# 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38卷 第11期 2018年11月25日出版

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

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.rande.en

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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):010-85158180 Email: office@cma.org.cn

### 广告发布登记号

京东工商广登字 20170015 号

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: M389

### 订 购

全国各地邮政局 邮发代号: 4-928

### 邮购

中华生殖与避孕杂志编辑部 200237, 上海市老沪闵路 779 号 电话: 021-64438169, 64438975 Email: randc@sippr.org.cn

每期 20.00 元,全年 240.00 元

### 中国标准连续出版物号 ISSN 2096-2916 CN 10-1441/R

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## CHINESE JOURNAL OF REPRODUCTION AND

## **CONTRACEPTION** (Original title: Reproduction and Contraception)

Established in December 1980 Volume 38, Number 11 November 25, 2018



### **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

Editorial Board of Chinese Journal of Reproduction and Contraception

779 Laohumin Road, Shanghai 200237, China

Tel: 0086-21-64438169 Fax: 0086-21-64438975 http://zhszybyzz.yiigle.com http://www.medline.org.cn

### **Editor-in-Chief**

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### **Publishing**

Chinese Medical Journal Publishing House Co., Ltd

42 Dongsi Xidajie, Beijing 100710, China Tel(Fax):0086-10-85158180 Email: office@cma.org.cn

**Business Book Printing Shop** Shanghai Publishing Printing Co., Ltd.

### **Overseas Distributor**

China International Book Trading Corporation P.O.Box 339, 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

ISSN 2096-2916 CN 10-1441/R

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# 早期卵裂:移植胚胎选择的一个重要评估指标

毛献宝 薛林涛 谭卫红 成俊萍 王世凯 李政达 周亭亭 韦娉嫔 张小慧530021 南宁,广西壮族自治区人民医院生殖医学与遗传中心 通信作者: 谭卫红, Tel: +86-771-2186485, Email: ivftwh@163.com DOI: 10.3760/cma.j.issn.2096-2916.2018.11.001

【摘要】目的 探讨早期卵裂 (EC) 对常规新鲜体外受精 - 胚胎移植 (IVF-ET) 结局的影响,评估 EC 能否作为第 3 日移植胚胎选择的一个评估指标。方法 回顾性队列研究分析 267 个新鲜 IVF-ET 周期,移植胚胎均为第 3 日优质胚胎,根据移植胚胎中 EC 胚胎的数目分为 A 组 (移植 2 枚 EC 胚胎)、B 组 (移植 1 枚 EC 胚胎 +1 枚非 EC 胚胎)和 C 组 (移植 2 枚非 EC 胚胎)。分析比较 3 组之间生化妊娠率、种植率、临床妊娠率、自然流产率、异卵双胎率和活产率的差异。结果 ①患者临床及 IVF 特征各项指标 [ 女方年龄、男方年龄、不孕年限、促排卵方案、获卵数、 $M_{\rm II}$  卵数、受精率、移植胚胎质量和人绒毛膜促性腺激素 (hCG) 扳机日子宫内膜厚度 ]3 组间差异均无统计学意义 (P>0.05)。② A 组与 B 组相比,生化妊娠率较低,种植率、临床妊娠率、每移植周期活产率均较高,但差异均无统计学意义 (P>0.05)。③ B 组与 C 组相比,生化妊娠率和自然流产率较低,种植率、临床妊娠率、每移植周期活产率均较高,但差异均无统计学意义 (P>0.05)。④ A 组与 C 组相比,生化妊娠率和自然流产率较低,种植率、临床妊娠率、每移植周期活产率均较高,其中生化妊娠率 (1.3% 比 8.6%, $\chi^2=4.665$ ,P=0.031)、种植率(42.3% 比 31.7%, $\chi^2=4.315$ , $\chi^2=4.504$  的第 3 日优质胚胎可以获得更高的种植率、临床妊娠率和活产率,因此 EC 应作为第 3 日移植胚胎选择的一个重要评估指标。

【关键词】 早期卵裂 (EC); 体外受精 - 胚胎移植 (IVF-ET); 胚胎选择; 妊娠率; 活产率基金项目: 国家自然科学基金 (81360107); 广西卫计委科研课题 (Z2014193)

Early cleavage: an important evaluating indicator for selecting embryos to transfer Mao Xianbao, Xue Lintao, Tan Weihong, Cheng Junping, Wang Shikai, Li Zhengda, Zhou Tingting, Wei Pingpin, Zhang Xiaohui Reproductive Medical and Genetic Center, the People's Hospital of Guangxi Zhuang Autonomous Region, Nanning 530021, China (Mao XB, Xue LT, Tan WH, Cheng JP, Wang SK, Li ZD, Zhou TT, Wei PP, Zhang XH) Corresponding author: Tan Weihong, Tel: +86-771-2186485, Email: ivftwh@163.com

[Abstract] Objective To investigate the impact of early cleavage (EC) on the outcomes of in vitro fertilization-embryo transfer (IVF-ET) and assess whether EC can be used as an additional parameter for day-3 embryo selection. **Methods** This retrospective cohort study included 267 fresh IVF-ET cycles. The transplanted embryos were day-3 high-quality embryos. According to the number of EC embryos in the transplanted embryos, they were divided into three groups: group A (two EC embryos), group B (one EC embryo and one non-EC embryo) and group C (two non-EC embryos). The differences of biochemical pregnancy rate, implantation rate, clinical pregnancy rate, spontaneous abortion rate, fraternal twins rate and live-birth rate were compared among the three groups. **Results** 1) There was no significant difference among the three groups in clinical and in vitro fertilization characteristics [i.e. female age, male age, infertility duration, ovarian stimulation protocol, egg number, M<sub>II</sub> egg number, fertilization rate, embryo quality and endometrial thickness on the day of human chorionic gonadotropin (hCG) injection (P>0.05). 2) Compared with group B, group A had a lower biochemical pregnancy rate, and higher rates of implantation, clinical pregnancy and live-birth, but the differences were not statistically significant (P>0.05). 3) Compared with group C, group B had lower biochemical pregnancy rate and spontaneous abortion rate, and higher implantation rate, clinical pregnancy rate and live-birth rate, but the differences were not significant (P>0.05). 4) Compared with group C, the biochemical pregnancy rate and the spontaneous abortion rate in group A were lower but the implantation rate, the clinical pregnancy rate and the live-birth rate were higher, and the differences of biochemical pregnancy rate (1.3% vs 8.6%,  $\chi^2$ =4.665, P=0.031), implantation rate (42.3% vs 31.7%,  $\chi^2=4.315$ , P=0.038), clinical pregnancy rate (65.4% vs 49.0%,  $\chi^2$ =4.834, P=0.028) and live-birth rate (51.3% vs 35.6%,  $\chi^2$ =4.504, P=0.034) were statistically significant. Conclusion Transfer of EC day-3 high-quality embryos can achieve higher implantation rate, clinical pregnancy rate and live-birth rate. Therefore, EC can be used as an important evaluating indicator for embryo selection in day-3 transfer.

