对照研究, 入组的 226 例 PGT 患者均于 FET 周期胚胎移植前 1 天进行了三维超声子宫内膜容受性评估, 根据妊娠结局分为临床妊娠组 ($n=155$) 及未妊娠组 ($n=71$)。比较两组患者一般情况及移植前 1 天子宫内膜容受性超声参数。妊娠影响因素分析采用

二元 logistic 回归。结果 两组患者年龄、原发不孕占比、抗苗勒管激素、窦卵泡计数等基线情况比较, 差异均无统计学意义 (均 $P>0.05$), 临床妊娠组不孕年限 [(2.79±2.45) 年] 显著低于未妊娠组 [(3.44±1.68) 年, $P=0.046$], 基础黄体生成素水平 [(4.37±3.02) U/L] 高于未妊娠组 [(3.59±2.02) U/L, $P=0.047$]; 临床妊娠组胚胎移植前 1 天单平面子宫内膜血流分支 (4.83±1.57) 与非妊娠组 (3.44±1.51) 对比, 差异有统计学意义 ($P=0.001$), 子宫内膜形态分型 A 型 [5.2% (8/155)]、B 型 [25.8% (40/155)] 及 C 型 [69.0% (107/155)] 与未妊娠组 [16.9% (12/71)、33.8% (24/71)、49.3% (35/71)] 对比, 差异有统计学意义 ($P=0.003$), 临床妊娠组围移植期内膜蠕动波次数 [1 (0, 2)] 少于未妊娠组 [1 (0, 4)], $P=0.046$]。两组子宫内膜厚度、蠕动波分型、子宫内膜容积分、内膜及内膜下血流搏动指数/阻力指数差异均无统计学意义 (均 $P>0.05$)。二元 logistic 回归分析显示内膜血流分支、子宫内膜蠕动波及基础黄体生成素水平是影响行 PGT 患者 FET 妊娠结局的独立因素 ($OR=1.855$, 95% CI : 1.478~2.327, $P=0.001$; $OR=0.813$, 95% CI : 0.667~0.990, $P=0.040$; $OR=1.163$, 95% CI : 1.000~1.351, $P=0.049$), 其中内膜血流分支对 PGT-FET 妊娠结局预测受试者工作特征曲线下面积为 0.725, $P=0.001$ 。结论 代表血流灌注强度的子宫内膜血流分支计数对 FET 周期助孕患者妊娠结局具有较好的临床预测价值。

【关键词】 植入前遗传学检测; 妊娠结局; 子宫内膜容受性; 内膜血流分支

基金项目: 成都市医学科研课题 (2022-171); 成都市妇女儿童中心医院英才计划资助项目 (YC2023013)

Clinical application value of ultrasonic blood flow detection in predicting frozen-thawed embryo transfer outcomes

Wang Yacong, Ke Xue, Xie Ruihua, Yang Xiaoxi, Luo Wen, Wang Fang

Department of Reproductive Medicine, Chengdu Women's and Children's Central Hospital; Women's and Children's Hospital Affiliated to the School of Medicine, University of Electronic Science and Technology of China, Chengdu 611731, China

Corresponding author: Wang Fang, Email: wangfcd2022@163.com

【Abstract】 **Objective** To explore the clinical application value of ultrasound detection of endometrial blood flow perfusion in evaluating the pregnancy outcomes of frozen-thawed embryo transfer (FET) cycles. **Methods** A case-control study of 226 patients underwent preimplantation genetic testing (PGT) in the Department of Reproductive Medicine of Chengdu Women's and Children's Central Hospital was conducted. Patients enrolled from December 2021 to August 2024 underwent three-dimensional ultrasound endometrial receptivity testing on the day before FET. According to the pregnancy outcomes, they were divided into clinical pregnancy group ($n=155$) and non-pregnancy group ($n=71$). The general characteristics and endometrial receptivity parameters were compared between the two groups. Binary logistic regression was used to analyze the factors affecting pregnancy. **Results** There was no significant difference in age, proportion of primary infertility, anti-Müllerian hormone, and antral follicle count between the two groups (all $P>0.05$). The duration of infertility in the clinical pregnancy group [(2.79±2.45) years] was significantly lower than that in the non-pregnancy group

