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编 辑

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

总编辑

乔 杰

编辑部主任

王黎茜

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Editorial Board of Chinese Journal of Reproduction and Contraception

779 Laohumin Road, Shanghai 200237, China

Tel: 0086-21-64438169
Fax: 0086-21-64438975
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Editor-in-Chief

Qiao Jie

Managing Director

Wang Lixi

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不全流产保守治疗专家共识

中华医学会计划生育学分会

通信作者：顾向应，Email: gxy6283@163.com，电话：+86-18622186957

【摘要】 不全流产为流产常见并发症，其治疗手段主要包括清宫术、药物保守治疗和期待治疗，其中清宫术有效率较高，但仍为一种有创操作，可能对患者身心造成一定的创伤。近年研究显示：药物治疗不全流产尤其是宫腔内残留物较小时（直径 ≤ 2.5 cm），疗效较明显，依从性好，不仅减少清宫术相关的手术并发症，并且可增加患者满意度，但我国目前尚缺乏明确的指南或共识。为了进一步指导和规范药物保守治疗及期待疗法在不全流产中的应用，中华医学会计划生育学分会专家根据国内外的研究进展，结合我国的实际情况，针对药物保守治疗不全流产的适应证、禁忌证、用药剂量、疗程、监测指标、注意事项等各方面及期待疗法的适应证进行了充分讨论，并制定了本共识，为临床医疗工作提供指导建议。

【关键词】 不全流产；米索前列醇；卡前列甲酯栓；米非司酮；期待疗法

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· 标准与规范 ·

Expert consensus on conservative treatment of incomplete abortion

Family Planning Branch of the Chinese Medical Association

Corresponding author: Gu Xiangying, Email: gxy6283@163.com, Tel: +86-18622186957

【Abstract】 Incomplete abortion is a common complication of abortion, and its treatment methods mainly include curettage, expectant treatment and conservative treatment of drugs. The effective rate of uterine curettage is higher, but it may create a certain imitation on the body and mind of patients as an invasive operation. It has shown that medication for incomplete abortion is especially effective. When the intrauterine remnants are small (diameter ≤ 2.5 cm), its curative effect is obvious and the compliance is good. It not only reduces the complications of uterine curettage, but also increases the satisfaction of patients. However, there is no clear guidance or consensus. In order to further guide and standardize the application of drug conservative therapy and expectant therapy in incomplete abortion, based on the research progress at home and abroad and combining with the actual situation of our country, experts of the Chinese Medical Accounting Family Planning Society has mainly discussed about the indications, contraindications, dosage, course of treatment, monitoring, precautions and other aspects of conservative treatment of incomplete abortion with drugs and has drawn up the consensus to provide some guidance and suggestions for clinical medical work.

【Key words】 Incomplete abortion; Misoprostol; Carboprost methylate suppositories; Mifepristone; Expectant therapy

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超生理剂量雌激素是新鲜胚胎移植单胎子代小于胎龄儿及低出生体质量的危险因素

张俊韦 孙丽君 杜明泽 李哲 王璐璐 胡继君 赵贝 冯莹莹

郑州大学第三附属医院生殖医学中心 450052

通信作者: 孙丽君, Email: docslj@163.com, 电话: +86-13253528099

【摘要】 目的 探讨人绒毛膜促性腺激素 (hCG) 注射日超生理剂量的血清雌二醇水平与小于胎龄儿 (small for gestational age, SGA) 及低出生体质量 (low birth weight, LBW) 的关系。方法 回顾性队列分析 2008 年 7 月—2017 年 7 月期间在郑州大学第三附属医院生殖医学中心行新鲜胚胎移植的卵巢反应正常并分娩单胎的年轻患者作为研究对象。根据 hCG 注射日血清雌二醇水平分组, A 组: 雌二醇 ≤ 2000 ng/L; B 组: 雌二醇 2001~3000 ng/L; C 组: 雌二醇 3001~4000 ng/L; D 组: 雌二醇 4001~5000 ng/L; E 组: 雌二醇 5001~6000 ng/L; F 组: 雌二醇 >6000 ng/L, 分析 6 组患者基础资料、临床及实验室数据, 并以 A 组为参照组, 分别计算其余各组 SGA、LBW、极低出生体质量 (very low birth weight, VLBW)、足月 LBW、早产 (preterm birth, PT) 的比值比 (odds ratio, OR) 及 95% 置信区间 (confidence interval, CI), 并采用多因素逻辑回归, 校正混杂因素 [年龄、产次、体质量指数 (body mass index, BMI)、不孕时间、不孕类型、不孕原因、hCG 注射日子宫内膜厚度、助孕方式、移植胚胎阶段、移植胚胎个数、新生儿性别], 比较不同组间上述观察指标校正后的 OR 值 (adjusted odds ratio, aOR)。结果 与 A 组相比, D 组、E 组、F 组的 SGA、LBW、足月 LBW 的发生率明显增加, 差异均有统计学意义 ($P < 0.001$)。然而 VLBW、PT 的发生率随雌二醇水平的增长无明显变化 ($P = 0.70$; $P = 0.85$)。经多因素逻辑回归分析校正混杂因素后, 雌二醇 ≥ 4001 ng/L 是 SGA (D 组 aOR=1.69, 95% CI=1.03~2.75, $P = 0.04$; E 组 aOR=1.94, 95% CI=1.12~3.36, $P = 0.02$; F 组 aOR=2.31, 95% CI=1.38~3.87, $P < 0.001$)、LBW (D 组 aOR=1.95, 95% CI=1.11~3.44, $P = 0.02$; E 组 aOR=2.57, 95% CI=1.38~4.78, $P < 0.001$; F 组 aOR=3.36, 95% CI=1.89~5.98, $P < 0.010$)、足月 LBW (D 组 aOR=5.36, 95% CI=2.00~14.37, $P < 0.001$; E 组 aOR=7.35, 95% CI=2.64~20.49, $P < 0.001$; F 组 aOR=12.02, 95% CI=4.55~31.78, $P < 0.001$) 的独立危险因素。同时, BMI 与 SGA 的发生率相关, 即 BMI 较低的患者分娩 SGA 子代风险更大 (aOR=0.88, 95% CI=0.83~0.90, $P < 0.001$)。结论 超生理剂量的雌二醇是新鲜胚胎移植单胎子代 SGA、LBW 及足月 LBW 的独立危险因素。

【关键词】 雌激素; 小于胎龄儿; 新鲜胚胎移植; 低出生体质量

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Supraphysiological estradiol level is a risk factor of small for gestational age and low birth weight of fresh embryo transfer

Zhang Junwei, Sun Lijun, Du Mingze, Li Zhe, Wang Lulu, Hu Jijun, Zhao Bei, Feng Yingying

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

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

【Abstract】 Objective To investigate the relationship between supraphysiologic estradiol levels on the human chorionic gonadotropin (hCG) injection day and small for gestational age (SGA) and low birth weight (LBW). **Methods** It was a retrospective cohort study. Patients with singleton pregnancies with delivered after transfer of fresh embryos during the period of July 2008 to July 2017 at the Reproductive Center of the Third Affiliated Hospital of Zhengzhou University were included. According to the serum estradiol level on the day of hCG trigger, we divided all patients into 6 groups. Group A: estradiol \leq 2000 ng/L (referent group), group B: estradiol 2001–3000 ng/L, group C: estradiol 3001–4000 ng/L, group D: estradiol 4001–5000 ng/L, group E: estradiol 5001–6000 ng/L, group F: estradiol >6000 ng/L. The outcome measures were SGA, LBW, very low birth weight (VLBW), preterm birth (PT) and full-term LBW. We compared the odds ratio (OR) of SGA, LBW, VLBW, PT and full-term LBW among the groups. Then multivariable logistic regression [age, parity, body mass index (BMI), infertility time, type of infertility, cause of infertility, endometrial thickness of hCG injection day, mode of assisted pregnancy, stage of embryo transfer, the number of transplanted embryos, the sex of the newborn] was used to analyze whether these outcome measures could be explained by the estradiol level on the hCG trigger day. **Results** Compared with group A, the incidence of SGA, LBW and term LBW in group D, group E and group F increased significantly. However, the incidence of VLBW and PT did not change significantly with the increase of estradiol levels ($P=0.70$, $P=0.85$). After adjusting for confounding factors by logistic regression analysis, estradiol \geq 4001 ng/L was an independent risk factor for SGA (group D: $aOR=1.69$, 95% $CI=1.03-2.75$, $P=0.04$; group E: $aOR=1.94$, 95% $CI=1.12-3.36$, $P=0.02$; group F: $aOR=2.31$, 95% $CI=1.38-3.87$, $P<0.001$), LBW (group D: $aOR=1.95$, 95% $CI=1.11-3.44$, $P=0.02$; group E: $aOR=2.57$, 95% $CI=1.38-4.78$, $P<0.001$; group F: $aOR=3.36$, 95% $CI=1.89-5.98$, $P<0.001$), and full-term LBW (group D: $aOR=5.36$, 95% $CI=2.00-14.37$, $P<0.001$; group E: $aOR=7.35$, 95% $CI=2.64-20.49$, $P<0.001$; group F: $aOR=12.02$, 95% $CI=4.55-31.78$, $P<0.001$). At the same time, we also found that BMI was associated with the incidence of SGA, patients with lower BMI had a higher risk of SGA ($aOR=0.88$, 95% $CI=0.83-0.90$, $P<0.001$). **Conclusion** Supraphysiologic serum estradiol level was an independent risk factor for SGA, LBW and full-term LBW birth of fresh embryo transfer.