**【Key words】** Early cleavage (EC); *In vitro* fertilization-embryo transfer (IVF-ET); Embryo selection; Pregnancy rate; Live-birth rate

**Fund program**: National Natural Science Foundation of China (81360107); Scientific Research Project of the Guangxi Zhuang Autonomous Region Health and Family Planning Commission (Z2014193)

# 冷冻膜及冷冻环在人早期胚胎玻璃化冷冻中的应用比较

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DOI: 10.3760/cma.j.issn.2096-2916.2018.11.002

【摘要】目的 探讨冷冻膜和冷冻环 2 种载体行玻璃化冷冻对人卵裂期胚胎和囊胚的效果。方法 用回顾性队列研究分析 912 个解冻复苏周期,比较 2 种载体行玻璃化冷冻后胚胎复苏结局和临床结局的差 异及其相关危险因素。结果 ① 385 枚卵裂期胚胎中,冷冻环组 (n=251) 和冷冻膜组 (n=134) 的胚胎复苏率、 完整胚胎存活率、临床妊娠率、种植率、流产率、移植周期出生率、双胎出生率、早产率及出生男女比率 差异均无统计学意义(P>0.05); 冷冻环组新鲜周期优质胚胎率(24.78%)、平均移植周期数(1.3±0.6)、复苏后 优质胚胎率 (40.76%)、复苏后平均移植胚胎数 [(2.1±0.4) 个] 及低体质量儿出生率 (19.01%) 均明显高于冷冻 膜组 [18.59%, P=0.002; 1.2±0.4, P=0.001; 28.13%, P=0.001; (1.9±0.4) 个, P=0.000; 4.08%, P=0.015]。 ② 527 枚囊胚中,冷冻环组 (n=287) 和冷冻膜组 (n=240) 的平均移植周期数、胚胎复苏率、完整胚胎存活率、 复苏后囊胚扩张率、流产率、双胎出生率、早产率、低体质量儿出生率及出生男女比率差异均无统计学意 义 (P>0.05); 冷冻环组的临床妊娠率 (67.94%)、种植率 (49.72%)、移植周期出生率 (52.96%)、新鲜周期优质 胚胎率 (27.0%)、平均移植胚胎数  $[(1.9\pm0.4) \land ]$  显著高于冷冻膜组 [54.17%, P=0.001; 39.58%, P=0.002;41.25%, P=0.047; 23.0%, P=0.002; (1.8±0.5) 个, P=0.004]。Logistic 回归显示, 新鲜周期优质胚胎数、 内膜厚度及冷冻胚胎所用载体类型与冷冻囊胚复苏移植后临床妊娠密切相关 (P=0.017、P=0.049、P=0.044), 而年龄、复苏后平均移植胚胎个数、复苏后囊胚扩张数、平均移植周期数及内膜分型等差异均无统计学意 义(P>0.05)。结论 对于卵裂期胚胎,冷冻膜和冷冻环冷冻胚胎的复苏结局和临床结局均是相当的。对于囊 胚,冷冻环组的临床结局优于冷冻膜组。

【关键词】 玻璃化冷冻载体;冷冻膜;冷冻环;卵裂期胚;囊胚

基金项目: 首都临床特色应用研究与成果推广项目(Z171100001017130)

### A comparative study of using the cryotop and cryoloop in vitrification of human preimplantation embryos

Shi Cheng, Wang Shan, Liang Rong, Yang Mei, Wang Ping, Duan Shengnan, Shen Huan, Chen Xi Reproductive Medicine Center, Peking University People's Hospital, Beijing 100044, China (Shi C, Wang S, Liang R, Wang P, Duan SN, Shen H, Chen X); Reproductive Medicine Center, Beijing Perfect Family Hospital, Beijing 100034, China (Yang M)

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[Abstract] Objective To compare the effect of vitrification on human cleaved embryos and blastocysts using cryotop and cryoloop. **Methods** Retrospectively cohort analysis on the documents of 912 frozen embryo transfer (FET) cycles was performed to find out the differences and the potential factors in the embryo developmental and clinical results after vitrification with cryotop and croloop. Results For frozen-thawed cleavage embryos (n=385), no differences were found between the two groups (cryoloop, n=251; cryotop, n=134) in survival rate, fully intact blastomere rate, clinical pregnancy rate, implantation rate, miscarriage rate, delivery rate per transfer, twin birth rate, premature birth rate and ratio of male to female infant. The good-quality embryo rate in fresh (24.78%) and frozen-thawed cycles (40.76%), the number of ET cycles (1.3 $\pm$ 0.6), the mean number of frozen-thawed transferred embryos  $(2.1\pm0.4)$  and low birth weight rate (19.01%) in the cryoloop group were significantly higher than those in the cryotop group (18.59%, P=0.002; 28.13%, P=0.001; 1.2 $\pm$ 0.4, P=0.001;  $1.91\pm0.41$ , P=0.000; 4.08%, P=0.015). For frozen-thawed blastocysts (n=527), no differences were found between the two groups (cryoloop, n=251; cryotop, n=134) in the number of ET cycles, survival rate, fully intact blastocyst rate, expanded frozen-thawed blastocyst rate, miscarriage rate, twin birth rate, premature birth rate, low birth weight rate and ratio of male to female infants. However, the clinical pregnancy rate (67.94%), the implantation rate (49.72%), the delivery rate per transfer (52.96%), the good-quality embryo rate in fresh cycles (27.0%) and the mean number of frozen-thawed transferred embryos (1.9 $\pm$ 0.4) in the cryoloop group were significantly higher than those in the cryotop group (54.17%, P=0.001; 39.58%, P=0.002; 41.25%, P=0.047; 23.0%, P=0.002; 1.8 $\pm$ 0.5, P=0.004). The further binary logistic analysis confirmed that the number of good-quality embryos in fresh cycles, the type of loading embryos in vitrification (cryoloop or cryotop) and the thickness of endometrium were potential factors of clinical pregnancy in vitrification-thawed blastocysts ET cycles (P=0.017, P=0.049, P=0.044). There were no differences in the age, the mean number of vitrificationthawed transferred embryos, the number of expanded vitrification-thawed blastocyst, the number of ET cycles and the type of endometrium. Conclusion Both vitrification-thawed survival and clinical outcome equal between cryotop and cryoloop in day 3 cleavage embryos cryopreservation embryo-transfer cycles; for blastocyst cryopreservation embryo-transfer cycles, the clinical outcomes in cryoloop group are superior to cryotop group.

**Key words** Vitrification carrier; Cryotop; Cryoloop; Cleavage embryo; Blastocyst

Fund program: Application of Clinical Features of Capital Special Subject (Z171100001017130)

# 子宫内膜异位症生育指数对子宫内膜异位 症合并内膜息肉宫腹腔镜术后自然妊娠结 局的评估价值

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【摘要】目的 研究子宫内膜异位症 (EMS) 与内膜息肉 (EPs) 的关系,并探讨 EMS 生育指数 (EFI) 评分对 EMS 合并 EPs 患者生育力的评估价值。方法 回顾性分析接受宫、腹腔联合手术治疗的 248 例 EMS 相关不孕患者的临床资料,按是否合并 EPs 分为息肉组 (105 例)和非息肉组 (143 例),随访并比较其妊娠情况和妊娠结局。结果 EMS 患者 EPs 的发生率为 42.3%,中重度 EMS 患者 (III~IV期) EPs 的发生率 (50.8%)略高于轻度患者 (I~II期)(39.6%),但差异无统计学意义 (P>0.05)。EFI 评分越高,在同一 EFI 分值中,合并 EPs 的患者所占比例越低,差异有统计学意义 (P=0.000)。息肉组术后的自然妊娠率 (37.1%)、活产率 (27.6%)均低于非息肉组 (57.3%,P=0.002;48.3%,P=0.001)。同一 EFI 分值,息肉组的妊娠率低于非息肉组,但差异无统计学意义 (P>0.05)。息肉组与非息肉组组内比较,EFI 分值越高,妊娠率越高,差异有统计学意义 (P=0.000)。96.7%患者多在术后 2 年内成功妊娠,息肉组术后 1 年内妊娠 35 例,占其妊娠总人数的 89.7%,高于非息肉组的 73.1%,差异有统计学意义 (P=0.038)。结论 EPs 在 EMS 合并不孕患者中的发生率明显升高。宫、腹腔镜联合手术治疗能明显提高 EMS 合并 EPs 患者的生育力,术后 2 年内是妊娠的最佳时期;EFI 评分对合并 EPs 的 EMS 患者术后生育力的评估价值有待商榷。