[(3.44±1.68) years, $P=0.046$], the basal luteinizing hormone (LH) level in clinical pregnancy group [(4.37±3.02) U/L] was higher than that in the non-pregnancy group [(3.59±2.02) U/L, $P=0.047$]. On the day before embryo transfer, the single-plane endometrial blood flow branch in the pregnancy group (4.83±1.57) was more than that in the non-pregnancy group (3.44±1.51), the difference was statistically significant ($P=0.001$). The clinical pregnancy group had significantly different endometrial morphology types A [5.2% (8/155)], B [25.8% (40/155)], and C [69.0% (107/155)] compared with the non-pregnancy group [16.9% (12/71), 33.8% (24/71), 49.3% (35/71), $P=0.003$], respectively, the number of peristalsis waves in the clinical pregnancy group [1(0, 2)] was less than that in the non-pregnancy group [1(0, 4), $P=0.046$]. There were no significant differences in endometrial thickness, peristaltic wave classification, endometrial volume, endometrial and subendometrial blood flow pulse index/resistance index between the two groups (all $P>0.05$). Binary logistic regression analysis showed that the endometrial blood flow branch, endometrial peristalsis and basal LH level were independent factors affecting the pregnancy outcome of patients underwent PGT during FET cycle ($OR=1.855$, 95% CI : 1.478–2.327, $P=0.001$; $OR=0.813$, 95% CI : 0.667–0.990, $P=0.040$; $OR=1.163$, 95% CI : 1.000–1.351, $P=0.049$). Among them, the area under the receiver operating characteristic curve of endometrial blood flow branches for the prediction of PGT-FET pregnancy outcome was 0.725, $P=0.001$.

Conclusion Endometrial blood flow branch, which represents the intensity of blood perfusion, has a good clinical value in evaluating the pregnancy outcome during FET cycle.

【Key words】 Preimplantation genetic testing; Pregnancy outcome; Endometrial receptivity; Endometrial blood flow branch

Fund program: Chengdu Medical Research Project (2022-171);Chengdu Women's and Children's Central Hospital Talent Program Funding Project (YC2023013)

·临床报道·

DOI: 10.3760/cma.j.cn101441-20241118-00424

收稿日期 2024-11-18 本文编辑 王李艳

引用本文: 祝俊, 吴迪, 杨扬, 等. 药物流产后即时加用米非司酮对完全流产率影响的随机对照试验[J]. 中华生殖与避孕杂志, 2025, 45(6): 612-617. DOI: 10.3760/cma.j.cn101441-20241118-00424.

药物流产后即时加用米非司酮对完全流产率影响的随机对照试验

祝俊 吴迪 杨扬 姜丽蓉 何茶英

杭州市妇产科医院计划生育中心, 杭州 310016

通信作者: 何茶英, Email: 13506819778@163.com

【摘要】 目的 探究药物流产后即时加用米非司酮片对提高药物流产完全流产率的临床疗效。方法 本研究为随机对照试验研究, 采用随机数字表法随机选取 2022 年 1 月至 2023 年 12 月杭州市妇产科医院计划生育中心 300 例因非意愿妊娠而药物流产患者, 分为高剂量组、低剂量组和对照组, 每组 100 例。低剂量组为药物流产后即时加用米非司酮片 25 mg bid×5 d; 高剂量组为药物流产后即时加用米非司酮片 50 mg bid×5 d。对照组药物流产后不使用米非司酮。比较 3 组完全流产率、阴道流血持续时间、阴道流血量情况以及并发症等不良事件发生率。结果 完全流产率、阴道流血持续时间和流血量大于本人月经量的比例 3 个指标, 低剂量组分别为 92.0% (92/100)、(9.0±2.8) d 和 0%, 高剂量组分别为 89.0% (89/100)、(10.8±3.0) d 和 0%, 对照组分别为 67.0% (67/100)、(16.5±2.6) d 和 11.0% (11/100)。高、低剂量组完全流产率均显著高于对照组 (均 $P<0.001$), 而阴道流血时间、流血量大于本人月经量的比例均显著低于对照组 (均 $P<0.001$), 差异均有统计学意义。并发症发生率及其他不良事件发生水平, 高、低剂量组与对照组接近, 差异均无统计学意义 (均 $P>0.05$)。结论 药物流产后即时给予米非司酮片能有效提高完全流产率, 显著减少患者阴道流血量, 缩短阴道流血持续时间, 且用药安全性良好。

【关键词】 米非司酮; 药物流产; 即时加用; 完全流产

基金项目: 杭州市科学技术局科研项目 (2020120313224); 杭州市医药卫生科技重点项目 (ZD20210058)

