

中华生殖与避孕杂志[®]



原刊名《生殖与避孕》

CHINESE JOURNAL OF REPRODUCTION AND CONTRACEPTION

月刊 1980年12月创刊 第41卷 第11期 2021年11月25日出版

主 管

中国科学技术协会

主 办

中华医学会
上海市计划生育科学研究所
复旦大学附属妇产科医院

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出 版

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

广告发布登记号

京东市监广登字20200006号

印 刷

上海商务联西印刷有限公司

发 行

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

订 购

全国各地邮政局
邮发代号4-928

邮 购

中华生殖与避孕杂志编辑部
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电话:(021)64438169,64438975
Email:rande@sippr.org.cn

定 价

每期30.00元,全年360.00元

中国标准连续出版物号

ISSN 2096-2916

CN 10-1441/R

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本刊稿约见本卷第1期封三、第7期封二

本期责任编辑 乔杰

本期责任编辑 王李艳

本期责任编辑 年利红

CHINESE JOURNAL OF REPRODUCTION AND CONTRACEPTION

(Original title: *Reproduction and Contraception*)

Monthly

Established in December 1980

Volume 41, Number 11

November 25, 2021



Responsible Institution

China Association for Science and Technology

Sponsor

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

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779 Laohumin Road, Shanghai 200237, China
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Chinese Medical Journals Publishing House Co., Ltd.
42 Dongsi Xidajie, Beijing 100710, China
Tel(Fax): 0086-10-51322059
Email: office@cmaph.org

Printing

Business Book Printing Shop Shanghai Printing Co., LTD

Overseas Distributor

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

Mail-Order

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

CSSN

ISSN 2096-2916
CN 10-1441/R

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DOI: 10.3760/cma.j.cn101441-20201119-00629

收稿日期 2020-11-23 本文编辑 孙敏

引用本文: 钱易, 张园, 袁纯, 等. 比较早卵泡期长效方案和拮抗剂方案在不明原因不孕人群中的应用[J]. 中华生殖与避孕杂志, 2021, 41(11): 957-965. DOI: 10.3760/cma.j.cn101441-20201119-00629.

·临床研究·

比较早卵泡期长效方案和拮抗剂方案在不明原因不孕人群中的应用

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【摘要】 目的 探讨不明原因不孕人群进行早卵泡期长效方案和拮抗剂方案诱导排卵的临床效果及妊娠结局。方法 检索南京医科大学第一附属医院生殖医学科临床辅助生殖技术管理系统软件数据库, 收集 2018 年 1 月至 2019 年 1 月期间进行体外受精/卵胞质内单精子注射-胚胎移植 (*in vitro fertilization/intracytoplasmic sperm injection and embryo transfer*, IVF/ICSI-ET) 的不明原因不孕患者临床资料共 642 例, 根据促排卵方案不同分为拮抗剂方案组 (记为拮抗剂组, 共 359 例) 和早卵泡期长效方案组 (记为早长组, 共 283 例)。通过回顾性队列研究分析两组患者的临床妊娠率、活产率、胚胎种植率以及其他诱导排卵临床指标及实验室指标。在此基础上, 进一步针对患者年龄、体质指数 (body mass index, BMI) 分别进行分层分析。结果 ①拮抗剂组患者 BMI [(22.17 ± 2.96) kg/m²] 高于早长组患者 [(21.68 ± 2.29) kg/m², $P=0.018$], 其余指标差异均无统计学意义 (P 均 >0.05)。②早长组患者促性腺激素 (gonadotropin, Gn) 启动剂量 [(149.74 ± 36.24) IU] 显著低于拮抗剂组 [(177.97 ± 38.85) IU, $P<0.001$], Gn 使用时间 [(11.93 ± 2.26) d]、Gn 使用总量 [(1908.35 ± 632.36) IU] 显著高于拮抗剂组 [(8.86 ± 1.45) d, (1638.57 ± 497.23) IU, P 均 <0.001]。两组患者行卵裂期胚胎移植早长组胚胎种植率 [57.14% (152/266)]、临床妊娠率 [66.48% (121/182)]、活产率 [59.89% (109/182)] 均显著高于拮抗剂组 [39.53% (68/172), $P<0.001$; 51.72% (60/116), $P=0.011$; 40.52% (47/116), $P=0.001$], 中重度卵巢过度刺激综合征发生率组间比较差异无统计学意义 ($P>0.05$)。多因素 logistic 回归分析结果显示治疗方案、年龄均是卵裂期胚胎移植临床妊娠、活产的危险因素 [2.261 (95% CI=1.333~3.836), $P=0.002$; 0.928 (95% CI=0.869~0.991), $P=0.026$; 2.598 (95% CI=1.535~4.397), $P<0.001$; 0.906 (95% CI=0.849~0.967), $P=0.003$]。③ <35 岁患者行早长方案新鲜胚胎周期移植临

床妊娠率、活产率均高于拮抗剂组，但差异均无统计学意义（ P 均 >0.05 ）。35~39岁患者早长方案新鲜胚胎周期移植种植率、临床妊娠率、活产率均高于拮抗剂组，但差异均无统计学意义（ P 均 >0.05 ）。④正常 BMI 人群中早长组种植率[55.71%（122/219）]、临床妊娠率[63.58%（96/151）]、活产率[58.94%（89/151）]均显著高于拮抗剂组[37.82%（45/119）， $P=0.002$ ；46.99%（39/83）， $P=0.014$ ；39.76%（33/83）， $P=0.005$]。超重人群中，早长组种植率[68.09%（32/47）]、临床妊娠率[81.25%（26/32）]均显著高于拮抗剂组[43.40%（23/53）， $P=0.013$ ；57.14%（20/35）， $P=0.034$]，但活产率差异无统计学意义（ $P>0.05$ ）。结论与拮抗剂方案相比，给予不明原因不孕症患者进行早卵泡期长效长方案促排卵可获得较满意的 IVF 新鲜周期移植临床妊娠结局，但其增加患者降调节时间及 Gn 使用时间、总剂量。

【关键词】 受精，体外； 胚胎移植； 早卵泡期长效长方案； 拮抗剂方案； 不明原因不孕

基金项目：国家自然科学基金重点项目（81730041）；国家重点研发计划子课题（2017YFC1001604）；国家自然科学基金青年基金（81701517）；江苏省科技厅项目（青年基金）（BK20161067）

Comparison of the early follicular long-term protocol and antagonist protocol in unexplained infertility patients

Qian Yi, Zhang Yuan, Yuan Chun, Jiang Chunyan, Wu Wei, Huang Jie, Mao Yundong, Liu Jiayin, Ma Xiang

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【Abstract】 **Objective** To investigate the clinical effects and pregnancy outcomes of the early follicular long-term protocol and antagonist protocol in the treatment of unexplained infertility patients. **Methods** From January 2018 to January 2019, 642 cases of unexplained infertility patients with early follicular long-term protocol and antagonist protocol in *in vitro* fertilization/intracytoplasmic sperm injection and embryo transfer (IVF/ICSI-ET) were collected using the clinical assisted reproductive technologies management system software database of the Department of Reproductive Medicine of the First Affiliated Hospital of Nanjing Medical University. Patients were divided into early follicular long-term protocol ($n=283$) and antagonist protocol ($n=359$) groups. The clinical outcomes of the two groups were analyzed retrospectively, including the implantation rate, the clinical pregnancy rate, and the live birth rate. Furthermore, the pregnancy outcomes of different age and body mass index (BMI) patients were further analyzed. **Results** 1) The BMI in the antagonist protocol group was higher than that in early follicular long-term protocol group [(22.17 \pm 2.96) kg/m² vs. (21.68 \pm 2.29) kg/m², $P=0.018$]. The other based data did not exhibit remarkable difference between the two groups ($P>0.05$). 2) The starting dosage of gonadotropin (Gn) in early follicular long-term protocol group was less than that of antagonist group [(149.74 \pm 36.24) IU vs. (177.97 \pm 38.85) IU, $P<0.001$]. While the total duration and dosage of Gn used in early follicular long-term protocol group were significantly higher than those in