【关键词】子宫内膜异位症 (EMS);内膜息肉 (EPs);不孕症;腹腔镜;子宫内膜异位症生育指数 (EFI)

基金项目: 重庆市基础研究与前沿探索项目 ( 重庆市自然科学基金 )(cstc2018jcyjax0648)

Predictive value of endometriosis fertility index in natural pregnancy outcome of patients with endometriosis and endometrial polyps after hysteroscopy combined with laparoscopic surgery Feng Xue,

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[Abstract] Objective To investigate the relationship of endometrial polyps (EPs) and endometriosis (EMS), and evaluate the predictive value of EMS fertility index (EFI) for women's fertility with EMS combined with EPs. Methods A total of 248 infertile patients with EMS and EPs who underwent laparoscopic and hysteroscopic surgery were analyzed. The patients were divided into EPs group and non-EPs group. Then the pregnancy outcome was compared between the two groups. Results The incidence of EPs was 42.3%. The incidence of EPs in patients with moderate to severe EMS (stages III-IV) was slightly higher than that in mild patients (stages I-II), but there was no significant difference between the two groups (P>0.05). The higher the EFI score, the lower the proportion of patients with EPs in the same EFI score, the difference was statistically significant (P=0.000). The natural pregnancy rate (37.1%) and the live birth rate (27.6%) were lower in the EPs group than in the non-EPs group (57.3%, P=0.002; 48.3%, P=0.001). At the same EFI score, the pregnancy rate of the EPs group was lower than that of the non-EPs group, but there was no statistical difference (P>0.05). Within the EPs group and non-EPs group, the spontaneous pregnancy rate increased with increasing EFI score, the difference was statistically significant (P=0.00). Most of the patients got pregnant within 2 years after operation (96.7%). The EPs group had 35 pregnancies within 1 year, accounting for 89.7% of the total number of pregnancies, which was higher than that in the non-EPs group of 73.1%, the difference was statistically significant (P=0.038). Conclusion There was a higher incidence of EPs among infertile patients with EMS. Hysteroscopy combined with laparoscopic surgery can significantly improve fertility for patients with EMS and EPs. The best time for pregnancy was within 2 years after surgery. The value of EFI score for predicting pregnancy rate for women with EMS and EPs remains to be discussed.

**[Key words]** Endometriosis (EMS); Endometrial polyps (EPs); Infertility; Laparoscopy; Endometriosis fertility index (EFI)

**Fund program:** Chongqing Basic Research and Frontier Exploration Project (Chongqing Natural Science Fund) (cstc2018jcyjax0648)

# 孕早期促甲状腺素和 β- 人绒毛膜促性腺 激素联合预测子痫前期的应用价值

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DOI: 10.3760/cma.j.issn.2096-2916.2018.11.004

【摘要】目的 评价在孕早期应用促甲状腺素 (thyroid stimulating hormone, TSH) 和 β- 人绒毛膜促性腺 激素 (β-human chorionic gonadotropin, β-hCG) 联合预测子痫前期 (preeclampsia, PE) 的诊断价值。方法 对 有早期产检并分娩的 368 例产妇的资料进行回顾性队列研究分析,根据是否发生 PE 分为 PE 组 (52 例 ) 和 对照组 (316 例 ), 分析患者一般资料、甲状腺功能、β-hCG 以及妊娠相关血浆蛋白 A(pregnancy-associated plasma proteins A, PAPP-A) 等指标,并以临床诊断作为"金标准",应用受试者工作特征 (receiver operating characteristic, ROC) 曲线比较不同指标对于预测 PE 的诊断价值以及诊断效能。结果 单因素分析显示, PE 组产妇的孕前体质量指数 [BMI, (24.41±2.11) kg/m<sup>2</sup>]、TSH[(2.79±0.83) mIU/L]、PAPP-A[(1.27±0.28) mIU/L)] 水平明显高于对照组 [(23.72 $\pm$ 1.96) kg/m², (1.99 $\pm$ 0.53) mIU/L, (0.98 $\pm$ 0.39) mIU/L](P=0.021、0.000、 0.000),而 β-hCG 水平 [(3.06±1.72)×10<sup>4</sup> IU/L] 显著低于对照组 [(5.48±2.29)×10<sup>4</sup> IU/L](P=0.000)。 Logistic 回 归 分 析 显 示, TSH(OR=15.423, 95% CI=12.963~59.162, P=0.000) 和 PAPP-A(OR=9.794, 95% CI=4.195~22.867, P=0.000) 是 PE 的 独 立 危 险 因 素, β-hCG(OR=0.889, 95% CI=0.853~0.927, P=0.000) 是 PE 的保护因素。ROC 曲线显示, TSH 和 β-hCG 预测 PE 的曲线下面积 (AUC=0.780, 0.788) 高于 PAPP-A(AUC=0.705) 和孕前 BMI(AUC=0.575), Youden 指数得出 TSH 和 β-hCG 的最佳截点 分别为 TSH  $\geq$  2.54 mIU/L 和 β-hCG  $\leq$  3.96×10<sup>4</sup> IU/L; 应用 TSH 联合 β-hCG(AUC=0.927) 的诊断价值 明显高于两者单独预测。TSH 联合 β-hCG 预测 PE 的敏感度为 96.15%,均显著高于 TSH 的 84.62% 和 B-hCG 的 82.69%(χ²=3.983、4.981; P=0.046、0.026), 而诊断准确率差异均无统计学意义(χ²=0.363、 3.160; P=0.547、0.075)。 **结论** 在孕早期应用 TSH 和 β-hCG 联合预测 PE 具有较高的应用价值,其中 TSH  $\geq$  2.54 mIU/L 和 β-hCG  $\leq$  3.96×10<sup>4</sup> IU/L 是较好的截点。

【关键词】 促甲状腺素 (TSH); 人绒毛膜促性腺激素 (hCG); 子痫; 子痫前期 (PE); 敏感度; 特异度

Value of thyroid stimulating hormone combined with β-human chorionic gonadotropin in the prediction of preeclampsia in the first trimester of pregnancy

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[Abstract] Objective To observe the value of thyroid stimulating hormone (TSH) combined with β-human chorionic gonadotropin (β-hCG) in the prediction of preeclampsia (PE) in the first trimester of pregnancy. **Methods** A retrospectively cohort analysis was performed on 368 pregnant women who had undergone early clinical examination and delivery. The patients were divided into PE group (52 cases) and control group (316 cases) according to whether PE occurred. The general data, thyroid function, β-hCG and pregnancy-associated plasma protein A (PAPP-A) were comparatively analyzed. Using the clinical diagnosis as the "golden standard", the receiver operating characteristic (ROC) curves were used to compare the diagnostic value and diagnostic efficacy of those indicators for predicting adverse pregnancy outcomes. **Results** Univariate analysis showed that pre-pregnancy body mass index [BMI,  $(24.41 \pm 2.11) \text{ kg/m}^2$ ], TSH [ $(2.79 \pm 0.83) \text{ mIU/L}$ ] and PAPP-A [(1.27 ± 0.28) mIU/L)] levels in PE group were significantly higher than those in control group  $[(23.72\pm1.96) \text{ kg/m}^2, (1.99\pm0.53) \text{ mIU/L}, (0.98\pm0.39) \text{ mIU/L}](P=0.021, 0.000, 0.000), \text{ while } \beta\text{-hCG}$ level  $[(3.06\pm1.72)\times10^4\,\text{IU/L}]$  was significantly lower than that in control group  $[(5.48\pm2.29)\times10^4\,\text{IU/L}]$ (P=0.000). Multivariate logistic regression analysis showed that TSH (OR=15.423, 95% CI=12.963~59.162, P=0.000) and PAPP-A (OR=9.794, 95% CI=4.195~22.867, P=0.000) were independent risk factors for PE, while  $\beta$ -hCG (OR=0.889, 95%  $CI=0.853\sim0.927$ , P=0.000) was a protective factor of PE. ROC curves showed that the area under the curve of TSH and β-hCG (AUC=0.780, 0.788) was higher than that of PAPP-A (AUC=0.705) and pre-pregnancy BMI (AUC=0.575), the Youden index showed that the best cut-off of TSH and β-hCG were TSH  $\geqslant 2.21$  mIU/L and β-hCG  $\leqslant 3.96 \times 10^4$  IU/L. The diagnostic value of TSH combined with β-hCG (AUC=0.927) was significantly higher than that of TSH or β-hCG alone. The sensitivity of TSH combined with β-hCG in predicting PE was 96.15%, which was significantly higher than that of TSH and  $\beta$ -hCG ( $\chi^2$ =3.983, 4.981; P=0.046, 0.026), while no statistical differences were found in the diagnostic accuracy  $(\chi^2=0.363, 3.160; P=0.547, 0.075)$ . Conclusion TSH combined with  $\beta$ -hCG have a high value in the prediction of PE in the first trimester of pregnancy, of which the best cut-off of TSH and  $\beta$ -hCG are TSH  $\geq 2.21$  mIU/L and  $\beta$ -hCG  $\leq 3.96 \times 10^4$  IU/L, respectively.