Randomized controlled trial on the effect of immediate addition of mifepristone after medical abortion on the complete abortion rate

Zhu Jun, Wu Di, Yang Yang, Jiang Lirong, He Chaying

Family Planning Center of Hangzhou Women's Hospital, Hangzhou 310016, China

Corresponding author: He Chaying, Email: 13506819778@163.com

【Abstract】 **Objective** To explore the clinical efficacy of immediately adding mifepristone tablets after medical abortion in improving the complete abortion rate. **Methods** This study was a randomized controlled trial. A total of 300 patients with medical abortion in Family Planning Center of Hangzhou Women's Hospital from January 2022 to December 2023 were randomly divided into high-dose group, low-dose group and control group by the digital table method, with 100 cases in each group. The low-dose group was given mifepristone tablets 25 mg bid×5 d immediately after medical abortion; the high-dose group was given mifepristone tablets 50 mg bid×5 d immediately after medical abortion; the control did not use mifepristone after medical abortion. The complete abortion rate, the duration of vaginal bleeding, the amount of vaginal bleeding and the incidence of adverse events such as complications were compared among the three groups.

Results For the three indicators of complete abortion rate, duration of vaginal bleeding and the proportion of vaginal bleeding volume exceeding the individual's customary menstrual flow, they were 92.0% (92/100), (9.0±2.8) d and 0% respectively in the low-dose group, 89.0% (89/100), (10.8±3.0) d and 0% respectively in the high-dose group, and 67.0% (67/100), (16.5±2.6) d and 11.0% (11/100) respectively in the control. The complete abortion rate in the high-dose group and low-dose group was significantly higher than that in the control (all $P<0.001$), while the duration and the proportion of vaginal bleeding volume exceeding the individual's customary menstrual flow were significantly lower than those in the control (all $P<0.001$), and the differences were statistically significant. The incidence of complications and the occurrence level of other adverse events were similar between the high-dose and low-dose groups and the control, and the differences were not statistically significant (all $P>0.05$). **Conclusion** Immediately giving mifepristone tablets after medical abortion can effectively improve the complete abortion rate, significantly reduce the amount and duration of vaginal bleeding in patients, and the security of the medication is good.

【Key words】 Mifepristone; Medical abortion; Immediate addition; Complete abortion

Fund program: Research Project of Hangzhou Science and Technology Bureau (2020120313224); Hangzhou Medical and Health Technology Key Project (ZD20210058)

个案报道

DOI: 10.3760/cma.j.cn101441-20241105-00405

收稿日期 2024-11-05 本文编辑 王李艳
引用本文: 胡玥玥, 王千一, 闫旭, 等. *PLCZ1* 复合杂合突变患者行 ICSI 结合卵母细胞辅助激活 1 例并文献复习 [J]. 中华生殖与避孕杂志, 2025, 45(6): 618-622. DOI: 10.3760/cma.j.cn101441-20241105-00405.

PLCZ1 复合杂合突变患者行 ICSI 结合卵母细胞
辅助激活 1 例并文献复习

胡玥玥 王千一 闫旭 孙志丰 张鑫 张颖 张昌军
湖北医药学院附属人民医院生殖医学中心 湖北省生殖医学临床医
学研究中心 湖北医药学院生物医学工程学院, 十堰 442000

通信作者: 张昌军, Email: 542690700@qq.com

【摘要】 回顾性分析 1 例男性不育患者多次受精失败及挽救受精的治疗过程。患者在外院行体外受精 (*in vitro* fertilization, IVF) 和卵胞质内单精子注射 (intracytoplasmic sperm injection, ICSI) 治疗 3 个周期均受精异常, 在湖北医药学院附属人民医院生殖医学中心经不孕不育基因 panel 检测及 Sanger 测序验证, 确定患者 *PLCZ1* 基因复合杂合突变, 基因突变分别来源于父母双方; 女方基因检测未发现异常突变。本中心给予女方改良高孕激素状态下促排卵方案, 取卵 9 枚, 9 枚成熟卵母细胞全部行 ICSI 结合 $10\ \mu\text{mol/L}$ 离子霉素卵母细胞辅助激活 (assisted oocyte activation, AOA), 正常受精 7 枚, 形成 7 枚卵裂期胚胎, 冷冻 2 枚优质卵裂期胚胎。2 个月后女方行冻融胚胎移植获生化妊娠。同时我们对国内外关于 *PLCZ1* 基因突变的文献和 AOA 相关文献进行复习。从本病例得出如下提示: ①当 IVF 周期出现不受精或多精受精, 并且 ICSI 全受精失败时, 需进行夫妻双方基因检测查找遗传因素。②*PLCZ1* 基因突变主要导致受精失败, ICSI 结合 AOA 是挽救受精失败的有效方法, 离子霉素对卵母细胞活化效果显著, 胚胎形成未受影响, 优质胚胎具有着床能力。但仍需要积累病例数据, 验证离子霉素 AOA 的安全性。