antagonist group [(11.93±2.26) d vs. (8.86±1.45) d, $P<0.001$; (1 908.35±632.36) IU vs. (1 638.57±497.23) IU, $P<0.001$). The cleavage embryo implantation rate, the clinical pregnancy rate and the live pregnancy rate in fresh cycle in early follicular long-term protocol group were significantly higher than those in the antagonist group [57.14% (152/266) vs. 39.53% (68/172), $P<0.001$; 66.48% (121/182) vs. 51.72% (60/116), $P=0.011$; 59.89% (109/182) vs. 40.52% (47/116), $P=0.001$]. The incidence of moderate and severe ovarian hyperstimulation syndrome between the two groups were not statistically different ($P>0.05$). Multivariate logistic regression analysis showed that different protocols and age were both risk factors for clinical pregnancy and live birth of cleavage embryo transfer [2.261(95% $CI=1.333-3.836$), $P=0.002$; 0.928(95% $CI=0.869-0.991$), $P=0.026$; 2.598(95% $CI=1.535-4.397$), $P<0.001$; 0.906(95% $CI=0.849-0.967$), $P=0.003$]. 3) In patients under 35 years old, the clinical pregnancy rate and the live birth rate in early follicular long-term protocol group were higher than those of the antagonist group, but there was no statistical difference (all $P>0.05$). The fresh embryo cycle implantation rate, the clinical pregnancy rate and the live birth rate of 35-39 years old patients in the early follicular long-term protocol group were higher than those in the antagonist group, but there was no statistical difference (all $P>0.05$). 4) In normal BMI group, the implantation rate, the clinical pregnancy rate and the live birth rate in early follicular long-term protocol group were significantly higher than those in the antagonist group [55.71% (122/219) vs. 37.82% (45/119), $P=0.002$; 63.58% (96/151) vs. 46.99% (39/83), $P=0.014$; 58.94% (89/151) vs. 39.76% (33/83), $P=0.005$]. In the overweight population, the implantation rate and the clinical pregnancy rate in early follicular long-term protocol group were significantly higher than those in the antagonist group [68.09% (32/47) vs. 43.40% (23/53), $P=0.013$; 81.25% (26/32) vs. 57.14% (20/35), $P=0.034$], but there was no statistically significant difference in the live birth rate ($P>0.05$). **Conclusion** Compared with the antagonist protocol, early follicular long-term protocol for unexplained infertility patients may achieve higher clinical pregnancy outcomes in IVF fresh cycle, but it could increased the duration of descending, the duration and dosage of Gn used.

【Key words】 Fertilization *in vitro*; Embryo transfer; Early follicular long-term protocol; Antagonist protocol; Unexplained infertility

Fund program: Key Project of National Natural Science Foundation of China (81730041); National Key Research and Development Program Sub-project (2017YFC1001604); National Natural Science Foundation of China (Youth Foundation) (81701517); Jiangsu Provincial Science and Technology Department Project (Youth Foundation) (BK20161067)

DOI: 10.3760/cma.j.cn101441-20200511-00275

收稿日期 2020-05-12 本文编辑 王李艳

引用本文: 张文, 于晓娜, 任炳楠, 等. 三种黄体支持方案在激素替代周期冻融胚胎移植中妊娠结局的比较[J]. 中华生殖与避孕杂志, 2021, 41(11): 966-972. DOI: 10.3760/cma.j.cn101441-20200511-00275.

·临床研究·

三种黄体支持方案在激素替代周期冻融胚胎移植中妊娠结局的比较

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【摘要】 目的 探讨三种不同黄体支持方案对激素替代周期冻融胚胎移植(hormone replacement therapy frozen-thawed embryo transfer, HRT-FET)中妊娠结局的影响。方法 回顾性队列研究分析 2016 年 1 月至 2019 年 2 月期间在郑州大学第三附属医院生殖中心接受 HRT-FET 的 3288 个周期, 根据不同黄体支持方案分为三组。A 组为黄体酮软胶囊联合地屈孕酮片组(478 个周期), B 组为黄体酮阴道缓释凝胶联合地屈孕酮片组(1923 个周期), C 组为黄体酮针剂联合地屈孕酮片组(887 个周期)。分别比较三组的妊娠结局及新生儿结局。结果 A 组、B 组和 C 组间的临床妊娠率、12 周妊娠率、移植周期活产率差异均无统计学意义(P 均 >0.05), 早产率和双胎分娩率 C 组高于 B 组[19.90% (78/392) 比 13.61% (109/801), $P=0.011$; 30.61% (120/392) 比 20.47% (164/801), $P<0.001$], 差异均有统计学意义, B 组新生儿体质量[$(3\ 178.60\pm635.38)$ g] 高于 C 组[$(3\ 033.01\pm682.54)$ g], 差异有统计学意义($P<0.001$), 三组间新生儿出生缺陷发生率差异无统计学意义($P>0.05$)。logistic 回归分析显示, 三组不同黄体支持方案并不是 12 周妊娠率的独立影响因素。结论 在 HRT-FET 周期中, 黄体酮软胶囊或黄体酮阴道缓释凝胶联合地屈孕酮片, 均能取得与黄体酮针剂联合地屈孕酮片相似的妊娠结局, 但仍需要大样本前瞻性研究证实。

【关键词】 黄体支持; 冻融胚胎移植; 激素替代周期; 妊娠结局

Comparison of pregnancy outcomes of three luteal support protocols in frozen-thawed embryo transfer during the hormone replacement cycle

Zhang Wen, Yu Xiaona, Ren Bingnan, Guan Yichun, Qiao Hongwu, Wang Jingyan

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【Abstract】 Objective To investigate the effects of three different luteal phase support protocols on pregnancy outcomes in hormone replacement therapy frozen-thawed embryo transfer(HRT-FET). **Methods** The clinical data of 3288 HRT-FET cycles in Reproductive Center of the Third Affiliated Hospital of Zhengzhou University from January 2016 to February 2019 were retrospective cohort study analyzed. The cycles were divided into three groups according to luteal phase

support protocols. The patients received a combination of progesterone soft capsule and dydrogesterone in group A (478 cycles), the patients received a combination of progesterone vaginal sustained-release gel and dydrogesterone in group B (1293 cycles), the patients received a combination of progesterone injection and dydrogesterone in group C (887 cycles). Pregnancy outcomes and neonatal outcomes in group A, group B and group C were compared. **Results** The clinical pregnancy rate, the 12-week pregnancy rate and the live birth rate had no significant difference among the three groups ($P>0.05$). The rates of premature delivery and twin delivery [19.90% (78/392), 30.61% (120/392)] in group C were higher than those in group B [13.61% (109/801), $P=0.011$; 20.47% (164/801), $P<0.001$]. The birth weight [(3 178.60 \pm 635.38) g] in group B was significantly higher than that in group C [(3 033.01 \pm 682.54) g, $P<0.001$]. There was no significant difference in the incidence of birth defects among the three groups ($P>0.05$). Logistic regression analysis showed that three different luteal phase support regimens were not associated with 12-week pregnancy rate. **Conclusion** In HRT-FET cycle, progesterone soft capsule or progesterone vaginal sustained-release gel combined with dydrogesterone can achieve the same pregnancy outcome as progesterone injection combined with dydrogesterone, but a large-scale prospective study is needed.

【Key words】 Luteal phase support; Frozen-thawed embryo transfer; Hormone replacement therapy; Pregnancy outcome

DOI: 10.3760/cma.j.cn101441-20200513-00276

收稿日期 2020-05-18 本文编辑 王李艳

引用本文: 王娜玉, 张娜, 吕翠婷, 等. 降调节后激素替代方案中应用生长激素对冻融胚胎移植周期结局的影响[J]. 中华生殖与避孕杂志, 2021, 41(11): 973-979. DOI: 10.3760/cma.j.cn101441-20200513-00276.