**Key words** Thyroid stimulating hormone (TSH); Human chorionic gonadotropin (hCG); Preeclampsia (PE); Eclampsia; Sensitivity; Specificity

·实验研究 ·

## dl- 扁桃酸热敏凝胶对兔阴道黏膜 炎症反应的研究

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【摘要】目的 探讨 dl- 扁桃酸热敏凝胶 (dl-mandelic acid thermosensitive in situ gel,MA Gel) 对兔阴 道黏膜的刺激性及炎症反应情况。方法 将 40 只雌兔随机分为基质对照组、MA Gel 低剂量组 (10 g/L)、MA Gel 中剂量组 (20 g/L)、MA Gel 高剂量组 (40 g/L) 和市售壬苯醇醚凝胶 (nonoxynol 9,N-9 Gel) 组,每组 8 只,阴道给药 2.5 mL,qd,连续 10 d。在给药前、给药第 4 日以及末次给药后 24 h 与 72 h,收集基质对照组、MA Gel 高剂量组和 N-9 Gel 组阴道灌流 (cervicovaginal lavage,CVL) 液,流式细胞仪计数 CVL 中炎性细胞和中性粒细胞数目,并对 CD45<sup>+</sup>细胞进行分析。取阴道组织做组织病理切片,免疫组织化学检测阴道黏膜内 CD45 的表达。结果 MA Gel 高剂量组 CVL 液中炎性细胞、中性粒细胞以及 CD45<sup>+</sup>细胞数目显著低于 N-9 Gel 组 (P=0.036)。MA Gel 各剂量组与基质对照组相比,阴道黏膜 CD45<sup>+</sup>表达无显著上升,主要表达在黏膜上皮层。结论 dl-扁桃酸热敏凝胶仅引起家兔阴道黏膜较轻微的炎症反应,未诱导局部炎性细胞的明显活化,安全性较好,具有研发成为阴道外用避孕药的前景。

【关键词】 dl- 扁桃酸; 流式细胞术; 阴道灌流液; 炎症细胞; CD45

基金项目: 国家重点研发计划 (2016YFC1000905); 国家科技重大专项 (2018ZX10301403-005-001); 上海市卫生和计划生育委员会重点学科建设项目 (15GWZK0201); 上海市科委实验动物专项 (1514091200); 上海市科委生物医药科技支撑项目 (18431900200); SIPPR 攀登计划 (PD2017-8)

•实验研究•

### Vaginal mucosa immune inflammatory response of dl-mandelic acid thermosensitive in situ gel in rabbits

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**[Abstract]** Objective To study the vaginal mucosal irritation and inflammatory response of dl-mandelic acid thermosensitive *in situ* gel (MA Gel) in rabbits. **Methods** Forty female rabbits were randomly divided into 5 groups: matrix control group, MA Gel low-dose group (10 g/L), MA Gel middle-dose group (20 g/L), MA Gel high-dose group (40 g/L), and nonoxynol 9 (N-9) Gel group. Gels were administered to rabbits through vagina at 2.5 mL once a day for 10 consecutive days. Cervicovaginal lavage (CVL) fluid of matrix control group, MA Gel high-dose group and N-9 Gel group was collected at 4 different time-points (before administration, 4th day of administration, 24 h and 72 h after last administration). The number of inflammatory cells, neutrophilic granulocytes, and CD45<sup>+</sup> cells in CVL was detected by flow cytometry. The vaginal tissue was taken for histopathological slices and immunohistochemistry was used to detect CD45<sup>+</sup> cells in vaginal mucosa. **Results** The number of inflammatory cells, neutrophilic granulocytes and CD45<sup>+</sup> cells of MA Gel high dose group was significantly lower than that of N-9 Gel group (*P*=0.036). Compared with the matrix control group, the number of CD45<sup>+</sup> cells in all MA Gel groups showed no significant increase, and the CD45<sup>+</sup> cells mainly located in the vaginal epithelium. **Conclusion** MA Gel caused far lower vaginal mucosal irritation in rabbits than N-9 Gel, and it was not likely to induce significant local activation of inflammatory cells. Owing to its promising pharmaceutical effects and safety profile, MA Gel has the potential to be developed as a novel spermicide.

**[Key words]** dl-mandelic acid; Flow cytometry; Cervicovaginal lavage fluid; Inflammation cell; CD45

Fund program: National Key Research and Development Plan (2016YFC1000905); National Science and Technology Major Project (2018ZX10301403-005-001); Shanghai Key Academic Discipline Project on Environmental Health and Occupational Health (15GWZK0201); Special Project for Experimental Animals of STCSM (1514091200); Biomedical Technology Support Project of STCSM (18431900200); "Climbing" Program of SIPPR (PD2017-8)

·流行病学研究 ·

## 听力障碍学生生殖健康知识状况调查

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DOI: 10.3760/cma.j.issn.2096-2916.2018.11.006

【摘要】目的 了解城市和农村地区听力障碍学生的生殖健康知识现状、获取途径和障碍,为加强听力障碍学生性与生殖健康教育提供科学依据。方法:采用定性研究和定量研究相结合的方法在上海市区和陕西农村地区进行调查。定性研究包括对 4 组听障学生的小组访谈,对 7 名听力障碍学生家长和 7 名学校老师的个人深入访谈;定量研究包括 4 所特殊学校 207 名 15~24 岁听力障碍学生的匿名问卷调查。结果 听力障碍学生生殖生理知识、艾滋病知识和避孕知识水平均较低,对月经和遗精的知晓情况分别为 21.26% 和 41.55%;对艾滋病传播途径的知晓率为 47.83%~62.32%;分别有 17.87% 和 20.29% 的调查对象没有听说过任何避孕方法和不知道从何处获取避孕药具。各类知识知晓情况均是城市高于农村。听力障碍学生生殖健康知识来源主要为学校、同伴、父母和网络,希望获取知识的途径与之类似,在获取生殖健康知识过程中存在的主要困难是"不知道从哪里获取知识"(42.51%)、"不好意思去了解这方面的知识"(41.06%)。结论 听力障碍学生生殖健康知识十分匮乏,特别是农村学生,应重视和加强听力障碍学生性与生殖健康教育。