【关键词】 精子注射; 细胞质内; 卵母细胞辅助激活; 离子霉素; *PLCZ1*; 全受精失败

A case of *PLCZ1* complex heterozygous mutation underwent ICSI combined assisted oocyte activation and literature review

Hu Yueyue, Wang Qianyi, Yan Xu, Sun Zhifeng, Zhang Xin, Zhang Ying, Zhang Changjun

Reproductive Medicine Center, Renmin Hospital, Hubei University of Medicine; Hubei Clinical Research Center for Reproductive Medicine; Biomedical Engineering College, Hubei University of Medicine, Shiyan 442000, China

Corresponding author: Zhang Changjun, Email: 542690700@qq.com

【Abstract】 The treatment process of multiple fertilization failure and salvage fertilization in a male infertile patient was retrospectively analyzed. The patient underwent *in vitro* fertilization (IVF) and intracytoplasmic sperm injection (ICSI) in another hospital for 3 cycles, all of which had fertilization abnormalities. The complex heterozygous mutation of *PLCZ1* gene was detected by infertility gene panel and confirmed by Sanger sequencing in the Reproductive Medicine Center of Renmin Hospital, Hubei University of Medicine, and the gene mutation was derived from both parents. No abnormal mutations were found in the woman's genetic testing. The woman underwent progestin-primed ovarian stimulation, resulting in the retrieval of 9 oocytes. ICSI combined with $10\ \mu\text{mol/L}$ ionomycin assisted oocyte activation (AOA) was applied to all mature eggs, resulting in 7 normal fertilized oocytes and 7 cleavage embryos, 2 high-quality cleavage embryos were frozen. Two months later, the woman underwent frozen-thawed embryo transfer to obtain biochemical pregnancy. Simultaneously, we reviewed the literature on *PLCZ1* gene mutations and AOA related literature at home and abroad. From this case we can draw the following conclusions: 1) When no fertilization or polyspermia occurs in

an IVF cycle and total fertilization fails in ICSI, genetic testing of both spouses is required to find genetic factors. 2) The mutation of *PLCZ1* gene mainly leads to fertilization failure. ICSI combined with AOA is an effective method to rescue fertilization failure. Ionomycin has a significant effect on oocyte activation, and has no effect on embryo formation. However, we still need to accumulate case data to verify the safety of ionomycin AOA.

【Key words】 Sperm injection, intracytoplasmic; Assisted oocyte activation; Ionomycin; *PLCZ1*; Total fertilization failure

个案报道

DOI: 10.3760/cma.j.cn101441-20241025-00384

收稿日期 2024-10-25 本文编辑 王李艳

引用本文: 张静, 田文艳, 田烨, 等. 早期子宫内膜癌患者孕期复发再次保留生育功能治疗 1 例[J]. 中华生殖与避孕杂志, 2025, 45(6): 623-627. DOI: 10.3760/cma.j.cn101441-20241025-00384.

早期子宫内膜癌患者孕期复发再次保留生育功能治疗 1 例

张静 田文艳 田烨 张妍 白晓红 宋学茹 王颖梅

天津医科大学总医院妇产科 天津市女性生殖健康与优生重点实验室, 天津 300052

通信作者: 王颖梅, Email: wangyingmei@tmu.edu.cn

【摘要】 回顾性分析 1 例早期子宫内膜癌(early-stage endometrial cancer, EEC) 保留生育功能治疗后孕期发现复发患者, 经再次保留生育功能治疗后顺利分娩的病例并进行文献复习。该患者经保留生育功能治疗后, 行 2 次控制性卵巢刺激周期和 3 次解冻胚胎移植周期, 移植后早期妊娠胚胎停育, 清宫时病理发现子宫内膜癌复发, 结合患者生育意愿、妇科超声、盆腔磁共振成像等检查, 多学科讨论后再次予以保留生育功能治疗, 完全缓解后结合胚胎植入前遗传学检测技术将患者剩余冻存胚胎进行筛选, 选择整倍体胚胎移植后成功妊娠足月分娩。EEC 患者保留生育功能治疗需综合管理来降低复发风险, 复发患者在全面评估病情下可选择再次保留生育功能治疗。