【Key words】 Estradiol; Small for gestational age; Fresh embryo transfer; Low birth weight

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体质量指数对新鲜及首次冻融胚胎移植周期临床结局的影响

金海霞 吕爱香 宋文妍 李刚 戴善军 孙莹璞

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

通信作者: 金海霞, Email: jhxgl@126.com, 电话: +86-13523488589

【摘要】目的 探讨体质量指数 (BMI) 对女性行体外受精 / 卵胞质内单精子显微注射 - 胚胎移植 (IVF/ICSI-ET) 治疗的新鲜及首次冻融胚胎移植临床结局的影响。**方法** 回顾性分析 2011 年 1 月—2016 年 12 月期间在郑州大学第一附属医院生殖医学中心就诊的 <35 岁首次行 IVF/ICSI 治疗后的患者临床资料, 分为新鲜周期和冻融周期, 并按照 BMI 分为低体质量组 (BMI<18.5 kg/m²)、正常体质量组 (18.5~23.9 kg/m²) 和超重组 (BMI ≥ 24 kg/m²)。比较新鲜周期及冻融周期不同 BMI 组的妊娠结局。**结果** ①新鲜周期中, 超重组不孕年限、基础内分泌、促性腺激素 (Gn) 用量及获卵数高于其他两组; 超重组患者活产率 (48.86%) 明显低于正常体质量组 (51.93%)($P=0.007$), 而流产率 (14.36%) 明显高于正常体质量组 (11.61%)($P=0.005$)。单胎分娩周期中随 BMI 增高巨大儿比例逐渐增高 (低体质量组比正常体质量组 $P=0.02$, 正常体质量组比超重组 $P=0.001$, 低体质量组比超重组 $P<0.001$)。双胎分娩周期中分娩低出生体质量儿的比例随 BMI 增高呈下降趋势 ($P=0.009$)。②解冻周期中, 不同 BMI 组间基础黄体生成素 (LH)、移植日内膜厚度、活产率也随 BMI 的增高而降低 ($P=0.015$, $P<0.001$, $P<0.001$)。解冻移植单胎分娩周期中随 BMI 增高分娩巨大儿比例明显增高 (低体质量组比正常体质量组 $P=0.01$, 正常体质量组比超重组 $P=0.02$, 低体质量组比超重组 $P<0.001$)。双胎分娩周期中超重组孕周相比正常体质量组出生孕周明显缩短 ($P<0.001$)。③在各 BMI 组中新鲜周期平均移植胚胎数低于解冻周期 ($P<0.001$), 而胚胎种植率、临床妊娠率及活产率高于解冻周期 (P 均 <0.001)。此外, 正常体质量组患者新鲜周期流产率 (11.61%) 低于解冻周期 (16.10%)($P<0.001$)。单胎分娩者中正常体质量组新鲜周期的早产率 (4.24%)、巨大儿 (7.23%) 及低出生体质量儿比例 (2.55%) 低于解冻周期 (7.52%, 9.47%, 4.38%; $P<0.001$, $P=0.05$, $P=0.01$)。各组 BMI 组新鲜周期双胎出生孕周 ($P<0.001$, $P=0.007$, $P<0.001$) 及低出生体质量儿比例 ($P=0.01$, $P<0.001$, $P=0.01$) 均高于解冻周期。平均出生体质量在低体质量组新鲜周期高于解冻周期组 ($P=0.016$), 而正常体质量组新鲜周期出生体质量低于解冻周期组 ($P=0.031$)。**结论** 育龄女性高 BMI 将导致 Gn 用量增加且会对妊娠结局产生不利影响。对于高 BMI 患者, 建议患者积极减重后再进行助孕治疗。行冻融胚胎移植并不能明显改善妊娠结局, 且会增加患者的经济和时间成本; 在行 IVF 助孕患者无其他并发症的情况下, 建议尽量行新鲜周期移植。

【关键词】 体质量指数; 胚胎移植; 肥胖症; 妊娠结局

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Effect of body mass index on clinical outcomes of the first fresh and frozen-thawed embryo transfer cycle

Jin Haixia, Lyu Aixiang, Song Wenyan, Li Gang, Dai Shanjun, Sun Yingpu

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

Corresponding author: Jin Haixia, Email: jhxgl@126.com, Tel: +86-13523488589

【Abstract】 Objective To investigate the effect of body mass index (BMI) on the clinical outcomes of fresh and frozen-thawed embryo transfer in women undergoing *in vitro* fertilization/intracytoplasmic sperm injection-embryo transfer (IVF/ICSI-ET) cycles. **Methods** A retrospective analysis was performed at the Center for Reproductive Medicine of the First Affiliated Hospital of Zhengzhou University. The patients who were <35 years and underwent IVF/ICSI treatment were treated with fresh/frozen-thawed embryo transfer for the first time. Patients were divided into low body mass group (BMI<18.5 kg/m²), normal body mass group (18.5–23.9 kg/m²), high body mass group (BMI ≥ 24 kg/m²). The basic conditions of fresh cycles in each group and frozen-thawed cycle pregnancy outcomes were compared. **Results** 1) The period of infertility, basal endocrine level, gonadotropin (Gn) used dosage and the number of oocytes obtained from the high body mass group were higher than those from the other two groups. Compared with the normal body mass group, the live birth rate (51.93% vs. 48.86%, $P=0.007$) significantly decreased in the high body mass group, while the abortion rate (14.36% vs. 11.61%, $P=0.005$) significantly increased. The proportion of macrosomia increased gradually with the increase of BMI in single birth cycle (low body mass group vs. normal body mass group $P=0.02$, normal body mass group vs. high body mass group $P<0.001$, low body mass group vs. high body mass group $P<0.001$). The proportion of low birth weight births in twin delivery cycle decreased with the increase of BMI ($P=0.009$). 2) During thawing cycles, basal luteinizing hormone (LH), endometrial thickness and live birth rate decreased with the increase of BMI in different BMI groups ($P=0.015$, $P<0.001$, $P<0.001$). The proportion of macrosomia was significantly increased with the increase of BMI in the single birth cycle of frozen-thawed cycles (low body mass group vs. normal body mass group $P=0.01$, normal body mass group vs. high body mass group $P=0.02$, low body mass group vs. high body mass group $P<0.001$). Compared with normal body mass group, the gestational weeks of high body mass group in twin birth cycle were significantly shorter ($P<0.001$). 3) In each BMI group, the average number of embryos transferred in fresh cycles was lower than that in frozen-thawed cycles ($P<0.001$), while the embryo implantation rate, clinical pregnancy rate and live birth rate were higher than those in frozen-thawed cycles ($P<0.001$). In addition, the fresh cycle abortion rate (11.61%) in normal body mass group was lower than that in frozen-thawed cycle (16.10%, $P<0.001$). Premature birth rate (4.24%), macrosomia (7.23%) and low birth weight (2.55%) in normal birth weight group were lower than those in frozen-thawed cycle (7.52%, 9.47%, 4.38%; $P<0.001$, $P=0.05$, $P=0.01$). The freshly born gestational weeks and the proportion of low birth weight infants in each BMI group were higher than those in frozen-thawed cycle ($P<0.001$, $P=0.007$, $P<0.001$; $P<0.001$, $P=0.0048$, $P=0.01$). The average birth weight in the low body mass group was higher than that in frozen-thawed cycle ($P=0.016$), while that in the normal body mass group was lower than that in frozen-thawed cycle ($P=0.031$). **Conclusion** High BMI in women increases the dosage of Gn used in IVF-ET therapy and may have an adverse effect on oocyte quality and endometrial receptivity. For patients with high BMI, even though the embryo is frozen, clinical pregnancy outcomes cannot be improved. Fresh embryo transfer should be recommended when the patients undergo IVF without other complications.