【关键词】听力障碍;青少年;学生;生殖健康;知识

基金项目:联合国教科文组织驻华代表处项目 (4500251526-A1); 上海市卫生和计划生育委员会资助项目 (201540091)

### ·流行病学研究 ·

**Sexual and reproductive health knowledge of students with hearing impairment** *Qi Wenjuan, Hu Tajing, Li Hongyan, Lou Chaohua, Lian Qiguo, Zuo Xiayun, Tu Xiaowen* 

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[Abstract] Objective To understand sexual and reproductive health (SRH) knowledge, accessibility and access barriers to SRH information among students with hearing impairment in urban and rural areas. Methods Qualitative and quantitative methods were employed to collect data in Shanghai and rural Shaanxi province. Semi-structured focus group interview was adopted for 4 groups of students with hearing impairment, and in-depth interview was adopted for 7 parents and 7 teachers. A total of 207 students with hearing impairment aged 15 to 24 years from 4 special schools were surveyed using anonymous questionnaires. Results Hearing impaired students had poor knowledge about sexual physiology, human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS) and contraception, Respectively 21.26% and 41.55% were aware of menstruation and spermatorrhea. Ranged from 47.83% to 62.32% students knew transmission routes of AIDS. About 17.87% and 20.29% of the respondents didn't know any kind of contraceptive methods and where to obtain contraceptives, respectively. Urban students had better awareness about each category of SRH knowledge than rural students. The main sources of SRH knowledge of students with hearing impairment were schools, peers, parents and internet. Their preferred channels to obtain SRH knowledge were similar to their main sources. The main difficulties they faced in accessing information on SRH were "don't know where to acquire the knowledge" (42.51%), "feel embarrassed to get the knowledge" (41.06%). Conclusion hearing impairment severely lacked SRH knowledge, especially those in rural areas. More attention should be paid to strengthen SRH education among hearing impaired students.

**[Key words]** Hearing impairment; Adolescents; Students; Reproductive health; Knowledge **Fund program**: UNESCO Beijing Office (4500251526-AI); Shanghai Municipal Commission of Health and Family Planning (201540091)

·循证医学 ·

# 添加重组黄体生成素对高龄患者体外受精 - 胚胎移植妊娠结局影响的 Meta 分析

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【摘要】目的 评价高龄患者添加重组黄体生成素 (rLH) 的必要性。方法 计算机检索 PubMed、EMbase、Ovid Medline、Cochrane Library 等中外生物医学数据库。筛选出高龄患者促排卵方案中是否添加 rLH 的随机对照研究 (RCTs)。按 Cochrane 系统评价的方法对所纳入的研究进行质量评价,并提取相关数据,采用 RevMan5.3 软件进行分析。结果 共纳入 9 个 RCTs,1 469 例患者,试验组 736 例,对照组 733 例。Meta 分析结果显示:高龄患者添加 rLH 对临床妊娠率 (RR=1.00, 95%  $CI=0.84\sim1.19$ , P=0.97)、活产率 (RR=1.01, 95%  $CI=0.84\sim1.23$ , P=0.88)、种植率 (RR=1.01, 95%  $CI=0.74\sim1.38$ , P=0.94) 及早期流产率 (RR=1.10, 95%  $CI=0.71\sim1.69$ , P=0.68) 无影响,但降低了获卵数 (WMD=-1.55, 95%  $CI=0.71\sim1.78\sim1.31$ ,  $P<0.000\ 01$ ) 及激动剂方案中  $M_{\parallel}$  卵数 (WMD=-1.40, 95%  $CI=0.71\sim1.01$ ,  $P<0.000\ 01$ )。结论 高龄患者添加 rLH 会减少获卵数及激动剂方案中的  $M_{\parallel}$  卵数,但对临床妊娠率、活产率、种植率及早期流产率无影响。

【关键词】 重组黄体生成素 (rLH); 高龄; 体外受精 - 胚胎移植 (IVF-ET); 妊娠结局; Meta 分析基金项目: 新疆维吾尔自治区自然科学基金 (2017D01C284)

### ·循证医学·

Effect of recombinant luteinizing hormone supplementation on the pregnancy outcome of elderly women undergoing in vitro fertilization-embryo transfer: a Meta-analysis Wang Zhihui, Gong Xiaoyun, Zhao Jing, Hu Bo, Wang Peng, Zhu Yuejie, La Xiaolin

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**[Abstract] Objective** To evaluate the necessity of recombinant luteinizing hormone (rLH) supplementation in elderly women. **Methods** We electronically searched biomedical databases such as Pubmed, EMbase, Ovid Medline and Cochrane library. Randomized controlled trials (RCTs) were identified about rLH supplementation in women of 35 years or older. Study selection and Meta-analysis were conducted which according to the Cochrane Handbook for systematic reviews. Date were extracted from these trials by 3 reviewers independently and analyzed by RevMan5.3 software. **Results** A total of 9 RCTs involving 1 469 cases were included, of which 736 cases were in experimental group while the other 733 cases were in control group. Meta-analysis indicated that, rLH supplementation had no beneficial on the clinical pregnancy rate (*RR*=1.00, 95% *CI*=0.84-1.19, *P*=0.97), the live-birth rate (*RR*=1.01, 95% *CI*=0.84-1.23, *P*=0.88), the implantation rate (*RR*=1.01, 95% *CI*=0.74-1.38, *P*=0.94) and the early miscarriage rate (*RR*=1.10, 95% *CI*=0.71-1.69, *P*=0.68). However, it reduced the No. of oocytes retrieved (WMD=-1.55, 95% *CI*=-1.78--1.31, *P*<0.000 01) in both groups and metaphase II oocytes (WMD=-1.40, 95% *CI*=-1.79--1.01, *P*<0.000 01) in patients with GnRH agonist protocol. **Conclusion** rLH supplementation can significantly reduce the No. of oocytes retrieved in both groups and metaphase II oocytes in patients with a GnRH agonist protocol, and no significant differences were found between the two groups in parameters of pregnancies.

**[Key words]** Recombinant LH (rLH); Advanced age; *In vitro* fertilization-embryo transfer (IVF-ET); Pregnancy outcome; Meta-analysis

Fund program: Natural Science Foundation of Xinjiang Uygur Autonomous Region (2017D01C284)

·循证医学 ·

# 透明质酸钠凝胶预防人工流产术后宫腔 粘连有效性及安全性的 Meta 分析

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【摘要】目的 系统评价透明质酸钠凝胶预防人工流产术后宫腔粘连 (IUA) 的有效性及安全性。方法 检索 PubMed 数据库、Springer 电子期刊数据库、Cochrane 图书馆、Elsevier ScienceDirect 数据库、CNKI数据库、万方数据库、维普数据库,查找关于透明质酸钠凝胶预防人工流产术后 IUA 的有效性及安全性的随机对照试验 (randomized controlled trial,RCT) 文献,检索时限自各数据库建库至 2017 年 12 月。按纳入和排除标准进行文献筛选、资料提取和质量评价后,采用 ReVman5.3 软件进行 Meta 分析。结果 最终共纳入 14 篇 RCT 文章。Meta 分析结果显示:试验组术后 IUA 以及粘连严重程度的发生率均较对照组低,差异均有统计学意义 (P<0.000 01);与对照组相比,试验组术后阴道流血时间短,量少,月经复潮时间短,且月经经量减少、闭经、周期性下腹痛等发生率更低,差异有统计学意义 (P<0.000 01)。结论 人工流产术后应用透明质酸钠凝胶可降低 IUA 的发生率,减轻粘连严重程度,促进子宫恢复以及减少术后并发症的发生。

【关键词】 宫腔粘连 (IUA); 透明质酸钠凝胶; Meta 分析

基金项目: 国家自然科学基金 (81402404, 81403163); 宜昌市科技攻关项目 (A14301-04)