·临床研究·

降调节后激素替代方案中应用生长激素对冻融胚胎移植周期结局的影响

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【摘要】 目的 探讨冻融胚胎移植(frozen-thawed embryo transfer, FET)周期中应用生长激素是否能改善患者的妊娠结局。方法 回顾性队列研究 2015 年 1 月至 2018 年 7 月期间于河北医科大学第四医院生殖医学科行 FET 的 1042 个降调节后激素替代周期的临床资料。根据是否应用生长激素将患者分为生长激素组(A 组)和未应用生长激素组(B 组),分别比较高龄(≥ 35 岁)、多囊卵巢综合征(polycystic ovary syndrome, PCOS)、反复种植失败患者中 A、B 两组间的临床结局。结果 A 组女方年龄 $[(31.1 \pm 4.5)$ 岁]、临床妊娠率 $[67.1\% (114/170)]$ 均高于 B 组 $[(30.1 \pm 4.4)$ 岁、 $57.5\% (501/872)]$ ($P=0.010$, $P=0.020$)。高龄患者 A 组与 B 组的胚胎种植率、临床妊娠率、流产率及活产率差异均无统计学意义(P 均 >0.05)。PCOS 患者 A 组的活产率 $[65.8\% (25/38)]$ 明显高于 B 组 $[42.3\% (96/227)]$ ($P=0.007$)。反复种植失败患者 A 组的种植率 $[37.3\% (57/153)]$ 、临床妊娠率 $[50.5\% (46/91)]$ 、活产率 $[37.4\% (34/91)]$ 明显高于 B 组 $[23.0\% (115/501)$ 、 $29.1\% (92/316)$ 、 $21.8\% (69/316)]$ ($P<0.001$ 、 $P<0.001$ 、 $P=0.003$)。结论 高龄患者应用生长激素并不能改善 FET 的妊娠结局。PCOS 患者应用生长激素可有效提高活产率。反复种植失败患者应用生长激素可以明显提高种植率、临床妊娠率和活产率。

【关键词】 冻融胚胎移植; 激素替代; 生长激素; 妊娠率; 反复种植失败

Effects of growth hormone in down-regulating hormone replacement cycle on the outcome of frozen-thawed embryo transfer

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【Abstract】 Objective To analyze whether the application of growth hormone (GH) in the frozen-thawed embryo transfer (FET) cycle can improve the pregnancy outcome of patients. **Methods** The retrospective cohort study including 1042 FET cycles was carried out between January 2015 to July 2018 in Reproductive Medicine Center, the Fourth Hospital of Hebei Medical University. According to medication before transfer, all patients were divided into GH group (group A) and no GH group (group B). The pregnancy outcomes were compared between the two groups in aged patients (≥ 35 years), polycystic ovary syndrome (PCOS) patients and repeated implantation failure (RIF) patients. **Results** In group A, the maternal age $[(31.1 \pm 4.5)$ years old] and the clinical pregnancy rate $[67.1\% (114/170)]$ were higher than those in group B $[(30.1 \pm 4.4)$ years old, $57.5\% (501/872)]$ ($P=0.010$, $P=0.020$). There were no significant differences in the implantation rate, the clinical pregnancy rate, the abortion rate and the live birth rate between group A and group B in aged patients (all $P>0.05$). In PCOS patients, the live birth rate in group A $[65.8\% (25/38)]$ was significantly higher than that in group B $[42.3\% (96/227)]$ ($P=0.007$). In the RIF patients, the implantation rate $[37.3\% (57/153)]$, the clinical pregnancy rate $[50.5\% (46/91)]$ and the live birth rate $[37.4\% (34/91)]$ in group A were significantly higher than those in group B $[23.0\% (115/501)$, $29.1\% (92/316)$, 21.8%

[69/316]] ($P<0.001$, $P<0.001$, $P=0.003$). **Conclusion** For the aged patients, adding GH could not improve pregnancy outcomes. The application of GH in PCOS patients could increase the live birth rate. For the RIF patients, the application of GH could increase the implantation rate, the clinical pregnancy rate and the live birth rate.

【Key words】 Frozen-thawed embryo transfer; Hormone replacement cycle; Growth hormone; Pregnancy rate; Repeated implantation failure

DOI: 10.3760/cma.j.cn101441-20200927-00536

收稿日期 2020-09-28 本文编辑 王李艳

引用本文: 周惠玲, 刘奇才, 邹亦庐, 等. 高孕激素状态下促排卵方案中不同促性腺激素在卵巢储备低下患者促排卵效果的研究[J]. 中华生殖与避孕杂志, 2021, 41(11): 980-985. DOI: 10.3760/cma.j.cn101441-20200927-00536.

·临床研究·

高孕激素状态下促排卵方案中不同促性腺激素对卵巢储备功能低下患者促排卵效果的研究

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【摘要】 目的 探讨体外受精 (*in vitro* fertilization, IVF) 周期中卵巢储备功能低下患者高孕激素状态下促排卵 (progestin primed ovarian stimulation, PPOS) 方案使用人绝经期促性腺激素 (human menopausal gonadotropin, hMG) 与卵泡刺激素 (follicle-stimulating hormone, FSH) 的促排卵效果差异及其临床意义。方法 采用回顾性队列研究方法, 收集福建医科大学附属第一医院生殖医学中心 2018 年 11 月至 2020 年 6 月期间接受 PPOS 方案 IVF 助孕的卵巢储备功能低下患者的临床资料, 共纳入 110 个周期。根据使用促性腺激素 (gonadotropin, Gn) 制剂不同分成 FSH 组 (63 个周期) 和 hMG 组 (47 个周期), 比较两组患者的一般资料、促排卵结局及妊娠结局。结果 两组的获卵总数、M_{II} 卵子数、受精总数、卵裂总数、第 3 日总胚胎数、冷冻总胚胎数、双原核受精率、囊胚形成率、第 5 日囊胚率、卵子利用率、生化妊娠率、流产率等差异均无统计学意义 (P 均 >0.05)。而 FSH 组较 hMG 组的第 3 日优质胚胎率、临床妊娠率及胚胎种植率更高 [64.2% (111/173) 比 50.0% (48/96), $P=0.024$; 45.8% (22/48) 比 21.2% (7/33), $P=0.023$; 36.5% (27/74) 比 16.7% (8/48)],

$P=0.018$], 差异具有统计学意义。结论 对卵巢储备功能低下患者而言, PPOS 方案中使用 FSH 较 hMG 可获得更高的第 3 日优质胚胎率、临床妊娠率及胚胎种植率。

【关键词】 卵巢储备功能低下; 高孕激素状态下促排卵; 诱导排卵; 卵泡刺激素

基金项目: 福建省卫健委青年基金 (2019-1-41、2019-1-46)

Effects of different gonadotropins in progestin primed ovarian stimulation protocol on ovulation induction of patients with diminished ovarian reserve

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【Abstract】 **Objective** In order to discuss the ovulation induction effect and clinical significance of human menopausal gonadotropin (hMG) and follicle-stimulating hormone (FSH) on progestin primed ovarian stimulation (PPOS) protocol in patients with diminished ovarian reserve during *in vitro* fertilization (IVF) cycle. **Methods** Using retrospective cohort study method, the patients with diminished ovarian reserve who received PPOS in IVF assisted reproduction in the Reproductive Medicine Center of the First Affiliated Hospital of Fujian Medical University from November 2018 to June 2020 were included, 110 cycles met requirements and were divided into FSH group (63 cycles) and hMG group (47 cycles) according to the different gonadotropin (Gn) used. General information and the outcome of IVF between the two groups were compared. **Results** The total number of retrieved oocytes, MII oocytes, fertilized oocytes, cleaved oocytes, day 3 (D3) embryos, all freezing embryo, two pronucleus (2PN) fertilization rate, the blastocyst formation rate, day 5 (D5) blastocyst rate and the utilization rate of oocytes, the biochemical pregnancy rate and the miscarriage rate had no statistical differences (all $P>0.05$). The rate of D3 high-quality embryos, the clinical pregnancy rate and the embryo implantation rate of FSH group were higher than those of hMG group [64.2% (111/173) vs. 50.0% (48/96), $P=0.024$; 45.8% (22/48) vs. 21.2% (7/33), $P=0.023$; 36.5% (27/74) vs. 16.7% (8/48), $P=0.018$] with statistical significances. **Conclusion** For patients with diminished ovarian reserve, the rate of D3 high-quality embryos, the clinical pregnancy rate and the embryo implantation rate of FSH group are higher.