【Key words】 Body mass index; Embryo transfer; Obesity; Clinical outcome

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卵泡抑素表达水平与子宫内膜异位症患者体外受精 - 胚胎移植结局预后相关性分析

张群芳 刘芸 陈国勇 何凌云

中国人民解放军联勤保障部队第九〇〇医院妇产科生殖中心, 福建医科大学福总临床医学院, 福建中医药大学教学医院, 厦门大学附属东方医院, 福州 350025

通信作者: 刘芸, Email: liuyunfj@126.com, 电话: +86-591-22859476

【摘要】目的 研究子宫内膜异位症 (EMS) 患者卵泡液和血清中卵泡抑素 (follistatin, FS) 表达水平与体外受精 - 胚胎移植 (IVF-ET) 妊娠结局的相关性, 探讨 EMS 患者 IVF 治疗时血清 FS 与卵泡液 FS 对妊娠结局的预测价值。**方法** 回顾性分析 2017 年 1 月—2017 年 6 月期间于中国人民解放军联勤保障部队第九〇〇医院妇产科生殖中心行 IVF-ET 治疗的 EMS 患者 (A 组, 84 例) 和输卵管因素不孕患者 (B 组, 80 例) 妊娠结局, 酶联免疫吸附法 (ELISA) 检测 FS 在患者卵泡液和血清中的表达, logistic 回归分析 FS 与 EMS 患者 IVF-ET 预后的相关性。**结果** 患者在年龄、不孕年限和抗苗勒管激素 (AMH)、体质量指数 (BMI)、基础性激素水平和促性腺激素 (Gn) 启动日激素水平组间比较, 差异均无统计学意义 (P 均 >0.05)。A 组 Gn 使用总量 $[(2\ 427.44 \pm 894.79)\text{ IU}]$ 显著高于 B 组 $[(2\ 124.69 \pm 567.30)\text{ IU}]$ ($P=0.01$)。A 组人绒毛膜促性腺激素 (hCG) 注射日雌激素水平 $[(3\ 079.46 \pm 1\ 594.12)\text{ ng/L}]$ 、获卵率 $[(79.25 \pm 13.56)\%]$ 显著低于 B 组 $[(3\ 701.23 \pm 1\ 829.01)\text{ ng/L}, (84.90 \pm 12.96)\%]$ ($P=0.021, P=0.007$)。Gn 使用时间、hCG 注射日内膜厚度、黄体生成素 (LH) 和孕酮水平、成熟卵率、双原核 (2PN) 受精率、优质胚胎率和优质囊胚形成率组间比较, 差异均无统计学意义 ($P>0.05$)。移植胚胎数、胚胎种植率和临床妊娠率在移植的 51 例 A 组和 44 例 B 组患者中差异均无统计学意义 ($P>0.05$)。A 组血清 FS 和卵泡液 FS 表达均显著高于 B 组 ($P<0.01$)。Logistic 回归分析显示, EMS 患者的血清 FS 与 IVF 妊娠结局呈负相关, 卵泡液 FS 与 IVF 妊娠结局呈正相关。**结论** 与输卵管因素不孕患者相比, EMS 患者血清 FS 和卵泡液 FS 表达均显著升高。EMS 不孕患者的血清 FS 升高和 / 或卵泡液 FS 降低与其不良妊娠结局有关。血清 FS 与卵泡液 FS 对 EMS 患者 IVF 治疗妊娠结局具有预测价值。

【关键词】 卵泡抑素; 子宫内膜异位症; 受精, 体外; 胚胎移植; 妊娠结局

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Relationship between follistatin expression and clinical outcomes in *in vitro* fertilization and embryo transfer women with endometriosis

Zhang Qunfang, Liu Yun, Chen Guoyong, He Lingyun

Reproductive Medicine Center, Department of Obstetrics & Gynecology, the 900th Hospital of the Joint Logistics Support Force PLA, Fuzhou General Clinic Medical College, Fujian Medical University, Teaching Hospital of Fujian University of Traditional Chinese Medicine, Dongfang Hospital Affiliated to Xiamen University, Fuzhou 350025, China

Corresponding author: Liu Yun, Email: liuyunfj@126.com, Tel: +86-591-22859476

【Abstract】 Objective To study the relevance of follistatin (FS) level in follicular fluid (FF) and serum with pregnancy outcomes of endometriosis (EMS) patients undergoing *in vitro* fertilization and embryo transfer (IVF-ET) and explore the predictive value of FS for IVF pregnancy outcomes in EMS patients. **Methods** Clinical outcomes and laboratory data from 84 EMS patients (group A) and 80 tubal infertile patients (group B) undergoing IVF-ET in Reproductive Medical Center Department of Obstetrics and Gynecology 900 Hospital PLA from January to June in 2017 were retrospectively analyzed. FS levels in FF on oocytes retrieved day and in serum on human chorionic gonadotropin (hCG) injection day were detected by enzyme linked immunosorbent assay (ELISA), and the correlation between FS and IVF prognosis in EMS patients was analyzed by ELISA. **Results** There were no significant differences of age, infertility duration, anti-Müllerian hormone (AMH), body mass index (BMI), level of basal endocrine and endocrine on the beginning of gonadotropin (Gn) used between the two groups ($P>0.05$). Total dosage of Gn used in group A [(2 427.44±894.79) IU] was significantly higher than that of group B [(2 124.69±567.30) IU] ($P=0.01$). Estradiol level on hCG injection day and oocyte recovery rate in group A [(3 079.46±1 594.12) ng/L, (79.25±13.56)%] were significantly lower than those of group B [(3 701.23±1 829.01) ng/L, (84.90±12.96)%] ($P=0.021$, $P=0.007$). There were no significant differences in Gn used duration, endometrial thickness, luteinizing hormone (LH) and progesterone on hCG injection day, M_{II} oocytes rate, two pronuclei (2PN) fertilization rate, high-quality embryo rate, high-quality blastocyst formation rate between the two groups ($P<0.05$). Finally, 51 cases in group A and 44 cases in group B underwent embryo transfer, and there were no significant differences in the number of embryos transferred, implantation rate and clinical pregnancy rate between the two groups ($P>0.05$). The levels of FS in FF and serum in group A were both significantly higher than those in group B ($P<0.01$). Logistic regression analysis showed that FS level in serum of EMS patients was negatively correlated with IVF pregnancy outcome, while FS level in FF was positively correlated with IVF pregnancy outcome. **Conclusion** The level of FS in FF and serum were significantly increased in EMS patients. High serum FS level and low FS level in FF were associated with adverse IVF-ET outcomes in EMS patients. The levels of FS in serum and FF have predictive value for IVF pregnancy outcomes in EMS patients.

【Key words】 Follistatin; Endometriosis; Fertilization *in vitro*; Embryo transfer; Pregnancy outcome

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高糖培养环境对小鼠胚胎发育潜能的影响

文亮 陈书强 郭翔宇 董杰 雷晖 马媛 王晓红

空军军医大学唐都医院生殖医学中心, 西安 710038

通信作者: 王晓红, Email: wangxh99919@163.com, 电话: +86-29-84777849, 传真: +86-29-84777690

【摘要】目的 评估植入前高糖培养环境对小鼠胚胎发育潜能的影响。方法 选择 SPF 级雌性 ICR 小鼠, 促排卵后与正常雄鼠交配获取原核胚, 分别在含 0.2 mmol/L 葡萄糖的 KSOM 培养液 (对照组)、含 10 mmol/L 葡萄糖的 KSOM 培养液 (中剂量组)、含 20 mmol/L 葡萄糖的 KSOM 培养液 (高剂量组) 培养至囊胚, 每组 15 只雌性小鼠, 记录 3 组桑葚胚率及囊胚率; 3 组囊胚移植入第 3.5 日 (D3.5) 代孕母鼠子宫, 于 D18.5 处死母鼠, 计算胚胎植入率、成活率、胚胎停育率; 提取 3 组小鼠囊胚 mRNA, 采用实时荧光定量聚合酶链式反应 (RT-qPCR) 检测细胞命运决定因子以及植入和早期血管发生相关基因的 mRNA 表达量。**结果** ①与对照组相比, 高剂量组囊胚形成率显著降低 ($P=0.016$)。②3 组胚胎植入率差异无统计学意义 ($P>0.05$), 但与对照组相比, 中剂量组和高剂量组植入后胚胎成活率显著降低 ($P=0.004$), 胚胎停育率显著增高 ($P=0.004$)。③与对照组相比, 中剂量组和高剂量组早期细胞命运决定因子 *Cdx2*、*Tead4*、*Fgfr2* 相对表达水平均显著下调 ($P<0.001$, $P=0.005$, $P=0.003$)。④与对照组相比, 中剂量组和高剂量组囊胚期胚胎植入及早期血管发生相关基因 *Adm*、*Plau*、*Timp1* 相对表达水平均显著下调 ($P<0.001$, $P=0.001$, $P=0.041$), *Mmp2*、*Timp3*、*Troap* 相对表达水平均显著上调 ($P=0.012$, $P=0.013$, $P=0.002$)。**结论** 植入前胚胎处于高糖培养环境, 降低了胚胎的发育潜能, 并导致了不良妊娠结局发生。

【关键词】 高糖; 囊胚; 植入率; 胚胎停育率; 葡萄糖代谢

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Effects of exposure to high glucose concentration on embryonic development potential of mouse