·循证医学 ·

Clinical efficacy and safety of sodium hyaluronate gel in the prevention of intrauterine adhesions after induced abortion: a Meta-analysis Xie Yan, Liu Qiang, Luo Youzhen, Zhou Yuanhong

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**[Abstract]** Objective To investigate the clinical effectiveness and safety of sodium hyaluronate gel in preventing intrauterine adhesion (IUA) after surgical abortion. Methods The databases including Pubmed database, Springer database, Cochrane library, Elsevier ScienceDirect database, CNKI database, Wanfang database, VIP database were systematically searched to collect the randomized control trail (RCT) about sodium hyaluronate gel in preventing IUA after artificial abortion, the retrieval time is from the building of each database to December 2017. According to the inclusion and exclusion criteria to search studies, data extraction and quality assessments were performed. RevMan 5.3 software was used for Meta-analysis. Results Fourteen RCTs were included. Meta-analysis showed that compared with control group, the incidence of IUA and the 3 stages (mild, moderate and severe) of adhesion in experimental group were statistically lower (P<0.000 01). In experimental group, the lasting time and the amount of vaginal bleeding after operation were less, the time of menstruation turnover was shorter, the incidence of hypomenorrhea, amenorrhea and the periodic hypogastralgia was lower, and all the differences were statistically significant (P<0.000 01). Conclusion Application of sodium hyaluronate gel after induced abortion can reduce the incidence of IUA, moderate the severity of adhesions, promote the recovery of the uterus and reduce postoperative complications.

**Key words** Intrauterine adhesion (IUA); Sodium hyaluronate gel; Meta-analysis

**Fund program**: National Natural Science Foundation (81402404, 81403163); Yichang Science and Technology Project (A14301-04)

## 早卵泡期雌激素补充对高龄无明显窦状卵泡患者的应用价值

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【摘要】目的 探讨早卵泡期雌激素补充对高龄无明显窦状卵泡患者的应用价值。方法 选取行体外受精/卵胞质内单精子显微注射 (IVF/ICSI) 治疗的 24 例高龄无明显窦状卵泡的不孕症患者,比较雌激素补充前、后卵巢储备功能指标的变化;根据所需雌激素补充时长分为 A 组 (1~5 d)、B 组 (6~10 d) 及 C 组 ( $\geq$ 11 d),比较各组促排卵周期相关指标的差异。结果 ①雌激素补充后患者出现卵泡,血清卵泡刺激素 (FSH) 水平 [(16.53±9.74) IU/L] 较基础 FSH 水平 [(24.87±11.02) IU/L] 显著降低 (P=0.032),血清雌二醇 (E2) 水平 [108.90(93.93,222.60) ng/L] 较前 [10.98(0.00,21.23) ng/L] 显著升高,差异均具有统计学意义 (P=0.001)。② A 组、B 组及 C 组患者雌激素补充后卵泡数均依次减少 [2.0(1.5,3.0),1.0(1.0,2.8),1.0(1.0,1.0)](P=0.019),各组的获卵率分别为 80.0%、70.8% 及 28.6%(P=0.039)。3 组间的雌激素补充后 FSH 和 E2 水平、获卵数及正常受精率的差异无统计学意义 (P>0.05)。③线性回归结果显示,雌激素补充时间与基础 FSH 水平呈正相关关系。结论 早卵泡期雌激素补充可能有助于高龄无明显窦状卵泡患者较快募集卵泡,继而获得卵母细胞并形成可移植胚胎,从而改善 IVF/ICSI 结局。

【关键词】 雌激素; 卵巢储备功能减退 (DOR); 体外受精/ 卵胞质内单精子显微注射 (IVF/ICSI)

**基金项目**: 国家自然科学基金 (81401177); 广东省自然科学基金资助项目 (2015A030313286); 南方医院高层次匹配项目基金 (G2014005)

Application of estrogen during early follicular phase to the elderly aged patients without apparent antral follicle Deng Ling, Chen Xin, Ye Desheng, Zhang Jun, Chen Shiling

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[Abstract] Objective To investigate the clinical value of estrogen supplementation during early follicular phase in the advanced aged patients with no apparent antral follicle. Methods Totally 24 elderly patients with no apparent antral follicle were included in the study, the ovarian reserve before and after estrogen supplementation was compared. They were categorized into group A (1-5 d), group B (6-10 d) and group C (≥ 11 d) according to the duration of estrogen administration that inducing follicle recruitment. Ovarian stimulation parameters and in vitro fertilization/intracytoplasmic sperm injection (IVF/ICSI) outcomes were compared among the three groups. Results 1) After estrogen supplementation, follicles appeared and the serum follicle stimulating hormone (FSH) levels  $[(16.53 \pm 9.74) \text{ IU/L}]$  significantly declined compared with the baseline FSH levels  $[(24.87 \pm 11.02) \text{ IU/L}]$ (P=0.032), as well as serum estradiol (E<sub>2</sub>) levels [(108.90 (93.93,222.60) ng/L, 10.98 (0.0,21.23) ng/L, P=0.001)] significantly increased. 2) The number of follicle after estrogen supplementation reduced in series among group A, group B and group C [2.0(1.5,3.0), 1.0(1.0,2.8), 1.0(1.0,1.0)](P=0.019) and the oocyte yield rate was 80.0%, 70.8% and 28.6%, respectively (P=0.039). After estrogen supplementation, the serum FSH and E<sub>2</sub> levels, the number of oocyte yield and normal fertilization rates were not statistically significant among the three groups. 3) The linear regression model identified that the duration of estrogen supplement was positively associated with baseline FSH levels. Conclusion Estrogen supplementation during early follicular phase might facilitate follicular recruitment to achieve oocytes and embryos as well as to improve IVF/ICSI outcomes in elderly aged patients with no apparent antral follicle.

**[Key words]** Estrogen; Diminished ovarian reserve (DOR); *In vitro* fertilization/intracytoplasmic sperm injection (IVF/ICSI)

**Fund program**: Natural Science Foundation of China (81401177); Guangdong Province Natural Science Foundation (2015A030313286); Nanfang Hospital High-level Project Matching Funds (G2014005)

# 激素人工周期联合金凤丸预防宫腔粘连分离术后再粘连的临床疗效观察

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【摘要】目的 观察金凤丸与激素人工周期干预宫腔粘连 (IUA) 分离术后的临床疗效。方法 选取 253 例 IUA 患者的临床资料进行随机对照研究,采用随机数字法分为 3 组,激素人工周期组 (n=83)、金凤丸组 (n=86) 和联合治疗组 (n=84),3 组均连续治疗 2 个月经周期,检测治疗前、后患者的月经情况、宫腔恢复情况及子宫动脉血流动力学指标。结果 激素人工周期组治疗后宫腔再粘连为 24 例,总有效率为 71.1%(59/83),金凤丸组治疗后宫腔再粘连为 11 例,总有效率为 87.2%(75/86),联合治疗组治疗后宫腔再粘连为 3 例,总有效率为 96.4%(81/84),三组间两两比较差异均有统计学意义(激素人工周期组和金凤丸组 P=0.036 8,激素人工周期组和联合治疗组 P=0.016 1,金凤丸组和联合治疗组 P=0.044 9)。与激素人工周期组比较,金凤丸组、联合治疗两组子宫动脉血流动力学指标显著改善(激素人工周期组 和金凤丸组 P=0.016 4,激素人工周期组和 联合治疗组 P=0.009 3)。结论 金凤丸在 IUA 分离术后使用,可改善子宫内膜修复,预防再次粘连的发生,同时与激素人工周期治疗方案具有协同作用,值得临床推广。