【Key words】 Diminished ovarian reserve; Progestin primed ovarian stimulation; Ovulation Induction; Follicle-stimulating hormone

Fund program: Youth Fund of Fujian Health Commission (2019-1-41, 2019-1-46)

DOI: 10.3760/cma.j.cn101441-20201207-00664

收稿日期 2020-12-10 本文编辑 王李艳

引用本文: 杜生荣, 杨雷, 黄志清, 等. 囊胚期胚胎嵌合发生主要影响因素分析[J]. 中华生殖与避孕杂志, 2021, 41(11): 986-990. DOI: 10.3760/cma.j.cn101441-20201207-00664.

囊胚期胚胎嵌合发生主要影响因素分析

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【摘要】 目的 分析染色体结构异常患者行卵胞质内单精子注射 (intracytoplasmic sperm injection, ICSI) 后形成的囊胚发生嵌合的主要影响因素。方法 回顾性队列研究福建省妇幼保健院生殖医学中心从 2018 年 1 月至 2019 年 12 月期间进行针对染色体结构异常的胚胎植入前遗传学检测 (preimplantation genetic testing for chromosomal structural rearrangement, PGT-SR) 周期 94 个和 ICSI 周期 551 个, 采用 SPSS21.0 软件分析女方年龄、获卵数、平均每个卵子的促性腺激素 (gonadotropin, Gn) 量 (Gn/卵)、囊胚分级, 以及不同性别染色体携带者与胚胎染色体嵌合的关系。结果 PGT-SR 周期中, 单因素分析显示嵌合体胚胎与年龄和精子浓度有关 ($P=0.01$, $P=0.04$), 而多因素 logistic 回归分析显示, 年龄 ($OR=3.41$, 95% $CI=1.34\sim8.66$, $P=0.01$)、精子浓度 ($OR=0.41$, 95% $CI=0.17\sim0.96$, $P=0.04$) 和不同性别的染色体易位携带 ($OR=2.21$, 95% $CI=1.04\sim4.70$, $P=0.04$) 是胚胎嵌合发生的主要影响因素。结论 PGT-SR 患者体外形成的囊胚发生嵌合现象可能与女方年龄、精子浓度和相互易位患者性别有关, 为选择性移植嵌合胚胎提供理论依据。

【关键词】 嵌合胚胎; 胚胎植入前遗传学检测; 高龄; 二代测序技术

基金项目: 福建省卫生计生科研人才培养项目 (2017117); 福建省妇幼保健院院内课题 (17-15)

Analysis of major factors of mosaic embryo in blastocyst stage

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【Abstract】 **Objective** To analyze of the main influecing factors of mosaic embryos during the preimplantation genetic test for chromosomal structural rearrangement (PGT-SR) to avoid the increase of risk of abortion and genetic abnormalities and to improve the diagnostic rate of mosaic embryos. **Methods** We

used a retrospective cohort study to analyze 94 cycles of infertile patients undergoing PGT-SR and 551 cycles of intracytoplasmic sperm injection (ICSI) from January 2018 to December 2019 in the Reproductive Medical Center of the Maternal and Child Health Hospital. The relationship of mosaic embryos was analyzed between the age, the number of oocytes, gonadotropin (Gn)/oocyte, the grade of blastocysts and chromosome carrier of different genders by the SPSS21.0 software. **Results** In the PGT-SR cycle, single factor analysis found that mosaic embryos were related to age and sperm concentration ($P=0.02$, $P=0.04$), but multivariate logistic regression analysis showed that age ($OR=3.41$, 95% $CI=1.34-8.66$, $P=0.01$), sperm concentration ($OR=0.41$, 95% $CI=0.17-0.96$, $P=0.04$) and chromosome carrier of different genders ($OR=2.21$, 95% $CI=1.04-4.70$, $P=0.04$) were the main factors of embryo mosaicism. **Conclusion** Female age, sperm concentration and chromosome carrier of different genders maybe affect the formation of mosaic embryos, providing theoretical basis for selective transfer of mosaic embryos.

【Key words】 Mosaic embryo; Preimplantation genetic testing; Advanced age; Next generation sequencing

Fund program: The Scientific Research Project of Health Family Planning in Fujian Province (2017-1-17); Research of Fujian Provincial Maternity and Children's Hospital (17-15)

DOI: 10.3760/cma.j.cn101441-20210628-00290

收稿日期 2021-07-21 本文编辑 孙敏

引用本文: 彭良玉, 杨菁. Galectin-1 调节子宫内膜容受性的机制研究[J]. 中华生殖与避孕杂志, 2021, 41(11): 991-1001. DOI: 10.3760/cma.j.cn101441-20210628-00290.

·实验研究·

Galectin-1 调节子宫内膜容受性的机制研究

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【摘要】 目的 探讨 Galectin-1 对子宫内膜容受性的影响以及在胚胎着床过程中所起的作用。方法 采用实时荧光定量 PCR 法、Western blotting 及细胞免疫荧光法检测 Galectin-1 在高容受性子宫内膜细胞 RL-95-2 和低容受性子宫内膜细胞 HEC-1-A 中的表达及定位情况, 通过 Transwell 实验和划痕实验检测两种细胞的侵袭和迁移能力。用 JAR 细胞模拟胚胎, 测 JAR 细胞在 RL-95-2 和 HEC-1-A 上的黏附能力。将 RL-95-2 与 HEC-1-A 分别转染 Galectin-1 siRNA 和 Galectin-1 过表达载体后, Western blotting 检测细胞中 Galectin-1 的表达水平、上皮间质转化 (epithelial-mesenchymal transition, EMT) 相关蛋白 (E-cadherin、N-cadherin 和 Vimentin 蛋白) 及 WNT/ β -catenin 信号通路相关蛋白 (β -catenin、WNT4a、WNT5a 和 WNT7a 蛋白) 的表达, 同时检测细胞的侵袭、迁移情况。将转染后的细胞分别加入 WNT 通路抑制剂 DKK1 及激活剂氯化锂 (LiCl), 检测 EMT 和 WNT 相关蛋白表达水平及细胞的侵袭、迁移情况。结果 ①RT-PCR 和 Western blotting 结果显示, Galectin-1 在 RL-95-2 中的表达量明显高于其在 HEC-1-A 中的表达 ($P=0.020$, $P=0.030$); 细胞免疫荧光实验显示, Galectin-1 主要表达于 RL-95-2 细胞质, 而在 HEC-1-A 细胞中, Galectin-1 主要表达于细胞核。②细胞黏附实验结果表明, JAR 细胞在 RL-95-2 细胞的黏附率明显高于 HEC-1-A 细胞 ($P=0.010$)。③Galectin-1 过表达后, HEC-1-A 细胞中 E-cadherin 蛋白表达量降低 ($P=0.001$), N-cadherin 和 Vimentin 蛋白表达量升高 ($P=0.003$, $P=0.023$); WNT 相关蛋白 β -catenin、WNT4a 和 WNT5a、WNT7a 蛋白表达量升高 ($P=0.025$, $P=0.004$, $P=0.005$, $P=0.001$), 细胞的迁移能力、侵袭能力明显增强 ($P=0.022$, $P=0.003$)。④DKK1 处理过表达 Galectin-1 的 HEC-1-A 细胞后, 与 DKK1 处理 HEC-1-A 细胞相比, E-cadherin 蛋白表达量降低 ($P=0.003$), N-cadherin 和 Vimentin 蛋白表达量升高 ($P=0.015$, $P=0.033$), 细胞的迁移能力以及侵袭能力均明显增加 ($P=0.030$, $P=0.040$)。⑤RL-95-2 细胞下调 Galectin-1 的表达后, E-cadherin 蛋白表达量升高 ($P=0.004$), N-cadherin 和 Vimentin 蛋白表达量明显降低 ($P=0.030$, $P=0.023$), β -catenin、WNT4a、WNT5a、WNT7a 蛋白表达量降低 ($P=0.001$, $P=0.005$, $P=0.023$, $P=0.020$)。⑥LiCl 处理下调 Galectin-1 表达的 RL-95-2 细胞后, 与 LiCl 处理 RL-95-2 细胞相比, E-cadherin 蛋白表达量增加, N-cadherin 蛋白和 Vimentin 蛋白表达量降低 ($P=0.012$, $P=0.035$, $P=0.020$); 细胞迁移率、侵袭数目降低 ($P=0.040$, $P=0.020$)。结论 与低容受性子宫内膜细胞相比, 高容受性的子宫内膜细胞中 Galectin-1 的表达水平增加; Galectin-1 可能通过 WNT/ β -catenin 信号通路调控 EMT 相关蛋白的表达, 从而影响胚胎的着床。