Wen Liang, Chen Shuqiang, Guo Xiangyu, Dong Jie, Lei Hui, Ma Yuan, Wang Xiaohong

Reproductive Medical Centre, Tangdu Hospital, the Fourth Military Medical University, Xi'an 710038, China

Corresponding author: Wang Xiaohong, Email: wangxh99919@163.com, Tel: +86-29-84777849, Fax: +86-29-84777690

【Abstract】 Objective To evaluate the effect of exposure to high glucose concentration on the developmental potential of preimplantation embryos. **Methods** Female ICR mice mated with males after ovulation induction to acquire zygotes, which were incubated to blastocysts in KSOM medium (0.2 mmol/L glucose, control group), KSOM medium supplemented with 10 mmol/L glucose (middle dose group) and KSOM medium supplemented with 20 mmol/L glucose (high dose group). The blastocyst rate of each group was recorded. The blastocysts were transplanted into day 3.5 (D3.5) pseudopregnant mice. The surrogate female mice were sacrificed in D18.5. Then, the embryo implantation rate, the live fetal rate after implantation and the embryo abortion rate were calculated. The blastocysts mRNA were extracted and the mRNA expression levels of relevant genes (*Cdx2*, *Tead4*, *Fgfr2*, *Adm*, *Plau*, *Timp1*) were detected by real-time quantitative polymerase chain reaction. **Results** 1) Compared with control group, the blastocyst rate of the high dose group was significantly decreased ($P=0.016$). 2) There was no statistical difference in the implantation rate of the three groups ($P>0.05$), but the live fetal rate after implantation of the middle dose group and high dose group was significantly decreased compared with control group ($P=0.004$). 3) Compared with control group, the mRNA relative expression levels of *Cdx2*, *Tead4* and *Fgfr2* were significantly down-regulated ($P<0.001$, $P=0.005$, $P=0.003$) in the blastocysts of middle and high dose groups. 4) Compared with control group, the mRNA relative expression levels of *Adm*, *Plau* and *Timp1* were significantly down-regulated ($P<0.001$, $P=0.001$, $P=0.041$), and *Mmp2*, *Timp3* and *Troap* were significantly up-regulated in the blastocysts of middle and high dose groups ($P=0.012$, $P=0.013$, $P=0.002$). **Conclusion** Before implantation, exposure to high glucose concentration decreases the developmental potential of the embryos, and leads to adverse pregnant outcomes.

【Key words】 High concentration of glucose; Blastocyst; Implantation rate; Embryo abortion rate; Glucose metabolism

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卵巢高反应判定标准和预测指标的系统评价

邓可¹ 李玲¹ 徐畅¹ 李蓉² 邹康¹ 孙鑫¹

¹ 四川大学华西医院中国循证医学中心, 成都 610041; ² 北京大学第三医院生殖医学中心 100191

通信作者: 孙鑫, Email: sunxin@wchscu.cn, 电话: +86-28-85164187

【摘要】 目的 系统总结卵巢高反应相关判定标准、危险因素和预测指标, 为科学制定卵巢高反应判定和预测标准提供依据。方法 计算机检索 PubMed、EMBASE、CBM、CNKI 和 Wanfang Data 数据库及美国国立指南库 (NGC)、英国国家卫生与临床优化研究所 (NICE)、苏格兰校际指南网络 (SIGN) 等临床实践指南库, 检索时限均为建库至 2018 年 1 月。2 名研究者采用预先制做的表格独立筛选文献、评价纳入研究的偏倚风险, 提取卵巢高反应判定标准、危险因素及预测指标相关资料进行 Meta 分析。结果 本研究最终共纳入 25 篇原始研究, 8 篇文献综述及 2 篇 Meta 分析。卵巢高反应的判定标准常用的单一指标为获卵数 >15、雌二醇浓度 >14 680~18 350 pmol/L 或卵巢敏感指数 (OSI)>10.07/IU。综合采用两个及以上指标的常用标准为获卵数 (>15 或 20) 和 / 或人绒毛膜促性腺激素 (hCG) 注射日血清雌二醇浓度 (>11 010 pmol/L)。多因素分析研究结果显示, 窦卵泡计数 (AFC) ≥ 11 、睾酮 $\geq 0.299 5 \mu\text{g/L}$ 、降调节后雌二醇 $\geq 15.355 \mu\text{g/L}$ 的患者发生卵巢高反应可能性较大。队列研究和文献综述中预测卵巢高反应的最佳临界值为抗苗勒管激素 (AMH)>3.04 $\mu\text{g/L}$ 或 $\geq 3.12 \mu\text{g/L}$ 、AFC>14; Meta 分析中纳入研究采用的预测临界值为 AMH>1.59~7.00 $\mu\text{g/L}$ 、AFC>9~18。Meta 分析结果表明, 在使用年龄作为预测指标的基础上, 结合卵泡刺激素 (FSH)、AMH、AFC 进行预测可提高结果的准确度, 综合 AFC+AMH 进行预测的准确度与年龄 +AFC+AMH 预测卵巢高反应的准确性相似。结论 卵巢高反应判定最常用的标准为控制性超促排卵 (COH) 方案促排卵后获卵数 >15 或 20 和 / 或雌二醇浓度 >11 010 pmol/L。AFC ≥ 11 、睾酮 $\geq 0.299 5 \mu\text{g/L}$ 、降调节后雌二醇 $\geq 15.355 \mu\text{g/L}$ 等可能是卵巢高反应的危险因素。AFC+AMH 综合使用的预测效果优于单独使用, 采用 AFC+AMH 综合进行预测的准确度与年龄 +AFC+AMH 预测卵巢高反应的准确性相似。目前国内外尚无卵巢高反应判定和预测的统一标准, 建议下一步组织专家形成共识, 建立卵巢高反应判定和预测的统一标准, 为临床指南的制定提供理论基础和参考依据。

【关键词】 卵巢高反应; 受精, 体外; 胚胎移植; 控制性超促排卵; 预测指标; 判定标准; Meta 分析

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Criteria and clinical predictors of high ovarian response: a systematic reviewDeng Ke¹, Li Ling¹, Xu Chang¹, Li Rong², Zou Kang¹, Sun Xin¹¹China Evidence Based Medicine Center, West China Hospital, Sichuan University, Chengdu 610041, China;²Reproductive Medical Science Center, Peking University Third Hospital, Beijing 100191, China

Corresponding author: Sun Xin, Email: sunxin@wchscu.cn, Tel: +86-28-85164187

【Abstract】 Objective To systematically summarize the criteria, risk factors and clinical predictors of high ovarian response, thus providing scientific basis and support for setting judgement and prediction criteria of high ovarian response. **Methods** We systematically searched PubMed, EMBASE, CBM, CNKI, Wanfang Data and clinical practice guideline database including National Guideline Clearinghouse (NGC), National Institute of Clinical Excellence (NICE), Scottish Intercollegiate Guidelines Network (SIGN) and so on, for eligible records from inception to January 2018. Two well-trained reviewers who had full understanding of the study protocol conducted the literature screening, risk of bias assessment and data extraction independently. Then the information of criteria, risk factors were summarized and analyzed, and clinical predictors of high ovarian response were collected. **Results** Totally 35 records were identified for analysis, including 25 original studies, 8 reviews and 2 Meta-analyses. For criteria of high ovarian response, the most frequently used single indexes were over 15 oocytes retrieved at oocyte pick-up, estradiol level between 14 680 pmol/L and 18 350 pmol/L on the day of human chorionic gonadotropin (hCG) injection, or ovarian sensitivity index (OSI)>10.07/IU. The most common condition in which two or more indexes combined were oocytes retrieved over 15 or 20 and/or peak estradiol concentration on hCG injection day over 11 010 pmol/L. As for risk factors, results from multiple-factor analysis showed that patients with antral follicle count (AFC) ≥ 11 , testosterone $\geq 0.299\ 5\ \mu\text{g/L}$ or peak estradiol $\geq 15.355\ \mu\text{g/L}$ were tend to have high ovarian response. As for clinical predictors, results from cohort studies and reviews showed that the most effective cutoff value for prediction of high ovarian response were anti-Müllerian hormone (AMH)>3.04 $\mu\text{g/L}$ or AMH $\geq 3.12\ \mu\text{g/L}$, or AFC>14. And studies included in Meta-analysis commonly used AMH>1.59–7.00 $\mu\text{g/L}$ or AFC>9–18 to predict high ovarian response. Moreover, results of Meta-analysis suggested that on basis of age, combing follicle stimulating hormone (FSH), AMH or AFC could improve the performance of prediction. AMH and AFC were better than FSH as predictors of high ovarian response. Combining AMH and AFC to predict high ovarian response would be more accurate than using them separately. Using AFC plus AMH to predict high ovarian response resulted in similar accuracy as using age plus AFC and AMH. **Conclusion** Current available evidence showed that the most commonly used criteria were oocytes retrieved over 15 or 20 and/or peak estradiol concentration on hCG injection day over 11 010 pmol/L, AFC ≥ 11 , testosterone $\geq 0.299\ 5\ \mu\text{g/L}$, peak estradiol $\geq 15.355\ \mu\text{g/L}$ may be risk factors for high ovarian response. Based on age, combing FSH, AMH or AFC could improve the performance of prediction. AMH and AFC were better than FSH as predictors of high ovarian response. Combining AMH and AFC to predict high ovarian response would be more accurate than using them separately. Using AFC plus AMH to predict high ovarian response resulted in similar accuracy as using age plus AFC and AMH. However, there were no uniform criteria worldwide for identifying or predicting high ovarian response, studies applying method such as expert consensus based on current results to set uniform criteria and clinical predictors of high ovarian response are warranted to provide theoretical basis and reference for relative study design and guideline development in the future.