【关键词】金凤丸; 宫腔粘连分离术; 激素人工周期; 子宫动脉血流动力学指标

Observation of clinical efficacy of hormone artificial cycle combined with Jinfeng pill in preventing readhesion after uterine cavity adhesion separation *Huang Donghong, Su Sisi, Yin Minghong* 

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[Abstract] Objective To observe the clinical efficacy of Jinfeng pill and post hormone artificial cycle interferes transcervical resection of adhesion. Methods A total of 253 clinical intrauterine adhesions (IUA) patients were selected and analyzed. By using the random number method, they were divided into 3 groups, hormonal artificial cycle group (n=83), Jinfeng pill group (n=86) and combined treatment group (n=84). Situations of menstruation period, uterine cavity recovery and uterine arteries haemodynamic index were compared before and after treatment for 2 continuous menstrual cycle. Results In hormonal artificial cycle group, group B, and group C, there were 24 cases, 11 cases, and 3 cases of IUA again after treatment respectively, the total effective rate was 71.1% (59/83), 87.2% (75/86), and 96.4% (81/84). Pairwise comparisons between the three groups were statistically significant (P=0.036 8 between hormonal artificial cycle group and Jinfeng pill group, P=0.016 1 between hormonal artificial cycle group and combined treatment group, P=0.044 9 between Jinfeng pill group and combined treatment group). Compared with hormonal artificial cycle group, uterine arterial flow mechanical indexes in Jinfeng pill group and combined treatment group were significantly improved (P=0.016 4 between hormonal artificial cycle group and Jinfeng pill group, P=0.009 3 between hormonal artificial cycle group and combined treatment group). Conclusion Jinfeng pill is an effective proposal for improving endometrial repairing and preventing intrauterine re-adhesion, whilst having synergistic effect with hormone artificial cycle proposal which is worth to popularizing in clinic.

**Key words** Jinfeng pill; Transcervical resection of adhesion; Hormone artificial cycle; Uterine arteries haemodynamic index

## 前置胎盘孕妇孕中晚期子宫动脉血流动力学变化的研究

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DOI: 10.3760/cma.j.issn.2096-2916.2018.11.011

【摘要】目的 探讨前置胎盘患者孕中、晚期子宫动脉血流动力学变化规律。方法 选取 105 例孕中、晚期胎盘距宫颈内口距离 <20 mm 的孕妇作为观察对象,监测其 21~26 周、28~31 周双侧子宫动脉收缩期与舒张末期最大血流速度比值 (S/D)、搏动指数 (PI) 及阻力指数 (RI) 的平均值,根据孕末期胎盘位置分为前置胎盘组 (观察组,31 例 ) 和对照组 (74 例 )。结果 观察组 2 次子宫动脉 S/D( $2.13\pm0.36$ 、 $1.87\pm0.24$ )、PI( $0.80\pm0.19$ 、 $0.67\pm0.14$ )、RI( $0.51\pm0.07$ 、 $0.45\pm0.07$ ) 平均值均低于对照组 [S/D( $2.38\pm0.48$ 、 $2.08\pm0.36$ )、PI( $0.94\pm0.25$ 、 $0.80\pm0.19$ )、RI( $0.55\pm0.07$ 、 $0.50\pm0.08$ )],差异均有统计学意义 (P<0.05)。结论 妊娠中晚期子宫动脉血流动力学参数变化与前置胎盘发生有一定相关性。

【关键词】 前置胎盘; 子宫动脉; 超声

Study on hemodynamic changes of uterine artery in patients with placenta previa during the second and the third trimester Wu Yilun, Lu Yu

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**[Abstract]** Objective To investigate the hemodynamic changes of uterine artery in patients with placenta previa during the trimester. **Methods** Totally 105 pregnant women whose placental edge was within 20 mm from the internal os during the second trimester were selected for observation. The systolic to diastolic velocity ratios (S/D), pulsatility index (PI) and resistance index (RI) of uterine artery were measured for all subjects in the second (21st–26th gestational weeks) and the third (28th–31th gestational weeks) trimester. All subjects were categorized into two groups according to the placenta position measured after 36 weeks gestation: placenta previa group (31 cases) and control group (74 cases). **Results** The mean values of S/D (2.13 $\pm$ 0.36, 1.87 $\pm$ 0.24), PI (0.80 $\pm$ 0.19, 0.67 $\pm$ 0.14) and RI (0.51 $\pm$ 0.07, 0.45 $\pm$ 0.07) of the uterine artery in the placenta previa group were lower than those in control group [S/D (2.38 $\pm$ 0.48, 2.08 $\pm$ 0.36), PI (0.94 $\pm$ 0.25, 0.80 $\pm$ 0.19), RI (0.55 $\pm$ 0.07, 0.50 $\pm$ 0.08)] (*P*<0.05). **Conclusion** The changes of uterine arterial blood flow parameters in middle and late pregnancy are correlated with placenta previa.

**Key words** Placenta previa; Uterine artery; Ultrasound

·个案报道·

## 卵母细胞内注射自体骨髓线粒体获得男婴活产1例病例报道

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【摘要】目的 探讨卵母细胞内注射自体骨髓线粒体对不孕患者反复助孕失败的治疗效果。方法 对本中心 1 例反复助孕失败不孕患者的临床资料进行分析,介绍卵母细胞内注射自体骨髓线粒体的过程。结果 患者孕 34<sup>+5</sup> 周活产一男婴。结论 卵母细胞内注射自体骨髓线粒体为解决原发不孕夫妇胚胎质量差及妊娠结局差等问题提供了新思路。

【关键词】骨髓间充质干细胞;线粒体移植;卵母细胞质量;胚胎质量

### ·个案报道·

A case of transferring mitochondria from autologous bone mesenchymal stem cells into oocytes resulting in a live baby boy Fang Cong, Huang Rui, Jia Lei, Cao Guokun, Liu Xiaoping, Chen Weixi, Liang Xiaoyan Reproductive Medicine Research Center, the Sixth Affiliated Hospital of Sun Yat-sen University, Guangzhou 510655, China (Fang C, Huang R, Jia L, Cao GK, Liu XP, Chen WX, Liang XY)
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**[Abstract]** Objective To explore the effect of transferring mitochondria from autologous bone mesenchymalstem cells on repeated pregnancy failure in infertility. **Methods** The clinical materials of an infertile patient undergoing repeated failure in *in vitro* fertilization (IVF) cycles was analyzed, and the process of transferring mitochondria from autologous bone mesenchymal stem cells (BMSCs) into oocytes was introduced. **Results** The patient underwent low-segment cesarean section at 34<sup>+5</sup> weeks of gestation and obtained a live baby boy. **Conclusion** Transferring mitochondria from autologous BMSCs into oocytes offers a new potential treatment to improve embryo quality and IVF outcome for infertile couples.

**[Key words]** Bone mesenchymal stem cells (BMSCs); Mitochondria transfer; Oocyte quality; Embryo quality

## 全氟及多氟类化合物与人类生殖关系的研究进展

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【摘要】 全氟和多氟烷酸类化合物 (PFASs) 是一类在环境和生物体内广泛存在、具有广泛毒性的环境内分泌干扰物 (EEDs),其中研究最多的是全氟辛烷磺酸 (PFOS) 和全氟辛酸 (PFOA)。已有大量实验和流行病学调查结果表明,PFASs 暴露与人类生殖健康有关。本文针对 PFASs 对人类生殖力,包括与生殖细胞发生发育、生殖激素分泌调节、出生子代健康等关系进行阐述,并对目前 PFASs 有关研究所存在的问题及今后的研究方向进行讨论和展望。

【关键词】全氟和多氟烷酸类化合物 (PFASs); 环境内分泌干扰物 (EEDs); 人类生殖基金项目: 国家重点基础研究发展计划 (973 计划 )(2014CB943300)

## Research progress of the relationship between perfluoroalkyl and polyfluoroalkyl substances and human reproduction Zhou Yuanyuan, Shen Juan, Mao Yuchan, Jin Fan

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[Abstract] Perfluoroalkyl and polyfluoroalkyl substances (PFASs) are a group of environmental endocrine disruptors (EEDs) that are widespread in the environment and organisms, including perfluorooctane sulfonate (PFOS) and perfluorooctanoic acid (PFOA). A large number of experimental and epidemiological investigations have shown that PFASs exposure is associated with disorders of human reproduction. The present review focuses on the effect of PFASs on the human reproduction, including their associations with the development of germ cells, the secretion of reproductive hormone, the health of the offspring and so on. The problems and prospect in the research of PFASs have been discussed.