【关键词】 子宫内膜癌; 早期; 胚胎植入前遗传学检测; 保留生育功能治疗

基金项目：国家重点研发计划（2022YFC2704402）；国家自然科学基金面上项目（82171625）；天津市医学重点学科（专科）建设项目（TJYXZDXK-031A）

A case of recurrence early-stage endometrial cancer during pregnancy recieved fertility-preserving retreatment

Zhang Jing, Tian Wenyan, Tian Ye, Zhang Yan, Bai Xiaohong, Song Xueru, Wang Yingmei

Department of Obstetrics and Gynecology, Tianjin Medical University General Hospital; Tianjin Key Laboratory of Female Reproductive Health and Eugenics, Tianjin 300052, China

Corresponding author: Wang Yingmei, Email: wangyingmei@tmu.edu.cn

【Abstract】 A retrospective analysis was conducted on a case of recurrence during pregnancy of early-stage endometrial cancer (EEC) after fertility-preserving treatment, and literature review was conducted. The patient underwent two cycles of controlled ovarian stimulation and three cycles of frozen-thawed embryo transfer after fertility-preserving treatment, early abortion after the third transfer and meanwhile the recurrence of endometrial cancer was found. Fertility-preserving retreatment was given after multidisciplinary discussion based on the patient's fertility intention, ultrasound, pelvic magnetic resonance imaging and other examinations. After complete remission, the remaining cryopreserved embryos of the patient were tested for euploidy by preimplantation genetic testing, and the euploid embryo was transferred and delivered at term successfully. Fertility-preserving treatment for patients with EEC need comprehensive management to reduce the recurrence rate. Recurrent patients can choose fertility-preserving retreatment under a comprehensive evaluation.

【Key words】 Endometrial cancer; Early stage; Preimplantation genetic testing; Fertility-preserving treatment

Fund program: National Key Research and Developmental Plan of China (2022YFC2704402); General Project of National Natural Science Foundation of China (82171625); Tianjin Key Medical Discipline (Specialty) Construction Project (TJYXZDXK-031A)

个案报道

DOI: 10.3760/cma.j.cn101441-20240307-00084

收稿日期 2024-03-07 本文编辑 王李艳

引用本文：卢颖莹，肖晶晶，谢淑武，等. 双侧输卵管妊娠 9 例临床诊治分析[J]. 中华生殖与避孕杂志, 2025, 45(6): 628-631. DOI: 10.3760/cma.j.cn101441-20240307-00084.

双侧输卵管妊娠 9 例临床诊治分析

卢颖莹¹ 肖晶晶¹ 谢淑武² 叶新红¹

¹ 复旦大学附属妇产科医院妇产科 上海市生殖内分泌相关疾病重点实验室, 上海 200011; ² 上海实验动物研究中心, 上海 201203

通信作者: 叶新红, Email: yexinhong1147@fckyy.org.cn

【摘要】 双侧输卵管妊娠是一种罕见的异位妊娠, 妊娠部位发生在双侧输卵管。为了探讨双侧输卵管妊娠的临床诊治要点、病理分析与治疗结局, 本文回顾性分析复旦大学附属妇产科医院妇产科 2003 年 1 月至 2023 年 12 月收治的 9 例双侧输卵管妊娠的临床资料。超声明确诊断为双侧输卵管妊娠, 都有胚胎移植史, 妊娠部位分布在输卵管壶腹部妊娠和间质部。治疗方式为双侧输卵管切除术。治疗后无一例二次手术, 1 例成功生育。总之双侧输卵管妊娠作为一种罕见、临床表现不典型的特殊异位妊娠类型, 应早期发现和诊治, 根据病情及患者需求制定个性化的治疗方案, 治疗后严密监测血 β -人绒毛膜促性腺激素变化, 结合多普勒超声检查等辅助检查方式, 警惕持续性异位妊娠, 甚至滋养细胞疾病的发生。

【关键词】 双侧输卵管妊娠; β -人绒毛膜促性腺激素; 胚胎移植

基金项目: 上海市自然科学基金 (17ZR1424300)

Clinical diagnosis and treatment analysis of 9 cases of bilateral tubal pregnancy