【Key words】 High ovarian response; Fertilization *in vitro*; Embryo transfer; Controlled ovarian hyperstimulation; Predictors; Judgement criteria; Meta-analysis

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染色体多态性对体外受精 / 卵胞质内单精子显微注射 - 胚胎移植结局的影响

胡卫华¹ 李文杰¹ 姜根凤¹ 阮健¹ 章志国²

¹ 皖南医学院第一附属医院弋矶山医院生殖医学中心, 芜湖 240001; ² 安徽医科大学第一附属医院妇产科生殖医学中心, 合肥 230031

通信作者: 胡卫华, Email: wnmchwh@163.com, 电话: +86-553-5739341

【摘要】 目的 探讨在辅助生殖技术助孕过程中染色体多态性对胚胎发育结局的影响。方法 回顾性病例对照研究分析 2014 年 12 月—2018 年 10 月期间在皖南医学院附属弋矶山医院生殖医学中心接受体外受精 / 卵胞质内单精子显微注射 - 胚胎移植 (IVF/ICSI-ET) 治疗的 712 例患者的染色体核型, 将其分为染色体多态性组 (多态性组, $n=191$) 和染色体正常组 (正常组, $n=521$), 比较组间的获卵数、 M_{II} 卵率、受精率、双原核 (2PN) 率、卵裂率、优质胚胎率和第 3 日可移植胚胎率。结果 多态性组和正常组的获卵数分别为 14.52 ± 8.43 和 13.74 ± 7.25 , M_{II} 卵率分别是 83.62% 和 84.54%, 组间差异均无统计学意义 ($P>0.05$); 多态性组的受精率 (84.98%) 和 2PN 率 (77.12%) 稍低于正常组 (85.03%, 77.16%), 但差异均无统计学意义 ($P>0.05$); 多态性组的优质胚胎率 (65.55%) 高于正常组 (64.77%), 差异无统计学意义 ($P>0.05$); 多态性组和正常组的卵裂率 (98.30% 比 98.19%) 和第 3 日可移植胚胎率 (93.95% 比 92.91%) 差异均无统计学意义 ($P>0.05$)。在所检出的 191 例染色体多态性中, 男方 Y 染色体多态性检出率最高, 占 57.59%; 女方各种染色体多态性占 32.98%, 男性高于女性, 但差异无统计学意义。结论 染色体多态性患者行辅助生殖技术助孕后的胚胎结局和正常人群差异无统计学意义, 但其妊娠结局及最终抱婴回家率有待严密随访跟踪。

【关键词】 辅助生殖技术; 染色体; 染色体多态性

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Effect of chromosome polymorphism on the outcome of embryos in *in vitro* fertilization/intracytoplasmic sperm injection-embryo transfer

Hu Weihua¹, Li Wenjie¹, Jiang Genfeng¹, Ruan Jian¹, Zhang Zhiguo²

¹Department of Reproductive Medicine Center, the First Affiliated Yijishan Hospital of Wannan Medical College, Wuhu 241001, China; ²Reproductive Medicine Center, Department of Obstetrics and Gynecology, the First Affiliated Hospital of Anhui Medical, Hefei 230031, China

Corresponding author: Hu Weihua, Email: wnmchwh@163.com, Tel: +86-553-5739341

【Abstract】 Objective To investigate the effect of chromosome polymorphism on embryonic development outcome during assisted reproductive technology (ART). **Methods** The chromosome karyotypes of 712 patients treated with *in vitro* fertilization/intracytoplasmic sperm injection-embryo transfer (IVF/ICSI-ET) from December 2014 to October 2018 in the Reproductive Center of the First Affiliated Yijishan Hospital of Wannan Medical College were retrospectively analyzed. They were divided into chromosome polymorphism group (polymorphism group, $n=191$) and chromosome normal group (normal group, $n=521$). The number of oocytes captured, M_{II} oocytes rate, fertilization rate, two pronuclei (2PN) rate, cleavage rate, excellent embryo rate and day 3 transplantable embryo rate were compared between the two groups. **Results** By comparing the number of oocytes obtained from polymorphism group and normal group, the number of oocytes obtained from the two groups was 14.52 ± 8.43 and 13.74 ± 7.25 respectively, and the rate of M_{II} oocytes was 83.62% and 84.54% respectively. There was no significant difference between the two groups ($P>0.05$); the fertilization rate (84.98%) and the 2PN rate (77.12%) of polymorphism group were lower than those of normal group (85.03%, 77.16%), but there was no significant difference ($P>0.05$). The rate of superior embryo (65.55%) was higher than that of normal group (64.77%), but there was no significant difference between the two groups ($P>0.05$), and there was no significant difference in cleavage rate (98.30% vs. 98.19%) and transplantable embryo rate (93.95% vs. 92.91%) on the third day between the two groups ($P>0.05$). There was no significant difference in statistics, but among 191 cases of chromosome polymorphism detected, the detection rate of Y chromosome polymorphism was the highest account for 57.59% in males, various chromosome polymorphisms also account for 32.98% in women. **Conclusion** Although there is no significant difference in embryonic outcomes between patients with chromosome polymorphism and normal population after ART, it is necessary to follow-up the final rate of carrying the baby home and the health of the newborn after three years.

【Key words】 Reproductive technology, assisted; Chromosomes; Chromosome polymorphism

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反复种植失败患者 T 型宫腔成形术后体外受精临床结局分析

楼晓芳¹ 房素萍² 张雯碧¹ 陈佳儗¹ 李路¹

¹ 复旦大学附属妇产科医院 上海集爱遗传与不育诊疗中心 200011; ² 上海交通大学医学院附属仁济医院 200001

通信作者: 李路, Email: lilu2ab@163.com, 电话: +86-13916394129

【摘要】目的 探讨反复种植失败 T 型宫腔患者在宫腔镜下行 T 型宫腔成形术前后体外受精 - 胚胎移植 (*in vitro* fertilization and embryo transfer, IVF-ET) 临床结局的差异。**方法** 回顾性分析 18 例 2016 年 3 月—2018 年 5 月期间在上海集爱遗传与不育诊疗中心, 因 IVF 反复种植失败 (移植失败 ≥ 3 次) 行宫腔镜检查术中诊断为 T 型宫腔的患者资料。所有患者行冷刀 T 型宫腔成形术, 评估术后 IVF-ET 临床结局。**结果** 18 例反复种植失败的患者行宫腔镜 T 型宫腔成形术, 术后第一次移植 14 例患者成功妊娠, 其中单胎足月分娩 8 例, 1 例双胎早产胎儿存活。**结论** 宫腔镜下宫腔成形术是诊断和治疗 T 型宫腔的一种有效手段, 降低了不良妊娠结局的发生, 改善部分 IVF 反复种植失败患者的临床妊娠结局。

【关键词】 T 型宫腔; 宫腔镜 T 型宫腔成形术; 反复移植失败; 生殖临床结局

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Analysis of the clinical reproductive outcome of repeated implantation failure after hysteroscopic metroplasty in women with a T shaped uterus

Lou Xiaofang¹, Fang Suping², Zhang Wenbi¹, Chen Jiazhou¹, Li Lu¹

¹Shanghai Jiai Heredity and Infertility Diagnosis and Treatment Center, Obstetrics and Gynecology Hospital of Fudan University, Shanghai 200011, China; ²Medical College of Shanghai Jiao Tong University Affiliated Renji Hospital, Shanghai 200001, China

Corresponding author: Li Lu, Email: lilu2ab@163.com, Tel: +86-13916394129

【Abstract】 Objective To investigate the outcome of repeated *in vitro* fertilization and embryo transfer (IVF-ET) failure patients with a T shaped uterus before and after hysteroscopic metroplasty. **Methods** A retrospective analysis of 18 cases of repeated IVF failure (3 or more failures) in our center was performed. The T shaped uterus was diagnosed and performed metroplasty with cold knife under hysteroscopy. The clinical outcome of IVF-ET was performed to evaluate the effect of the operation. **Results** Fourteen patients were transplanted successfully after the hysteroscopic operation, eight full-term single birth and one premature twin births were delivered. **Conclusion** Hysteroscopic T shaped uterus metroplasty is an effective method for diagnosis and treatment of T shaped uterus, which reduces the incidence of poor pregnancy and improves the clinical reproductive outcome of partial IVF repeated failure patients.