**【Key words 】** Perfluoroalkyl and polyfluoroalkyl substances (PFASs); Environmental endocrine disruptors (EEDs); Human reproduction

Fund program: National Key Basic Research Program of China (973 Program) (2014CB943300)

### 女性生殖道微生物组学在生殖医学中的研究进展

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DOI: 10.3760/cma.j.issn.2096-2916.2018.11.014

【摘要】 女性生殖道是动态变化的微生态体系,存在着多种正常的微生物群落。生殖道微生物组是人体重要的微生态体系之一,与宿主、环境之间构成了相互制约、相互协调的微生态平衡,在维护女性生殖道健康中起到关键作用。临床上通过检测与评价健康或疾病状态下的生殖道微生态状况,可以及时发现生殖道疾病的危险因素,为不孕症的治疗提供指导与帮助。本文主要对近年来女性生殖道微生物组学的研究进展,特别是与生殖医学相关的进展加以综述,并展望生殖医学领域微生物组学未来的研究方向。

【关键词】生殖道微生物组学;生殖医学;16S rRNA 测序

基金项目: 北京大学第三医院临床重点项目(BYSY2015002)

# Research progress of reproductive tract microbiome in female reproductive medicine Yang Puyu, Ma Caihong

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【Abstract】 Female reproductive tract is a dynamic microecological system with a variety of microbial communities. Female reproductive tract microbiology is one of the important microecosystems, which constitute a microecological balance of mutual restriction and coordination with host and environment and plays a key role in maintaining female reproductive tract health. By detecting and evaluating the microbiome of reproductive tract clinically, the risk factors of reproductive tract diseases can be found in time, providing guidance and help for the treatment of infertility. This paper mainly reviews the research progress of female reproductive microbiology in recent years, especially related to reproductive medicine, and looks forward to the future research direction of microbiology in the field of reproductive medicine.

**[Key words]** Reproductive tract microbiome; Reproductive medicine; 16S rRNA sequencing **Fund program**: Key Clinical Project of Peking University Third Hospital (BYSY2015002)

### 复发性流产的治疗进展

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DOI: 10.3760/cma.j.issn.2096-2916.2018.11.015

【摘要】 复发性流产 (recurrent spontaneous abortion, RSA) 是指与同一性伴侣, 28 周前 3 次或 3 次以上的妊娠丢失,该定义存在地域和种族的差异。RSA 的病因多样,仍有多数患者病因不明,临床诊疗存在很大难度。解剖异常引起的 RSA 通常需要手术治疗帮助患者恢复子宫、内膜、宫颈等的解剖和功能,尤其是宫腔粘连的患者,宫腔粘连松解术可有效改善患者的生育情况; 目前,尚无充足的证据表明,胚胎植入前遗传学诊断可以提高 RSA 患者的活产率; 对于甲状腺功能异常的 RSA 患者,其促甲状腺素应控制在一定的水平; 二甲双胍可改善 RSA 患者的胰岛素抵抗,但能否改善其妊娠结局尚缺乏依据; 没有充足的证据表明,补充孕激素治疗 RSA 伴黄体功能不全患者可以提高活产率; 合并典型抗磷脂抗体综合征 (APS) 的 RSA 患者,应联合使用低分子肝素和低剂量阿司匹林; 对于不明原因复发性流产患者,低分子肝素、粒细胞集落刺激因子、淋巴免疫治疗能否有效改善妊娠结局尚缺乏临床验证。本文根据国内外研究进展,对 RSA 主要病因的治疗进行综述。

【关键词】复发性流产(RSA);不明原因复发性流产(URSA);治疗

基金项目: 国家自然科学基金 (81571513)

Research advances in management of recurrent spontaneous abortion Yan Nana, Yang Jing Reproductive Medical Center, Renmin Hospital of Wuhan University, Wuhan 430061, China (Yan NN, Yang J) Corresponding author: Yang Jing, Tel: +86-13507182023, Email: 13507182023@163.com

**【Abstract】** Recurrent spontaneous abortion (RSA) was defined as three or more failed clinical pregnancies before 28 weeks with the same sexual partner, and the definition differs from areas and races. Factors associated with RSA are numerous, and the cause of most patients is still unknown. Clinical diagnosis and treatment are very difficult. RSA caused by anatomical abnormalities usually requires surgical treatment to help patients recover anatomy and function of uterus, endomembrane, cervix, etc., especially in patients with intrauterine adhesions, hysteroscopic adhesiolysis can effectively improve the pregnancy outcome of patients. Currently, there is no adequate evidence suggests that preimplantation genetic diagnosis can improve the live birth rate of RSA patients. For thyroid dysfunction in RSA patients, thyrotropin should be controlled to a certain level. Metformin can improve insulin resistance in RSA patients, but the efficacy to improve pregnancy outcome remains to be feather verified. There is insufficient evidence that progesterone supplement can improve live birth rate of RSA patients with luteal insufficiency. RSA patients with typical antiphospholipid syndrome (APS) should be treated with low molecular weight heparin (LMWH) and low dose aspirin. Whether LMWH, granulocyte colony-stimulating factor or lymphatic immunotherapy can effectively improve pregnancy outcome in patients with unexplained RSA is still unproven. This article reviewed the treatment of RSA according to different causes.

**Key words** Recurrent spontaneous abortion (RSA); Unexplained recurrent spontaneous abortion (URSA); Treatment

Fund program: National Nature Science Foundation of China (81571513)

## CFTR 基因在先天性双侧输精管缺如中的研究进展

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【摘要】 先天性双侧输精管缺如 (congenital bilateral absence of the vas deferens, CBAVD) 目前认为主要由囊性纤维化跨膜转导子 (cystic fibrosis transmembrane conductance regulator, CFTR) 基因变异导致,在欧美国家 CFTR 基因变异检测已经用于胚胎植入前遗传学诊断,以避免子代发生 CBAVD 或携带 CFTR 变异基因。但是该基因变异类型繁多,与种族密切相关,差异巨大。现将 CFTR 基因在 CBAVD 中的研究进展综述如下。

【关键词】囊性纤维化跨膜转导子(CFTR)基因; 先天性双侧输精管缺如(CBAVD); 基因变异

# Research progress of cystic fibrosis transmembrane conductance regulator gene mutations in congenital bilateral absence of the vas deferens Bai Song, Wu Bin

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【Abstract】 congenital bilateral absence of the vas deferens (CBAVD) is mainly caused by cystic fibrosis transmembrane conductance regulator (CFTR) gene variations. The detection of CFTR variations have been used for preimplantation genetic diagnosis in western countries for avoiding CBAVD happened in offspring or carrying CFTR gene mutations. However, there are numerous kinds of variations in CFTR gene and they are closely related to race. Now we review the literature of CFTR gene progress in CBAVD as follow.

**Key words** Cystic fibrosis transmembrane conductance regulator (CFTR) gene; Congenital bilateral absence of the vas deferens (CBAVD); Variation