【关键词】 Galectin-1; 子宫内膜容受性; WNT 信号通路; 上皮间质转化相关蛋白; 滋养细胞

Effect of Galectin-1 on the function of endometrial epithelial cells with different receptivity

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【Abstract】 Objective To observe the expression of Galectin-1 in human ectopic endometrial cells with different receptivity and its role in the process of embryo implantation. **Methods** The expression and localization of Galectin-1 in high tolerance endometrial cell RL-95-2 and low tolerance endometrial cell HEC-1-A were detected by real-time quantitative PCR (RT-qPCR), Western blotting and immunofluorescence assay. The invasion and migration of the two kinds of cells were detected by Transwell assay and scratch assay. JAR cells were used to mimic embryos and to detect the migration rate. The expression levels of Galectin-1, epithelial-mesenchymal transition (EMT)-related proteins and WNT/ β -catenin signaling pathway-related proteins were analyzed by transfecting Galectin-1 siRNA and Galectin-1 overexpression vector in the RL-95-2 cells and HEC-1-A cells, respectively. Then the transfected endometrial cells were added with WNT pathway inhibitor DKK1 and activator LiCl respectively, and the changes of EMT-related proteins and the invasion, migration of cells were examined. **Results** 1) RT-qPCR and Western blotting results showed that Galectin-1 was significantly higher in RL-95-2 than in HEC-1-A ($P=0.020$, $P=0.030$); immunofluorescence experiments showed that Galectin-1 was mainly expressed in the cytoplasm of RL-95-2, while in HEC-1-A cells, Galectin-1 was mainly expressed in the nucleus. 2) The results of cell adhesion assay showed that the adhesion rate of JAR cells to RL-95-2 cells was significantly higher than that to HEC-1-A cells ($P=0.010$). 3) After Galectin-1 overexpression, the expression of E-cadherin protein was decreased in the HEC-1-A cells ($P=0.001$), and the expressions of N-cadherin and Vimentin were increased ($P=0.003$, $P=0.023$); the expressions of β -catenin, WNT4a, WNT5a, and WNT7a were increased ($P=0.025$, $P=0.004$, $P=0.005$, $P=0.001$), and the migration ability and invasion ability of HEC-1-A cells were significantly enhanced ($P=0.022$, $P=0.003$). 4) After DKK1 treatment of HEC-1-A cells overexpressing Galectin-1, E-cadherin protein expression was decreased ($P=0.003$), N-cadherin and Vimentin protein expressions were increased ($P=0.015$, $P=0.033$), and the migratory ability as well as invasive ability of HEC-1-A cells were significantly increased ($P=0.030$, $P=0.040$). 5) After down-regulation of Galectin-1 expression in RL-95-2 cells, E-cadherin protein expression was increased ($P=0.004$), N-cadherin and Vimentin protein expressions were significantly decreased ($P=0.030$, $P=0.023$), and β -catenin, WNT4a, WNT5a, and WNT7a protein expressions were reduced ($P=0.001$, $P=0.005$, $P=0.023$, $P=0.020$). 6) After LiCl treatment of RL-95-2 cells with down-regulated Galectin-1 expression, E-cadherin protein expression was increased, and N-cadherin protein and Vimentin protein expressions were decreased compared with LiCl-treated RL-95-2 cells ($P=0.012$, $P=0.035$, $P=0.020$); RL-95-2 cells migration rate, and invasion number were decreased ($P=0.040$, $P=0.020$). **Conclusion** The expression level of Galectin-1 was increased in highly receptivity endometrium compared with low receptivity endometrium. Galectin-1 may regulate the expression of EMT-related proteins through WNT/ β -catenin signaling pathway, thus affecting embryo implantation.

【Key words】 Galectin-1; Endometrial receptivity; WNT pathway; Epithelial-mesenchymal transition related-protein; Trophoblast

DOI: 10.3760/cmaj.cn101441-20201015-00564

收稿日期 2020-10-29 本文编辑 王李艳

引用本文: 杨星, 张博伦, 李满超, 等. 分娩方式对生殖道微生物组影响的机理学研究[J]. 中华生殖与避孕杂志, 2021, 41(11): 1002-1010. DOI: 10.3760/cmaj.cn101441-20201015-00564.

分娩方式对生殖道微生物组影响的机理学研究

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【摘要】 目的 评价差异表达的宫颈外口和内膜组织微生物组与女性不孕的相关性。方法 纳入 2019 年 8 月至 2019 年 12 月期间于中山大学附属第六医院生殖医学研究中心助孕治疗的 14 名继发不孕患者进行病例对照研究, 根据既往分娩方式分为剖宫产组和顺产组。剖宫产组包含 9 例剖宫产继发不孕患者, 顺产组包含同期 5 例顺产后继发不孕患者, 并分别对患者的宫颈和内膜进行采样分析。提取两组宫颈外口和内膜表面组织的总 DNA 进行 16S rRNA 分析, 并对测序结果行生物信息学分析和统计学分析。结果 通过高通量测序方法对剖宫产宫颈组、剖宫产内膜组、顺产宫颈组和顺产内膜组进行测序, 共检测到 12 种微生物群, 其中含量最高的是菌门厚壁菌, 在四组中的水平由高到低依次为顺产宫颈组、顺产内膜组、剖宫产宫颈组和剖宫产内膜组。拟杆菌门丰度在顺产组表达较高, 而变形菌门在剖宫产组表达较高。菌科水平发现 14 个优势菌群, 含量最高的菌科为乳杆菌科, 在四组中的水平由高到低依次为顺产宫颈组、顺产内膜组、剖宫产宫颈组和剖宫产内膜组。进一步分析发现 13 个优势菌属, 含量最高的菌属为乳杆菌, 在四组中的水平由高到低依次为顺产宫颈组、顺产内膜组、剖宫产宫颈组和剖宫产内膜组。结论 剖宫产和顺产分娩妇女的生殖道微生物群落组成和丰度存在差异, 剖宫产妇女的生殖道乳杆菌菌群丰度相比顺产妇女显著降低。本研究提示剖宫产后妇女不孕状态与子宫腔内乳杆菌等群落丰度的差异相关, 提示从生殖道乳杆菌菌群丰度改善角度出发, 是寻求改善不孕结局, 进而提高辅助生殖成功率的新治疗策略。

【关键词】 生殖道微生物组; 不孕症; 高通量核苷酸测序; 瘢痕子宫

Effect of delivery way on reproductive tract microbiota

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【Abstract】 Objective To evaluate the correlation between the microbial flora differences of the external cervix and endometrium and female infertility. **Methods** It was a case-control study involving 14 patients who had delivered previously and underwent assisted reproduction treatment. Patients were divided into cesarean group (9 patients) and vaginal birth group (5 patients) according to their previous delivery method, and the patients' cervix and endometrium were analyzed separately. The total DNA of the two groups origin from external cervical and endometrial tissues were extracted for 16S rRNA analysis, and the sequencing results were further analyzed by bioinformatics and statistics. **Results** External cervical and endometrial tissues from each group were sequenced by high-throughput sequencing methods. Twelve kinds of microbial flora at the level of Phylum were detected. *Firmicutes* had the highest content, and its level in each group was as follows: vaginal birth cervix group > vaginal birth endometrium group > cesarean cervix group > cesarean endometrium group. The abundance of *Bacteroidetes* was higher in vaginal birth group, while the *Proteobacteria* was higher in cesarean group. Fourteen dominant bacterial groups were found at the level of family. *Lactobacillus* had the highest content and its level among four groups was as follows: vaginal birth cervix group > vaginal birth endometrium group > cesarean cervix group > cesarean endometrium group. Further analysis found 13 dominant bacteria genera, *Lactobacillus* had the highest content, the level among the four groups was as follows: vaginal birth cervix group > vaginal birth endometrium group > cesarean cervix group > cesarean endometrium group. **Conclusion** There were differences in the composition and abundance of female reproductive tract microbiota of women after cesarean delivery and vaginal birth. The abundance of genital tract lactobacillus flora of women after cesarean section was significantly lower than that of women after vaginal birth. This study revealed that the difference in the abundance of *Lactobacillus* and other communities is related to the decreased fecundity of women who had underwent cesarean section. Exploring the methods to balance microbial community environment in the uterus could promote fecundity and assisted reproductive technology success rate in cesarean scar patients.