【Key words】 T shaped uterus; Hysteroscopic T shaped uterus metroplasty; Repeated transplantation failure; Clinical reproductive outcome

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不孕症女性生育镜检查结果分析

张琬琳¹ 王鑫¹ 谢多² 刘瑾¹ 肖西峰¹

¹空军军医大学第二附属医院妇产科生殖医学中心, 西安 710038; ²解放军 323 医院妇产科, 西安 710054

通信作者: 肖西峰, Email: xxfeng926@163.com, 电话: +86-13992897709

【摘要】目的 探究生育镜在查找不孕症病因、指导进一步助孕方面的作用。**方法** 本文回顾了空军军医大学唐都医院生殖医学中心 2014 年 7 月—2018 年 4 月期间 487 例生育镜检查结果, 并对其中 216 例患者的妊娠结局进行了随访。对检查结果的分布频率进行描述性统计, 对不同年龄组及不同不孕症诊断组的检查结果分布进行 χ^2 检验。**结果** 487 例生育镜检查术成功率 100%, 无并发症发生。所有患者均可耐受手术。在所有检查结果中, 双侧或单侧输卵管通畅且不合并其他异常者 185 例 (38.0%); 双侧或单侧输卵管通畅且仅合并可纠正宫腔异常者 118 例 (24.2%)。有 2 种或 2 种以上解剖异常者所占比例 (62%) 大于仅有 1 种或 1 种以下解剖异常者 (38%)。随访的 216 例患者中, 生育镜检查距妊娠的时间间隔为 (8.15 ± 3.14) 个月 (1~35 个月)。总体活产率为 54.6%(118/216), 继续妊娠率为 10.2%(22/216), 流产率为 6.5%(14/216), 未妊娠率为 28.7%(62/216)。在活产者中, 至少一侧输卵管通畅者通过自然方式妊娠的比例 [77.0%(97/126)] 高于通过体外受精 - 胚胎移植术妊娠的比例 [23.0%(29/126)] ($P < 0.001$)。**结论** 生育镜是评估女性上生殖道解剖的一种全面、安全、痛苦小及便捷的检查方法。对于任何年龄、无论原发或继发不孕的患者, 若无明确盆腹腔病史, 生育镜检查可在查找不孕原因、指导进一步治疗方面使大多数患者获益。

【关键词】 不孕症; 生育镜; 经阴道注水腹腔镜

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Clinical analysis of outcomes of fertiloscopic examination for infertile women

Zhang Wanlin¹, Wang Xin¹, Xie Duo², Liu Jin¹, Xiao Xifeng¹

¹Reproductive Medical Center, Department of Gynecology and Obstetrics, the Second Filiated Hospital of the Fourth Military Medical University, Xi'an 710038, China; ²Department of Gynecology and Obstetrics of the 323 Military Hospital, Xi'an 710054, China

Corresponding author: Xiao Xifeng, Email: xxfeng926@163.com, Tel: +86-13992897709

【Abstract】 Objective To explore the implication of fertiloscopy in screening the etiology of female infertility and tailoring the treatment method for an individual infertile woman. **Methods** This article retrospectively analyzed the outcomes of fertiloscopic examination for 487 infertile women in the Reproductive Medical Center of Tangdu Hospital from June 2014 to April 2018. The frequency distribution of the examination outcomes was presented descriptively by numbers and percentages. The discrepancies of frequency distribution between groups of different ages and infertility diagnosis were examined with chi-square test. **Results** The success rate of the examination was 100%. No complication occurred. The procedures were all tolerable. In all outcomes of the examination, there were 118 cases (24.2%) with normal uterine cavity, normal bilateral patent tubes and without other anomalies; 67 cases (13.8%) with normal uterine cavity, unilateral patent tube and without other anomalies, and 8 cases (1.6%) with normal uterine cavity, bilateral obstructive tubes and without other anomalies. In groups of age younger than 30 years old and age of 30 years old or older, in groups of primary infertility and secondary infertility, the proportion of cases with at least one patent tube without other anomalies (38%) was significantly lower than cases with 2 or more anomalies (62%). Among 216 patients who were followed up, the average interval between fertiloscopic examination and pregnancy was (8.15 ± 3.14) months (1–35 months). The overall live birth rate was 54.6% (118/216), the ongoing pregnancy rate was 10.2% (22/216), the miscarriage rate was 6.5% (14/216), and there was 28.7% (62/216) patients who hadn't gotten pregnant at the time of data collection. The proportion of live births through natural intercourse [77.0% (97/126)] was significantly higher than that through *in vitro* fertilization-embryo transfer [23.0% (29/126)] in patients with at least one patent fallopian tube ($P < 0.001$). **Conclusion** For selected infertile women, fertiloscopy is a comprehensive, safe and convenient method with mild pain to explore all the anatomic condition of pelvic, ovaries, fallopian tubes and uterine. Fertiloscopic examination is benefit for most patients at any reproductive age of any infertility diagnosis in screening etiology of infertility and tailoring treatment program further.

【Key words】 Infertility; Fertiloscopy; Transvaginal hydrolaparoscopy

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体外受精 - 胚胎移植患者电子信息化健康教育模式的构建和效果评价

倪颖 童琛晔 韩迟迟 朱丽慧

上海交通大学医学院附属瑞金医院生殖医学中心 200025

通信作者: 倪颖, Email: ny21085@rjh.com.cn, 电话: +86-18917762718

【摘要】目的 探讨在辅助生殖助孕过程中, 构建电子信息化健康教育模式对体外受精 - 胚胎移植 (*in vitro* fertilization-embryo transfer, IVF-ET) 助孕患者心理状态、治疗用药依从性和满意度的应用效果评价。**方法** 选择 2017 年 7—12 月, 在上海交通大学医学院附属瑞金医院生殖医学中心首次行 IVF-ET 助孕的 100 例不孕症患者作为研究对象。将 2017 年 7—9 月实施助孕周期治疗的 50 例设为对照组, 采用常规健康教育模式; 2017 年 10—12 月助孕患者 50 例设为观察组, 采用电子信息化健康教育模式; 比较两组患者在不同健康教育后焦虑、抑郁评分, 治疗用药依从性和对护理满意度。**结果** 观察组患者的焦虑评分 (50.62 ± 3.64)、抑郁评分 (0.51 ± 0.04) 均显著低于对照组患者 (58.30 ± 2.60 , 0.58 ± 0.03) (P 均 < 0.001); 观察组的各项治疗行为依从性均显著高于对照组 (按时服药率 96% 比 80%; 按时复诊率 94% 比 76%; 排卵监测率 94% 比 78%; 术前准备率 100% 比 86%; 术后随访率 90% 比 70%) ($P < 0.05$); 观察组的护理满意度 (护理服务、专业知识技术、耐心聆听解释) 均高于对照组, 差异有统计学意义 ($P < 0.05$)。**结论** 构建电子信息化健康教育模式, 对助孕患者不同阶段进行针对性的教育和指导及提醒功能推送, 能有效地改善患者的心理状态, 提高治疗用药依从性及患者对护理工作的满意度。

【关键词】 不孕不育; 电子信息; 健康教育; 模式构建; 效果评价

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Pattern construction and effects evaluation of electronic health education on patients undergoing *in vitro* fertilization-embryo transfer

Ni Ying, Tong Chenye, Han Chichi, Zhu Lihui

Reproductive Medicine Center, Ruijin Hospital Affiliated to Shanghai Jiao Tong University School of Medicine, Shanghai 200025, China

Corresponding author: Ni Ying, Email: ny21085@rjh.com.cn, Tel: +86-18917762718

【Abstract】 Objective To explore the effect of electronic health education on the psychological status, compliance with medications and satisfaction with nursing of *in vitro* fertilization (IVF)-assisted patients during assisted reproductive pregnancy. **Methods** From July to September in 2017, 100 infertile women who received IVF-embryo transfer (ET) for the first time in Reproductive Medical Center of Ruijin Hospital, Shanghai Jiao Tong University School of Medicine were enrolled in this research. Fifty cases of control group received routine health education, while the other 50 cases of observation group received electronic health education. The anxious and depressive scores, compliance with medications and satisfaction with nursing between the two health education mode were to compare. **Results** The scores of anxiety (50.62 ± 3.64) and depression (0.51 ± 0.04) in the observation group were lower than those in control group significantly (58.30 ± 2.60 , 0.58 ± 0.03 , all $P < 0.001$). But the therapeutic compliance [timely taking medicine rates (96% vs. 80%), timely return visit rates (94% vs. 76%), ovulation monitoring rates (94% vs. 78%), preoperative preparation rates (100% vs. 86%) and postoperative follow-up rates (90% vs. 70%)] as well as their nursing satisfaction on our nursing services, professional knowledge and their reaction to our explanation in observation group were higher than those in control group ($P < 0.05$). **Conclusion** Constructing the electronic health education system can improve the patients' psychological status, compliance with medications and increase the nursing satisfaction by pushing notifications and applying specific educations during different treatment stages using electronic health education system.