Lu Yingying¹, Xiao Jingjing¹, Xie Shuwu², Ye Xinhong¹

¹ Obstetrics and Gynecology Department of Obstetrics & Gynecology Hospital of Fudan University; Shanghai Key Laboratory of Reproductive Endocrine Diseases, Shanghai 200011, China; ² Shanghai Laboratory Animal Research Center, Shanghai 201203, China

Corresponding author: Ye Xinhong, Email: yexinhong1147@fckyy.org.cn

【Abstract】 Bilateral tubal pregnancy is a rare ectopic pregnancy that occurs in both fallopian tubes. In order to explore the clinical diagnosis and treatment methods, pathological analysis, and treatment outcomes of the disease, we retrospectively analyzed the clinical data of 9 cases of bilateral tubal pregnancy admitted to the Obstetrics and Gynecology Department of Obstetrics & Gynecology Hospital of Fudan University from January 2003 to December 2023. All cases were confirmed as bilateral tubal pregnancy by preoperative ultrasound, and all with a history of embryo transfer, which pregnancy sites distributed in the ampulla and interstitial regions of the fallopian tubes. The treatment method was bilateral salpingectomy. After treatment, there were no cases of secondary surgery, and one case successfully gave birth. In summary, as a rare and atypical type of ectopic pregnancy, bilateral tubal pregnancy should be detected and diagnosed early. Personalized treatment plans should be developed based on the patient's condition and needs. After treatment, changes in blood β -human chorionic gonadotropin should be monitored strictly, and auxiliary examination methods such as Doppler

ultrasound should be used to alert to the occurrence of persistent ectopic pregnancy and even trophoblastic diseases

【Key words】 Bilateral tubal pregnancy; β -human chorionic gonadotrophin; Embryo transfer

Fund program: Natural Science Foundation of Shanghai (17ZR1424300)

综述

DOI: 10.3760/cma.j.cn101441-20250115-00019

收稿日期 2025-01-15 本文编辑 孙敏

引用本文: 侯思如, 吴珊珊, 张斯文, 等. 超重/肥胖对女性行辅助生殖助孕结局的影响及其作用机制[J]. 中华生殖与避孕杂志, 2025, 45(6): 632-636. DOI: 10.3760/cma.j.cn101441-20250115-00019.

超重/肥胖对女性行辅助生殖助孕结局的影响及其作用机制

侯思如 吴珊珊 张斯文 高姗 谭季春

中国医科大学附属盛京医院生殖二科, 沈阳 110004

通信作者: 谭季春, Email: tjczjh@163.com

【摘要】 近年来, 不孕症的发生率呈逐步上升趋势。肥胖作为一种慢性炎症性疾病, 不仅可能会引发高血压、糖尿病等一系列慢性疾病, 也能对女性生殖系统产生负面影响, 如稀发排卵、无排卵和月经紊乱, 甚至不孕等。即使在辅助生殖技术 (assisted reproductive technology, ART) 助孕的人群中, 超重/肥胖女性的助孕结局也不容乐观, 而超重及肥胖对 ART 结局的影响机制尚未明了。本文将对超重和肥胖对女性 ART 结局的影响及机制进行综述。

【关键词】 肥胖症; 生殖技术, 辅助; 活产; 妊娠并发症; 体质量指数

Effect of overweight/obesity on female ART outcomes and its mechanisms

Hou Siru, Wu Shanshan, Zhang Siwen, Gao Shan, Tan Jichun

The Second Reproductive Division, Shengjing Hospital Affiliated to China Medical University, Shenyang 110004, China

Corresponding author: Tan Jichun, Email: tjczjh@163.com

【Abstract】 In recent years, the incidence of infertility has been steadily increasing. Obesity, recognized as a chronic inflammatory condition, can not only lead to various chronic diseases such as hypertension and diabetes, but also

adversely affects female reproductive health,including rare ovulation, anovulation, menstrual irregularities, and even infertility. The reproductive outcomes of overweight/obese women are not optimistic even among people undergoing assisted reproductive technology (ART).However, the mechanisms of overweight and obesity on ART outcomes remain poorly understood. This review aims to summarize current evidence on the impact of overweight and obesity on ART outcomes in women and explore the potential mechanisms.