【 Key words 】 Female reproductive tract microbiota; Infertility; High-throughput nucleotide sequencing; Cesarean section uterus

DOI: 10.3760/cmaj.cn101441-20200615-00346

收稿日期 2020-06-19 本文编辑 王李艳

引用本文: 杨娟, 张月, 张东梅, 等. 深圳市 330 115 例孕前优生健康检查育龄女性 TORCH 筛查结果分析[J]. 中华生殖与避孕杂志, 2021, 41(11): 1011-1018. DOI: 10.3760/cmaj.cn101441-20200615-00346.

·流行病学研究·

深圳市 330 115 例孕前优生健康

检查育龄女性 TORCH 筛查结果分析

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杨娟和张月对本文有同等贡献

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【摘要】 目的 分析深圳市免费孕前优生健康检查育龄女性的 TORCH 筛查结果, 以期指导科学备孕。方法 对 2013 年 1 月至 2019 年 12 月期间参加深圳市免费孕前优生健康检查的 330 115 例育龄女性的 TORCH 筛查结果进行横断面研究, 通过 χ^2 检验分析 TORCH 筛查结果在不同年份、不同行政区域以及不同人口学特征育龄女性间的差异。结果 深圳市育龄女性风疹病毒(rubella virus, RV)-IgG、巨细胞病毒(cytomegalovirus, CMV)-IgG、CMV-IgM、刚地弓形虫(toxoplasma, TOX)-IgG、TOX-IgM 筛查总体阳性率分别为 85.54% (282 377/330 115)、96.36% (318 088/330 115)、0.31% (1009/330 115)、3.12% (10 292/330 115)、0.64% (2114/330 115), 2017 年至 2019 年较 2013 年至 2016 年育龄女性 RV-IgG、CMV-IgG 平均阳性率升高 ($P=0.003$, $P<0.001$), TOX-IgG、TOX-IgM 平均阳性率降低 ($P<0.001$)。五种抗体阳性率在不同行政区域间的差异均有统计学意义 (P 均 <0.001)。除 CMV-IgM、TOX-IgM 阳性率在不同年龄女性间的差异无统计学意义外, 五种抗体阳性率在其他人口学特征育龄女性间的差异均有统计学意义 (P 均 <0.05)。不同人口学特征女性在不同年份 TORCH 抗体阳性率的变化差异有统计学意义。结论 与 2013 年至 2016 年相比, 2017 年至 2019 年深圳市育龄女性 RV-IgG、CMV-IgG 阳性率有所升高, TOX-IgG、TOX-IgM 阳性率有所下降。五种抗体阳性率在各区之间、不同人口学特征育龄女性间存在差异, 提示在优生优育宣教时要因地制宜、因人而异地定改成订, 强化优生意识, 降低胎儿先天性宫内感染 TORCH 的风险。

【关键词】 弓形虫属； 风疹病毒； 巨细胞病毒； 孕前保健； 育龄女性

基金项目：国家重点研发计划（2016YFC1000307）；国家卫生健康委科学技术研究所所级课题（2018NRIFPJ03）

Analysis of TORCH screening results of 330 115 reproductive-age females who underwent pre-pregnancy health examination in Shenzhen

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【Abstract】 Objective To analyze the results of TORCH screening for reproductive-age females who underwent pre-pregnancy health examination in Shenzhen to guide scientific pregnancy preparation. **Methods** Cross-sectional study was performed on the TORCH screening results of 330 115 reproductive-age females who participated in free pre-pregnancy health examination in Shenzhen from January, 2013 to December, 2019. The χ^2 test was used to analyze the differences of TORCH screening results among reproductive-age females in different years, administrative regions and demographic characteristics. **Results** The overall positive rates of screening for rubella virus (RV)-IgG, cytomegalovirus (CMV)-IgG, CMV-IgM, toxoplasma gondii (TOX)-IgG and TOX-IgM among reproductive-age females in Shenzhen were 85.54% (282 377/330 115), 96.36% (318 088/330 115), 0.31% (1009/330 115), 3.12% (10 292/330 115) and 0.64% (2114/330 115), respectively. Compared with 2013 to 2016, the average positive rates of RV-IgG and CMV-IgG among reproductive-age females in Shenzhen increased ($P=0.003$, $P<0.001$), while the average positive rates of TOX-IgG and TOX-IgM decreased from 2017 to 2019 ($P<0.001$). There were statistically significant differences in the positive rates of the five antibodies among different administrative regions (all $P<0.001$). Except for the differences in the positive rates of CMV-IgM and TOX-IgM among women of different ages, there were statistically significant differences in the positive rates of these five antibodies among reproductive-age females with other demographic characteristics (all $P<0.05$). There were statistical differences in the positive rates of TORCH antibodies among women with different demographic characteristics in different years. **Conclusion** Compared with 2013 to 2016, the positive rates of RV-IgG and CMV-IgG in reproductive-age females in Shenzhen from 2017 to 2019 were on the rise, while the positive rates of TOX-IgG and TOX-IgM were on the decline. The positive rates of these five antibodies were different among different administrative regions and among reproductive-age females with different demographic characteristics, which suggested that plans should be made according to local conditions and different objects in order to

strengthen the awareness of eugenics and reduce the risk of congenital intrauterine infection with TORCH of the fetus during the propaganda and education of eugenics.

【Key words】 Toxoplasma; Rubella virus; Cytomegalovirus; Preconception care; Reproductive-age females

Fund program: National Key Research and Development Program of China (2016YFC1000307); Project of National Research Institute for Family Planning (2018NRIFPJ03)

DOI: 10.3760/cmaj.cn101441-20210623-00279

收稿日期 2021-07-22 本文编辑 孙敏

引用本文: 杜超, 于月新, 侯开波, 等. 新型冠状病毒肺炎疫情后辅助生殖患者心理压力调查分析[J]. 中华生殖与避孕杂志, 2021, 41(11): 1019-1025. DOI: 10.3760/cmaj.cn101441-20210623-00279.