【Key words】 Infertility; Electronic information; Health education; Pattern construction; Evaluation of effects

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酪氨酸羟化酶缺乏症两例的临床特征、基因诊断及其干预

肖云山¹ 张雪芹²

¹厦门市妇幼保健院产科遗传咨询门诊 361003; ²厦门市妇幼保健院产科 361003

通信作者: 张雪芹, Email: wind459@126.com, Tel: +86-13400677617

【摘要】目的 深化对酪氨酸羟化酶缺乏症 (THD) 进行医疗干预的认识。**方法** 回顾分析 2 例 THD 患儿的临床资料: 2 例患儿均于孕晚期出现宫内生长受限、宫内窘迫等, 出生后半年出现肌张力障碍症状。经知情同意, 抽取患者及其父母亲外周血。抽提 DNA, 进行全外显子组测序 (WES), 并经 Sanger 测序验证。**结果** 2 例患儿临床表现符合 THD, 经全外显子基因检测, 患儿 1 的 *TH* 基因检测到来源于父亲的 c.1196C>T 突变及来源于母亲的 c.457C>T 形成的复合杂合突变。患儿 2 的 *TH* 基因检测到来源于父亲的 c.698G>A 突变及来源于母亲的 c.1293+5G>C 形成的复合杂合突变。均为 *TH* 基因变异导致多巴反应性肌张力障碍。据此诊断, 采用口服美多巴治疗, 运动症状改善, 认知能力仍明显滞后。**结论** THD 患儿胎儿期发育异常与出生后临床表型严重有关, 深入了解其临床特征与基因型的关系有助于准确评估 THD 疾病的医疗干预效果。

【关键词】 酪氨酸羟化酶缺乏症; 全外显子组测序; 医疗干预

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Clinical characteristics, gene diagnosis, and intervention of tyrosine hydroxylase deficiency: 2 cases report

Xiao Yunshan¹, Zhang Xueqin²

¹Genetic Counseling Clinic, Department of Obstetrics, Xiamen Maternity and Child Health Care Hospital, Xiamen 361003, China; ²Department of Obstetrics, Xiamen Maternity and Child Health Care Hospital, Xiamen 361003, China

Corresponding author: Zhang Xueqin, Email: wind459@126.com, Tel: +86-13400677617

【Abstract】 Objective To deepen the understanding of the intervention effect of tyrosine hydroxylase deficiency (THD). **Methods** The clinical data of 2 patients with THD were retrospectively analyzed. In both cases, intrauterine growth restriction and intrauterine distress occurred in the late pregnancy, and dystonia symptoms were found in half a year after birth. After informed consent, the peripheral blood of the patients and their parents were collected, and DNAs were extracted. Whole exome sequencing (WES) was used to detect the gene mutations, and Sanger sequencing was performed to verify the results. **Results** The tyrosine hydroxylase gene mutation of the first patient came from c.1196C>T mutation in his father and c.457C>T compound heterozygous mutation in his mother. The tyrosine hydroxylase gene mutation of the second patient came from c.698G>A mutation in his father, and c.1293+5G>C compound heterozygous mutation in his mother. According to the diagnosis, oral dopamine therapy is effective in improving motor symptoms, and the cognitive ability of patients is still lagging behind. **Conclusion** The abnormal fetal development is related to the severe postnatal phenotype of THD children. It is essential to understand the relationship between the clinical features and genotypes of THD, which help to accurately evaluate the effect of the medical intervention on THD disease.

【Key words】 Tyrosine hydroxylase deficiency; Whole exome sequencing; Medical intervention

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体外受精 - 胚胎移植长方案降调节过程中多卵泡发育 1 例病例报告并文献复习

燕敏¹ 侯振² 郭小芹¹ 韩文权¹ 刘婧¹ 吉别克·瓦提别克¹ 夏拉帕提·阿布都外力¹
乌丽太·沙德尔伙加¹

¹伊犁州妇幼保健院生殖医学中心, 伊宁 835000; ²南京医科大学第一附属医院生殖医学中心 210029

通信作者: 侯振, Email: zhou1981@126.com, 电话: +86-13951814609

【摘要】目的 分析 1 例体外受精 - 胚胎移植 (*in vitro* fertilization-embryo transfer, IVF-ET) 长方案降调节过程中多卵泡发育病例并进行卵泡刺激素受体 (FSHR) 检测对临床诊疗的意义。**方法** 检索 FSHR、卵巢反应性、IVF, 检索历年来发表文献。**结果** 本例 IVF-ET 长方案降调节过程中多卵泡发育患者的 FSHR 基因存在 2 个变异位点, 综合国内外有 IVF/ 卵胞质内单精子注射 (ICSI) 治疗中进行 FSHR 检测的结果, 提示 IVF-ET 长方案降调节过程中多卵泡发育可能与 FSHR 变异有关。**结论** FSHR 的检测对于临床促排卵治疗可能有一定的指导意义。

【关键词】 卵巢反应性; 受精, 体外; 卵泡刺激素受体

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A case report of multiple ovarian follicles grew in the progress of gonadotrophin-releasing hormone agonist down-regulation of *in vitro* fertilization-embryo transfer and literatures review

Yan Min¹, Hou Zhen², Guo Xiaoqin¹, Han Wenquan¹, Liu Jing¹, Jibieke Watibieke¹, Xialapati Abuduwaili¹, Wulitai Shadeerhuojia¹

¹Center of Clinical Reproductive Medicine, Yili Prefecture Maternal and Child Health Hospital, Yining 835000, China; ²Center of Clinical Reproductive Medicine, First Affiliated Hospital, Nanjing Medical University, Nanjing 210029, China

Corresponding author: Hou Zhen, Email: zhhou1981@126.com, Tel: +86-13951814609

【Abstract】 Objective To analyze the case that multiple ovarian follicles grew in the progress of gonadotrophin-releasing hormone agonist down-regulation when a patient received *in vitro* fertilization (IVF) and to discuss the significance of follicle-stimulating hormone receptor (FSHR) determination that will guide the clinical diagnosis and treatment in *in vitro* fertilization. **Methods** The literatures that published about FSHR, ovarian response and IVF were searched. **Results** We detected two polymorphisms of *FSHR* in this patient. After reviewed the literatures we find that ovarian reaction is associated with FSHR polymorphisms. **Conclusion** FSHR determination may have some clinical significances to predict ovarian response in IVF. However, we should gather more data to prove this conclusion.

【Key words】 Ovarian response; Fertilization *in vitro*; Follicle-stimulating hormone receptor

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子宫内膜异位症合并不孕患者控制性促排卵方案的选择

杨璞玉 马彩虹

北京大学第三医院生殖医学中心 100191

通信作者: 马彩虹, Email: macaihong@263.net, 电话: +86-10-82268326

【摘要】 子宫内膜异位症 (EMS) 是引起育龄女性不孕的重要因素之一, 其原因与盆腔解剖结构改变、内分泌和免疫功能失调等有关。体外受精 - 胚胎移植 (IVF-ET) 技术是 EMS 合并不孕的有效助孕方法。促性腺激素释放激素激动剂 (GnRH-a) 超长方案是最常用的控制性促排卵方案, 但该方案可能导致过度的垂体抑制, 进而提高卵巢反应不良的风险。如何综合考量 EMS 不孕患者自身因素, 针对不同情况选择个体化的 GnRH-a 降调节方案是临床面临的挑战。本文综述了 EMS 合并不孕患者应用不同控制性促排卵方案的 IVF-ET 结局, 探讨个体化的控制性促排卵方案选择策略。

【关键词】 子宫内膜异位症; 受精, 体外; 胚胎移植; 控制性促排卵; 临床结局

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Choice of controlled ovarian stimulation protocols for women with endometriosis-related infertility

Yang Puyu, Ma Caihong

Reproductive Medicine Center, Peking University Third Hospital, Beijing 100191, China

Corresponding author: Ma Caihong, Email: macaihong@263.net, Tel: +86-10-82268326

【Abstract】 Endometriosis (EMS) is one of the important factors of female infertility. The possible causes of infertility include the abnormal pelvic anatomy, the decreased ovarian function and imbalance of immune function. The *in vitro* fertilization-embryo transfer (IVF-ET) is an effective method for EMS associated with infertility. Gonadotropin-releasing hormone agonists (GnRH-a) prolonged protocol is regarded as the most common treatment for patients with EMS-related infertility. However, long time pituitary suppression may lead to increase of total dosage of Gn used and the risk of poor ovarian response. How to consider the infertility factors of patients with EMS comprehensively and choose personalized GnRH-a protocols for different situations is a clinical challenge. In this review, we summarized the clinical outcomes of different pituitary down regulation protocols in women with EMS-related infertility undergoing IVF-ET and set up the individualized treatment strategy.