【Key words】 Obesity; Reproductive techniques, assisted; Live birth; Pregnancy complications; Body mass index

综述

DOI: 10.3760/cma.j.cn101441-20241221-00488

收稿日期 2024-12-21 本文编辑 李天琦

引用本文: 王诗敏, 张秀萍, 陈佳瑶, 等. 非经典型先天性肾上腺皮质增生症酶缺乏对女性生殖健康影响的研究进展 [J]. 中华生殖与避孕杂志, 2025, 45(6): 637-643. DOI: 10.3760/cma.j.cn101441-20241221-00488.

非经典型先天性肾上腺皮质增生症酶缺乏对女性生殖健康影响的研究进展

王诗敏¹ 张秀萍² 陈佳瑶¹ 朱鹏飞² 武学清²

¹山西医科大学临床学科建设中心, 太原 030001; ²山西省儿童医院

山西省妇幼保健院生殖医学中心 山西省生育力优化技术创新中心,

太原 030013

通信作者: 武学清, Email: xueqingwu416@126.com

【摘要】 非经典型先天性肾上腺皮质增生症 (non-classical congenital adrenal hyperplasia, NCAH) 是一种遵循常染色体隐性遗传模式的疾病。该病源于编码参与肾上腺类固醇激素酶和辅助因子的基因突变, 这些突变可导致 21-羟化酶、11 β -羟化酶、3 β -羟基类固醇脱氢酶、17 α -羟化酶及类固醇急性调节蛋白等关键酶和辅助因子的活性降低或功能丧失, 进而通过遗传与内分泌机制对女性生殖健康产生影响。本综述旨在探讨导致 NCAH 不同类型中各种酶缺陷的发病机制、临床特征及其对女性生育能力的影响, 希望有助于改善 NCAH 相关不孕症的诊断策略, 从而提高患者的生育能力, 并为该领域的进一步研究提供新的方向和机遇。

【关键词】 不孕； 先天性肾上腺皮质增生症； 21-羟化酶缺乏症； 非典型先天性肾上腺皮质增生症

基金项目：“四个一批”科技兴医创新计划项目之山西省生殖与遗传研究科技培育团队项目（2020TD19）；山西省基础研究计划自由探索类面上项目（202203021211062）

Research progress on the effect of enzyme deficiencies and female reproductive health in patients with non-classical congenital adrenal hyperplasia

Wang Shimin¹, Zhang Xiuping², Chen Jiayao¹, Zhu Pengfei², Wu Xueqing²

¹ Centre for Clinical Discipline Construction, Shanxi Medical University, Taiyuan 030001, China; ² Center of Reproductive Medicine, Children's Hospital of Shanxi; Shanxi Women and Children Hospital; Shanxi Fertility Optimisation Technology Innovation Centre, Taiyuan 030013, China

Corresponding author: Wu Xueqing, Email: xueqingwu416@126.com

【Abstract】 Non-classical congenital adrenal hyperplasia (NCCAH), an autosomal recessive disorder, stems from genetic mutations affecting the enzymes and cofactors integral to adrenal steroidogenesis. These mutations may result in diminished activity or a complete loss of function for critical enzymes, such as 21-hydroxylase, 11 β -hydroxylase, 3 β -hydroxysteroid dehydrogenase, 17 α -hydroxylase, and the steroidogenic acute regulatory protein (StAR). The impairment of these enzymatic processes has profound implications for reproductive health in females, mediated through both genetic and endocrine pathways. This review aims to explore the pathogenesis of various enzyme defects in different types of NCCAH, their clinical features, and their impact on female fertility. It is hoped that this will help refine the diagnostic strategies for infertility associated with NCCAH, thereby enhancing fertility of patients and providing new directions and opportunities for further research in this field.

【Key words】 Infertility; Adrenal hyperplasia, congenital; 21-hydroxylase deficiency; Non- classical congenital adrenal hyperplasia

Fund program: "Four batches" Science and Technology Innovation Plan Project of Shanxi Reproductive and Heritage Research Science and Technology Cultivation Team Program (2020TD19); Shanxi Provincial Basic Research Programme Free Exploration Top-level Project (202203021211062)

综述

DOI: 10.3760/cma.j.cn101441-20250111-00014

收稿日期 2025-01-11 本文编辑 王李艳

引用本文：晏天禧，赵晓丽，吴林玲，等. TET 蛋白介导的 DNA 去甲基化在哺乳动物胚胎发育与妊娠结局中的调控作用 [J]. 中华生殖与避孕杂志，2025，45(6): 644-648. DOI: 10.3760/cma.j.cn101441-20250111-00014.