·现场调查·

新型冠状病毒肺炎疫情后辅助生殖患者心理压力调查分析

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【摘要】 目的 利用中文版压力知觉量表 (Chinese perceived stress scale, CPSS) 调查新冠疫情过后不孕患者的心理压力并分析其相关因素。方法 利用问卷调查的方式搜集 2021 年 3 月 29 日至 2021 年 4 月 29 日期间于北部战区总医院行辅助生殖患者的基本情况、生育史、受疫情影响情况、心理现状等信息, 根据 CPSS, 采用组间比较和相关性分析探讨可能与患者心理压力相关的因素。结果 共收到有效问卷 251 份, 患者 CPSS 评分为 22.43 ± 7.07 , 疫情期间约 33.86% (85/251) 的不孕患者推迟了助孕计划, 81.27% (204/251) 的人表示不清楚注射新冠疫苗对后代是否有影响。不同性别、职业和在不同助孕阶段推迟助孕计划的患者间的心理压力差异具有统计学意义 ($P=0.001$, $P=0.005$, $P=0.002$), 是否推迟助孕计划的患者间心理压力差异无统计学意义 ($P>0.05$); 相关性分析显示, 患者心理压力大小与其年龄、收入、因疫情推迟的时间呈负相关 ($r=-0.192$, $P=0.002$; $r=-0.323$, $P<0.001$; $r=-0.282$, $P=0.009$)。结论 新冠肺炎疫情对于不孕夫妇的心理压力造成了一定影响, 针对不孕患者的心理护理尤为重要。为了消除不孕患者对于疫苗的疑虑, 治疗过程中应注意正确的新冠疫苗科普宣传。

【关键词】 COVID-19; 压力知觉量表; 辅助生殖; 疫苗

基金项目: 军委后勤保障部计生专项课题 (19JSZ12)

Investigation and analysis of psychological stress of assisted reproduction patients after COVID-19 epidemic

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【Abstract】 Objective To analyze the psychological stress of infertile patients after COVID-19 epidemic and its related factors by Chinese version of the perceived stress scale (CPSS). **Method** The basic information, reproductive history, impact of the epidemic, psychological status of patients undergoing assisted reproductive technology at the General Hospital of Northern Theater Command from March 29, 2021 to April 29, 2021 were collected by questionnaire. According to CPSS, group comparison and correlation analysis were used to explore factors related to patients' psychological stress. **Results** A total of 251 valid questionnaires were received. The average CPSS score of the patients was 22.43 ± 7.07 . During the epidemic, about 33.86% (85/251) of the infertility patients postponed the fertilization plan; there were significant differences in the psychological stress among patients of different genders, occupations, and postponed fertilization plans at different stages of fertilization ($P=0.001$, $P=0.005$, $P=0.002$). There was no significant difference in CPSS score between infertile patients who delayed treatment or not ($P>0.05$). Correlation analysis showed that the perceived stress of patients was negatively correlated with their age, income, and delay duration ($r=-0.192$, $P=0.002$; $r=-0.323$, $P=0.001$; $r=-0.282$, $P=0.009$). Among all patients who delayed treatment, patients with higher CPSS score would restart treatment sooner; most of the infertile patients knew little about the vaccine. **Conclusion** The COVID-19 epidemic has caused a certain impact on the psychological pressure of infertile couples who accepted treatment in our hospital. The psychological care for infertile patients is particularly important. In the future, in order to dispel the doubts of infertile patients about the vaccine, we should pay attention to the correct scientific promotion of the COVID-19 vaccine during the treatment process.

【Key words】 COVID-19; Chinese version of the perceived stress scale; Assisted reproduction; Vaccine

Fund program: Family Planning Project of the Logistics Support Department of the Military Commission (19JSZ12)

DOI: 10.3760/cmaj.cn101441-20210719-00312

收稿日期 2021-07-20 责任编辑 宋培培

引用本文: 孙宁霞, 李紫袁, 庞文娟, 等. 中国首例卵巢组织冷冻移植活产两年随访[J]. 中华生殖与避孕杂志, 2021, 41(11): 1026-1030. DOI: 10.3760/cmaj.cn101441-20210719-00312.

·个案报道·

中国首例卵巢组织冷冻移植活产 2 年随访

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【摘要】 目的 探讨卵泡体外激活 (*in vitro* activation, IVA) 联合冷冻卵巢组织移植技术在治疗早发性卵巢功能不全 (premature ovarian insufficiency, POI) 中的安全性及有效性。方法 对 1 例 POI 患者进行 IVA 联合冷冻卵巢组织移植, 并对该患者的诊疗过程进行详细报道以及随访分析。结果 该 POI 患者通过 IVA 联合冷冻卵巢组织移植术后成功自然妊娠, 产下健康婴儿, 成为中国首例卵巢组织冷冻后移植活产, 目前随访 2 年, 小儿体格发育、运动、精神神经发育正常。结论 卵巢组织冷冻移植联合 IVA 技术有助于激活 POI 患者的残余卵泡, 使 POI 患者得以孕育自己的遗传后代。提示 IVA 技术可能成为 POI 患者生育治疗的新选择。

【关键词】 冷冻保存; 早发性卵巢功能不全; 生育力保存; 体外激活; 卵巢组织移植

基金项目: 国家自然科学基金面上项目 (82071605); 宁夏重点研发计划 (2018YBZD1540); 上海卫计委面上项目 (201840315); 上海市科委医学引导项目 (19411960700)

Live birth after transplantation of cryopreserved ovarian tissue with two-year follow-up: report of the first Chinese case

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【Abstract】 Objective To investigate the safety and efficacy of *in vitro* activation (IVA) following cryopreserved ovarian tissue autotransplantation in the treatment of patients with premature ovarian insufficiency (POI). **Methods** We reported and reviewed the treatment and follow-up of a patient with POI, who underwent IVA combined with cryopreserved ovarian tissue transplantation. **Results** The patient naturally conceived and delivered a healthy baby boy, who became the first live birth after cryopreserved ovarian tissue transplantation in China. The baby showed normal physical, motor and mental development during two-year follow-up. **Conclusion** IVA combined with cryopreserved ovarian tissue transplantation can effectively activate residual follicles in some POI patients and allow them to conceive their own genetic offspring. IVA technology may become a new choice for fertility treatment of POI patients.

【Key words】 Cryopreservation; Premature ovarian insufficiency; Fertility preservation; *In vitro* activation; Ovarian tissue transplantation

Fund program: Surface Program of National Natural Science Foundation of China (82071605); Ningxia Key R & D Plan (2018YBZD1540); General Projects of Shanghai Health and Family Planning Commission (201840315); Medical Guidance Project of Shanghai Science and Technology Commission (19411960700)

DOI: 10.3760/cma.j.cn101441-20200901-00471

收稿日期 2020-09-04 本文编辑 宋培培

引用本文: 栾旭, 芦小单, 米旭光, 等. 干细胞治疗早发性卵巢功能不全的研究进展[J]. 中华生殖与避孕杂志, 2021, 41(11): 1031-1035. DOI: 10.3760/cma.j.cn101441-20200901-00471.

·综述·

干细胞治疗早发性卵巢功能不全的研究进展

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【摘要】 早发性卵巢功能不全已成为困扰育龄妇女的主要问题, 到目前为止, 尚无有效的治疗方法。干细胞具有自我更新和多向分化潜能, 越来越被考虑用于卵巢功能不全的治疗。从骨髓、脐带、外周血和羊水中提取的干细胞可以迁移到卵巢并增殖, 在特定的卵巢环境下分化成熟, 分泌相关因子, 促进卵巢功能修复, 增加卵巢各级卵泡质量和颗粒细胞的数量, 改善内分泌功能, 在一定程度上恢复生育能力。本文就各类干细胞治疗早发性卵巢功能不全的相关研究进展进行综述。

【关键词】 早发性卵巢功能不全; 干细胞; 颗粒细胞

基金项目: 吉林省科技厅项目 (20180201028YY、20200403081SF、20200801019GH、20200404125YY); 吉林省人才开发资金 (2019026)

Stem cell therapy in the treatment of premature ovarian failure

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【Abstract】 Premature ovarian insufficiency has become a major problem that plagues women of childbearing age. So far, there is no effective treatment method. Stem cells have the potential for self-renewal and multidirectional differentiation, and are increasingly being considered for the treatment of ovarian insufficiency. Stem cells extracted from bone marrow, umbilical cord, peripheral blood, and amniotic fluid can migrate to the ovary and proliferate, differentiate and mature in a specific ovarian environment, secrete related factors, promote ovarian function repair, and increase the quality of ovarian follicles and the number of granulosa cells at all levels. Improve endocrine function and restore fertility to a certain extent. This article reviews the research progress of various types of stem cells in the treatment of premature ovarian insufficiency.

【Key words】 Premature ovarian insufficiency; Stem cells; Granulosa cells

Fund program: Jilin Province Science and Technology Department Project (20180201028YY, 20200403081SF, 20200801019GH, 20200404125YY); Talent Development Fund of Jilin Province(2019026)

·综述·

DOI: 10.3760/cma.j.cn101441-20201114-00619

收稿日期 2020-11-23 本文编辑 孙敏

引用本文: 宫炳琛, 王敬婉, 李静, 等. 辅助生殖技术中导致子代出生性别差异的相关因素研究进展[J]. 中华生殖与避孕杂志, 2021, 41(11): 1036-1040. DOI: 10.3760/cma.j.cn101441-20201114-00619.