【Key words】 Endometriosis; Fertilization *in vitro*; Embryo transfer; Controlled ovarian stimulation; Clinical outcome

Fund program: Key Clinical Project of Peking University Third Hospital (BYSY2015002)

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肥胖与复发性流产的相关性研究进展

乔岩¹ 孙振高² 宋景艳¹ 夏庆昌¹ 牟珍妮³ 刘红根³

¹ 山东中医药大学第一临床学院, 济南 250014; ² 山东中医药大学附属医院生殖与遗传中心, 济南 250011; ³ 山东中医药大学中医学院, 济南 250014

通信作者: 孙振高, Email: doctorqiaoyan@163.com, 电话: +86-13708938621

【摘要】 肥胖是一种全身性代谢疾病, 近年来其发病率逐年上升。复发性流产是危害育龄期夫妇身心健康的妊娠并发症, 病因复杂。本文从染色体异常、免疫失衡、蜕膜化受损、内分泌紊乱、血栓前状态、表观遗传学 6 个方面探讨肥胖和复发性流产的相关性, 以期肥胖及其相关因素导致的复发性流产提供治疗思路。

【关键词】 免疫; 内分泌系统; 复发性流产; 肥胖; 蜕膜化

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Research progress on the correlation between obesity and recurrent pregnancy loss

Qiao Yan¹, Sun Zhengao², Song Jingyan¹, Xia Qingchang¹, Mu Zhenni³, Liu Honggen³

¹The First Clinical College of Shandong University of Traditional Chinese Medicine, Jinan 250014, China;

²Affiliated Hospital of Shandong University of Traditional Chinese Medicine, Reproductive Medicine Center, Jinan 250011, China; ³Traditional Chinese Medicine College, Shandong University of Traditional Chinese Medicine, Jinan 250014, China

Corresponding author: Sun Zhengao, Email: doctorqiaoyan@163.com, Tel: +86-13708938621

【Abstract】 Obesity is a systemic metabolic disease. The incidence of obesity has increased year by year. Recurrent pregnancy loss (RPL) is a pregnancy complication which endangers the physical and mental health of couples of reproductive age. The etiology of RPL is complicated. This article discusses the correlation of obesity and RPL on several aspects, including chromosomal abnormality, immune imbalance, impaired decidualization, endocrine disorder, prethrombotic state, and epigenetics, to provide treatment ideas for RPL caused by obesity and its related factors.

【Key words】 Immunity; Endocrine system; Recurrent pregnancy loss; Obesity; Decidualization

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下丘脑和垂体微小 RNAs 调控生殖功能的研究进展

贺璟 张善辉 王平平

泰州市第二人民医院检验科 225500

通信作者: 王平平, Email: wangpingping1972@126.com, 电话: +86-523-88112101

【摘要】 微小 RNAs(microRNAs, miRNAs) 是一类非编码 RNAs, 可通过靶标基因发挥多种生物功能。miRNAs 调控生殖功能的早期研究集中在性腺水平, 近年来的研究也有报道下丘脑和垂体 miRNAs 也能够调控生殖过程。在下丘脑中, miRNA-9 和 miRNA-200 家族能够调控促性腺激素释放激素神经元迁移, miRNA-155 和 miRNA-200 家族调控微小青春期, let-7 参与青春期启动。在垂体中, miRNA-200b/miRNA-429、miRNA-7a2 和 miRNA-132/miRNA-212 等参与调控垂体促性腺激素分泌, miRNA-27 等调控垂体细胞凋亡。这些研究使得 miRNAs 对生殖的调节从性腺水平提升到下丘脑 - 垂体 - 性腺轴的神经内分泌水平。本文就下丘脑和垂体 miRNAs 在生殖调控中的作用作一综述。

【关键词】 微小 RNAs; 下丘脑; 垂体; 生殖

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Review of microRNA regulation on reproduction in hypothalamus and pituitaries

He Jing, Zhang Shanhu, Wang Pingping

Department of Clinical Laboratory, Taizhou Second People's Hospital, Taizhou 225500, China

Corresponding author: Wang Pingping, Email: wangpingping1972@126.com, Tel: +86-523-88112101

【Abstract】 MicroRNAs (miRNA) belong to small, non-coding RNAs, which are involved in multiple biological processes by binding to target genes. Previous researches on miRNA regulating reproduction are restricted to the gonadal level. Recent novel findings illustrate that miRNAs in hypothalamus and pituitaries are also involved in reproduction regulation. In hypothalamus, miRNA-9 and miRNA-200 family can regulate GnRH neuron migration; miRNA-155 and miRNA-200 family regulate mini-puberty; let-7 is involved in puberty activation. In pituitary, miRNA-200b/miRNA-429, miRNA-7a2 and miRNA-132/miRNA-212 participate in regulating gonadotropin expression; miRNA-27 is fundamental for apoptosis of pituitary cells. These researches have improved the insights of miRNAs' roles in reproduction from the single gonadal level to the neuroendocrinology level of hypothalamus-pituitary-gonadal axis. In this review, we summarized the regulation of hypothalamic and pituitary miRNAs on reproduction.

【Key words】 MicroRNAs; Hypothalamus; Pituitary; Reproduction

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N6- 甲基腺苷在生殖领域研究进展

李玮¹ 郝翠芳²

¹ 青岛大学 266071; ² 青岛大学附属烟台毓璜顶生殖医学中心 264000

通信作者: 郝翠芳, Email: cuifang-hao@163.com, 电话: +86-18605359669

【摘要】 作为 RNA 上最丰富的一种甲基化修饰, N6- 甲基腺苷 (N6-methyladenosine, m⁶A) 广泛存在于生物界, 随着新技术的发展, m⁶A 相关结构、甲基转移酶, 去甲基化酶、m⁶A 结合蛋白被陆续发现, 其对 mRNA 及非编码 RNA 的重要生物学作用受到越来越多的重视。女性生殖健康是目前备受关注的医学问题, 本文就 m⁶A 对配子发生、合子发育的作用及对多囊卵巢综合征、早发卵巢功能不全、生殖道肿瘤的影响进行阐述。

【关键词】 N6- 甲基腺苷; 配子发生; 合子发育; 妇科内分泌疾病; 生殖系统肿瘤

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Research progress of N6-methyladenosine in reproduction area

Li Wei¹, Hao Cuifang²

¹Qingdao University Qingdao, Qingdao 266071, China; ²Reproductive Medicine Center, Affiliated Yantai Yuhuangding Hospital of Qingdao University, Yantai 264000, China

Corresponding author: Hao Cuifang, Email: cuifang-hao@163.com, Tel: +86-18605359669

【Abstract】 Among various RNA methylations, N6-methyladenosine (m⁶A) is the most common one. m⁶A is ubiquitous in diverse biological-process. Because of the development of new technologies, structures of m⁶A methyltransferases, demethylases and binding proteins were discovered in succession. Close attention was paid on m⁶A for its important biological functions to mRNA and non-coding RNA. The health of reproduction is growing concern in the medical field. In this paper, we reviewed the latest research of m⁶A's significant influences on gametogenesis; zygote development, gynecological endocrine disease and reproductive system tumor.

【Key words】 N6-methyladenosine; Gametogenesis; Zygote development; Gynecological endocrine disease; Reproductive system tumor

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移动医疗在生殖健康中的应用研究现状

雷林 朱文兵

中南大学基础医学院生殖与干细胞工程研究所, 长沙 410078

通信作者: 朱文兵, Email: zhuwenbing0971@sina.com, 电话: +86-18673159292

【摘要】 近年来移动医疗作为现代医疗模式与移动互联网技术相结合的产物, 得到飞速发展, 有着十分广阔的市场应用前景。移动医疗广泛应用于糖尿病、过敏及哮喘等疾病, 但在生殖健康领域的应用效果不明确。本文结合国内外移动医疗在男性和女性生殖健康中的应用情况, 从移动医疗的有效性、可行性、可接受性等方面进行综述, 并对移动医疗的前景作出展望。

【关键词】 移动医疗; 生殖健康; 应用程序

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Research progress of application of mobile health in reproductive health

Lei Lin, Zhu Wenbing

Institute of Reproductive & Stem Cell Engineering, School of Basic Medical Science, Central South University, Changsha 410078, China

Corresponding author: Zhu Wenbing, Email: zhuwenbing0971@sina.com, Tel: +86-18673159292

【Abstract】 In recent years, as a combination of modern medical model and mobile internet technology, mobile health has developed rapidly, which has a very broad market application prospect. Mobile health is widely used in diseases such as diabetes, allergy and asthma, but its effect in the field of reproductive health is not clear. Based on the application of mobile health in male and female reproductive health, this paper summarizes the effectiveness, feasibility and acceptability of mobile health in this field, and looks forward to the prospect of mobile health.

【Key words】 Mobile health; Reproductive health; Applications

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