TET蛋白介导的DNA去甲基化在哺乳动物胚胎发育与妊娠结局中的调控作用

晏天禧 赵晓丽 吴林玲 程诗蔓 吴宇 张海娇 孙娅瑄 李晨

曦 贾佳

天津中医药大学第一附属医院生殖医学科 国家中医针灸临床医学

研究中心, 天津 300381

通信作者: 吴林玲, Email: 154384118@qq.com

【摘要】 DNA 甲基化是哺乳动物中重要的表观遗传修饰方式, 对细胞分化、基因表达调控等生理进程具有关键作用。DNA 去甲基化酶 10-11 易位 (ten-eleven translocation, TET) 蛋白家族在调节 DNA 甲基化过程中起着核心作用, 通过将 5-甲基胞嘧啶氧化为 5-羟甲基胞嘧啶等产物, 实现 DNA 的去甲基化。在早期胚胎发育的 DNA 甲基化重编程过程中, 基因组会表现出大范围的 DNA 去甲基化, DNA 甲基化重编程的异常可能会导致胚胎发育异常、子代的生理缺陷等问题。TET 蛋白凭借其独特动态性以及功能多面性介导 DNA 去甲基化过程, 调节哺乳动物胚胎发育过程中的生殖细胞的发育和成熟、多能性建立、细胞谱系分化和转录进程, 与妊娠维持、子代疾病易感性等密切相关。此外, 基因突变、母体疾病状态、不良环境因素暴露等会影响 TET 蛋白活性, 进而导致 DNA 去甲基化模式异常。深入探究 TET 蛋白的相关机制对于理解生命早期的表观遗传调控机制、为临床上早期胚胎发育异常阻滞等相关疾病的诊断和治疗, 以及指导妊娠期预防保健等具有重要意义。本文对 TET 蛋白介导的 DNA 去甲基化在哺乳动物胚胎发育与妊娠结局中的调控作用作一综述。

【关键词】 胚胎发育; 妊娠结局; 表观遗传; TET 蛋白; DNA 去甲基化

基金项目: 国家自然科学基金面上项目 (82474562); 天津中医药大学第一附属医院“拓新工程”基金科研课题重点项目 (院 ZD202104)

Regulatory role of DNA demethylation mediated by TET protein in mammalian embryonic development and pregnancy outcome

Yan Tianxi, Zhao Xiaoli, Wu Linling, Cheng Shiman, Wu Yu, Zhang Haijiao, Sun Yaxuan, Li Chenxi, Jia Jia

Reproductive Center of the First Teaching Hospital of Tianjin University of Traditional Chinese Medicine; National Clinical Research Center for Chinese Medicine Acupuncture and Moxibustion, Tianjin 300381, China

Corresponding author: Wu Linling, Email: 154384118@qq.com

【Abstract】 DNA methylation is an important epigenetic modification in mammals, playing a crucial role in various physiological processes, including cell

differentiation and the gene expression regulation. The ten-eleven translocation (TET) protein family of DNA demethylases is integral to the regulation of DNA methylation, as it catalyzes the oxidation of 5-methylcytosine to form 5-hydroxymethylcytosine. During early embryonic development, the genome undergoes extensive DNA demethylation, and any aberration in this reprogramming process can result in abnormal embryonic development and physiological defects in offspring. The TET proteins, due to their unique dynamics and multifaceted roles, facilitate DNA demethylation and are involved in development and maturation of germ cells, the establishment of pluripotency, cell lineage differentiation, and transcriptional processes throughout mammalian embryogenesis. Furthermore, these proteins are closely associated with the maintenance of pregnancy and susceptibility of progeny to disease. Factors such as genetic mutations, maternal health conditions, and exposure to adverse environmental influences can impact TET protein activity, resulting in abnormal patterns of DNA demethylation. A comprehensive investigation of the related mechanisms of TET proteins is essential for enhancing our understanding of epigenetic regulation during early life, diagnosing and treating related diseases such as early fetal development retardation, and informing strategies for the prevention and management of pregnancy. This article reviews the regulatory role of DNA demethylation mediated by TET protein in mammalian embryonic development and pregnancy outcomes.

【Key words】 Embryonic development; Pregnancy outcome; Epigenetic modification; TET protein; DNA demethylation

Fund program: General Program of the National Natural Science Foundation of China (82474562); Key Research Project of the "Pioneering and Innovative Engineering" Fund for Scientific Research of the First Teaching Hospital of Tianjin University of Traditional Chinese Medicine (Hospital Grant No. ZD202104)