辅助生殖技术中导致子代出生性别差异的相关因素研究进展

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【摘要】 随着辅助生殖技术(assisted reproductive technology, ART)的发展,越来越多的不孕症夫妇拥有了自己的孩子。据不完全统计,截止到2010年,全球大约有500万婴儿经过ART治疗后出生。ART是否会对子代出生性别产

生影响，会产生何种影响，至今尚不明确。而随着 ART 新生儿数量的增加，未来可能会对人口构成产生深远影响。目前已知的可能影响 ART 新生儿性别比的因素有：双亲年龄、授精方式、胚胎移植阶段（卵裂期/囊胚期）、移植胚胎类型（新鲜胚胎/冷冻胚胎）等，本文拟就目前已知可能影响 ART 新生儿性别比的因素展开综述。

【关键词】 生殖技术，辅助； 性别比； 影响因素

基金项目：国家自然科学基金（81701404）

Advances in research on the related factors leading to sex ratio difference at birth of offspring in assisted reproductive technology

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【Abstract】 With the development of assisted reproductive technology (ART), more and more infertile couples have their own children. According to incomplete statistics, as of 2010, about 5 million babies worldwide were born after treatment with ART. It is not clear whether and how ART affects the sex of offspring at birth. And with the increase of the number of ART newborns, it may have a profound impact on the demographics in the future. At present, the known factors that may affect the sex ratio of newborns with ART include parental age, type of infertility, embryo transfer stage (cleavage stage/blastocyst stage), embryo transfer type (fresh embryo/frozen embryo), etc. This paper aims to review the factors that may affect the sex ratio of newborns with ART at present.

【Key words】 Reproductive technology, assisted; Sex ratio; Influencing factors

Fund program: National Natural Science Foundation of China (81701404)

·综述·

DOI: 10.3760/cmaj.cn101441-20200510-00273

收稿日期 2020-05-13 本文编辑 宋培培

引用本文：车嘉慧，陆鹏荣，赵婷. 子宫腺肌病的无创及微创诊断方法[J]. 中华生殖与避孕杂志, 2021, 41(11): 1041-1044. DOI: 10.3760/cmaj.cn101441-20200510-00273.

子宫腺肌病的无创及微创诊断方法

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【摘要】 子宫腺肌病是一种良性子宫疾病，是痛经和异常子宫出血的常见原因。近年来研究表明，经阴道超声因与核磁共振的敏感度和特异度相当，成为诊断子宫腺肌病的一线方法，但其诊断标准及流程迄今尚未规范。国际子宫形态学超声评估小组提出了子宫腺肌病超声下特征术语及标准化报告系统，具有较高的临床指导价值。弹性超声技术的发展，为超声下评估子宫腺肌病提供了新的手段。核磁共振、腹腔镜检查和宫腔镜检查也是诊断子宫腺肌病的备选方法。此外，超声引导下的子宫取样技术、腹腔镜及宫腔镜下子宫取样技术使在不切除子宫的情况下获得组织病理学诊断成为可能。上述检查手段为无创或微创诊断及评估子宫腺肌病提供了多种解决方案。应用上述方法诊断子宫腺肌病可规范诊断流程、提高检出率，因此具有重要的临床意义。本文拟对子宫腺肌病的无创及微创诊断及最新进展进行综述。

【关键词】 子宫腺肌病； 超声检查； 核磁共振； 腹腔镜； 宫腔镜

Non-invasive and minimally invasive diagnosis of adenomyosis

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【Abstract】 Adenomyosis is a benign uterine disease, which is a common cause of dysmenorrhea and abnormal uterine bleeding. In recent years, studies have shown that transvaginal ultrasound has the same sensitivity and specificity as magnetic resonance imaging (MRI), and it is a first-line method for the diagnosis of adenomyosis, but its diagnostic criteria and procedures have not yet been standardized. The team of Morphological Uterus Sonographic Assessment (MUSA) has put forward the ultrasonic characteristic terms and standardized reporting system of adenomyosis, which has high clinical guidance value. The development of elastic ultrasound technology provides a new method for ultrasound evaluation of adenomyosis. MRI, laparoscopy and hysteroscopy are also options for the diagnosis of adenomyosis. In addition, ultrasound-guided uterine sampling techniques, laparoscopic and hysteroscopic uterine sampling techniques make it possible to obtain histopathological diagnosis without hysterectomy. The above examination methods provide a variety of solutions for non-invasive or minimally invasive diagnosis and evaluation of adenomyosis. The application of the above methods in the diagnosis of adenomyosis can standardize the diagnosis process and improve the detection rate, so it has an important clinical significance. This article will review the current methods of non-invasive and minimally invasive diagnosis of adenomyosis.

【Key words】 Adenomyosis; Ultrasonography; Magnetic resonance imaging; Hysteroscopy; Laparoscopy

DOI: 10.3760/cma.j.cn101441-20200525-00307

收稿日期 2020-07-01 本文编辑 李天琦

引用本文: 张雅梦, 王建业, 周平, 等. 原始卵泡体外激活技术的研究进展[J]. 中华生殖与避孕杂志, 2021, 41(11): 1045-1051. DOI: 10.3760/cma.j.cn101441-20200525-00307.

·综述·

原始卵泡体外激活技术的研究进展

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【摘要】 体外激活 (*in vitro* activation, IVA) 技术是指 IVA 原始卵泡, 使其生长至可接受激素刺激的阶段, 结合促排卵获得成熟卵泡的技术, 最终通过体外受精-胚胎移植 (*in vitro* fertilization and embryo transfer, IVF-ET) 技术达到受孕目的。常用方法为激活 PI3K/Akt 信号通路和阻断 Hippo 信号通路。随着研究深入, 新的激活方法逐渐发展。现已有多例早发性卵巢功能不全 (primary ovarian insufficiency, POI) 患者应用 IVA 技术成功妊娠的案例报道, 结合生育力保存技术, 卵巢低反应 (poor ovarian response, POR) 以及女性恶性肿瘤患者都可能受益于 IVA 技术。然而 IVA 技术尚不完善, 仍在临床成功率、安全性等方面存在问题, 需要在机制和临床应用继续探索。本文针对 IVA 技术的机制、临床应用情况以及发展方向方面进行论述, 为 IVA 的研究和临床应用提供参考。

【关键词】 原始卵泡; 体外激活; 卵巢功能不全; 生育力保存

基金项目: 国家重点研发计划 (2017YFC1002004); 中国医学科学院中央级公益性科研院所基本科研业务费专项资金 (2019PT310002)

Research progress of primordial follicle activation technology *in vitro*

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【Abstract】 *In vitro* activation (IVA) technology refers to the process of activating primordial follicles to grow to a stage that can be stimulated by hormones *in vitro*, combined with the technology of controlled ovarian hyperstimulation to obtain mature follicles, and finally achieve the purpose of conception through *in vitro* fertilization and embryo transfer (IVF-ET) technology. The common methods are activating the PI3K/Akt pathway and disrupting the Hippo pathway. With the

deepening of research, new activation methods have gradually developed. Multiple cases of successful pregnancy with IVA technology have been reported in patients with primary ovarian insufficiency (POI). Combining with fertility preservation technology, patients with poor ovarian response (POR) and female malignant tumors may all benefit from IVA technology. However, the IVA technology is not perfect, and there are still problems in clinical success rate, safety and other aspects, and it is necessary to continue to explore the mechanism and clinical application. In this paper, the mechanism, clinical application and development direction of IVA technology were discussed, so as to provide reference for the research and clinical application of IVA.

【 Key words 】 Primordial follicle; *In vitro* activation; Primary ovarian insufficiency; Fertility preservation

Fund program: National Key Technology Research & Development Program of China (2017YFC1002004); The Non-profit Central Research Institute Fund of Chinese Academy of Medical Sciences (2019PT310002)