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编 辑

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

总编辑

乔 杰

编辑部主任

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Editing

Editorial Board of Chinese Journal of
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779 Laohumin Road, Shanghai 200237, China
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Fax: 0086-21-64438975
Email: randc@sippr.org.cn
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Editor-in-Chief

Qiao Jie

Managing Director

Wang Jian

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促性腺激素释放激素拮抗剂方案与超短方案对卵巢储备功能低下患者行体外受精-胚胎移植妊娠结局的影响

文雯 李娜 刘茜桐 周寒鹰 潘丹 李萍 王瑞 师娟子

西北妇女儿童医院生殖中心, 西安 710003

通信作者: 李娜, Email: linasmiling@126.com, 电话: +86-13891948999

【摘要】 目的 评价促性腺激素释放激素(GnRH)拮抗剂方案在卵巢储备功能低下(diminished ovarian reserve, DOR)患者行体外受精-胚胎移植(*in vitro* fertilization-embryo transfer, IVF-ET)中的应用效果。方法 回顾性队列研究分析2015年1月至2016年12月期间在西北妇女儿童医院生殖中心首次接受IVF-ET治疗的DOR患者的临床资料,根据促排卵方案不同,分为GnRH拮抗剂方案组和超短方案组。比较两组一般情况、临床及实验室指标、妊娠结局。结果 活产率、临床妊娠率、种植率组间比较差异均无统计学意义($P>0.05$)。GnRH拮抗剂方案组Gn用量[(3 082.04±1 004.40) IU]比超短方案组少[(3 510.05±1 119.09) IU]($P<0.001$), Gn使用时间[(9.66±2.13) d]比超短方案组短[(10.63±2.27) d, $P<0.001$], 获卵数(4.54±2.97)比超短方案组少(5.54±3.54, $P<0.001$)。结论 DOR患者采用GnRH拮抗剂方案超促排卵治疗与超短方案妊娠结局相似,且Gn用量更少、Gn使用时间更短。因此,GnRH拮抗剂方案也是DOR患者适宜的促排卵方案之一。

【关键词】 受精, 体外; 卵巢储备功能低下; 促性腺激素释放激素拮抗剂方案; 活产率

基金项目: 陕西省卫生健康科研项目(2018D035)

Effects of gonadotropin-releasing hormone antagonist protocol and gonadotropin-releasing hormone agonist short protocol on diminished ovarian reserve patients

Wen Wen, Li Na, Liu Xitong, Zhou Hanying, Pan Dan, Li Ping, Wang Rui, Shi Juanzi

Reproductive Center of Northwest Women's and Children's Hospital, Xi'an 710003, China

Corresponding author: Li Na, Email: linasmiling@126.com, Tel: +86-13891948999

【Abstract】 Objective To evaluate the effect of gonadotropin-releasing hormone antagonist (GnRH-A) protocol on *in vitro* fertilization-embryo transfer (IVF-ET) in patients with diminished ovarian reserve (DOR). **Methods** A retrospective cohort study was performed to analyze the clinical data of the DOR patients who received IVF-ET treatment for the first time at the Northwest Women's and Children's Hospital Reproductive Center during January 2015 to December 2016. They were divided into a GnRH-A protocol group and an gonadotropin-releasing hormone agonist (GnRH-a) short protocol group according to different ovulation induction protocols. The general conditions, clinical and laboratory indicators, and pregnancy outcomes of the two groups were compared. **Results** There was no statistically significant difference in live birth rate, clinical pregnancy rate and

implantation rate between the two groups ($P>0.05$). The dosage of gonadotropin (Gn) used in GnRH-A protocol group [$3\ 082.04\pm1\ 004.40$] IU was less than that in GnRH-a short protocol group [$3\ 510.05\pm1\ 119.09$] IU, $P<0.001$], the duration of Gn used [9.66 ± 2.13] d was shorter than that in GnRH-a short protocol group [10.63 ± 2.27] d, $P<0.001$], the number of eggs (4.54 ± 2.97) was less than that in GnRH-a short protocol group (5.54 ± 3.54 , $P<0.001$). **Conclusion** DOR patients using GnRH-A protocol for hyperovulation therapy have similar outcomes to GnRH-a short protocol pregnancy, with less Gn used dosage and shorter Gn used duration. Therefore, the GnRH-A protocol is also one of the suitable ovulation induction for DOR patients.

【Key words】 Fertilization *in vitro* ; Diminished ovarian reserve ; Gonadotropin-releasing hormone antagonist protocol ; Live birth rate

Fund program : Health Research Fund Project of Shaanxi Province (2018D035)

·临床研究·

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16 458 个供精人工授精自然周期妊娠结局的多因素分析

张清健 宋革 钟小英 姜荣华 刘晓玲 郑炜炜 祝晓丽 黎敏茹 詹泽虎 蔡晓林 陈翔
国家卫生健康委员会男性生殖与遗传重点实验室 广东省计划生育科学技术研究所生殖中心, 广州 510600

通信作者: 宋革, Email: songgepp@126.com, 电话: +86-20-87622440, 传真: +86-20-87777331

【摘要】 目的 探讨多种因素对自然周期供精人工授精(AID)妊娠结局的影响。方法 回顾性分析 2011 年 1 月至 2018 年 12 月期间在广东省计划生育科学技术研究所生殖中心治疗的 16 458 个自然周期, 对女性因素、供精精液质量以及周期相关因素与术后妊娠结局进行 χ^2 和广义估计方程多因素分析。结果 女方年龄 ≤ 30 岁($OR=1.865$, $P<0.001$)、年龄 31~35 岁($OR=1.215$, $P<0.001$)、不孕年限 <5 年($OR=1.139$, $P=0.007$)、第 3 日促黄体生成素水平 >8.10 IU/L($OR=1.309$, $P=0.022$)、第 3 日雌激素水平 ≤ 77.10 pmol/L($OR=1.301$, $P=0.012$)、第 3 日雌激素水平 77.11~293.60 pmol/L($OR=1.099$, $P=0.044$)、优势卵泡数 1 个($OR=1.473$, $P=0.038$)、宫颈黏液评分 ≥ 10 分($OR=1.256$, $P=0.026$)、子宫内膜分型为 A 型($OR=1.114$, $P=0.005$)、尿促黄体生成素强阳性($OR=1.171$, $P=0.002$)、精子冻融复苏后活力 $>54\%$ ($OR=1.142$, $P=0.002$)、精子冻融复苏后前向运动精子总数 $\geq 35\times 10^6$ ($OR=1.217$, $P=0.001$)以及每周期 AID 授精 2 次($OR=1.376$, $P=0.001$)显著影响授精妇女的妊娠率。结论 在自然周期 AID 中, 女方年龄、不孕年限、第 3 日促黄体生成素水平、

第3日雌激素水平、优势卵泡数、宫颈黏液评分、子宫内膜分型、尿促黄体生成素、精子冻融复苏后活力、精子冻融复苏后前向运动精子总数以及每周授精次数影响女性的妊娠率。

【关键词】 供精人工授精； 妊娠； 广义估计方程

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Multivariate analysis of the clinical outcome of 16 458 natural artificial insemination cycles with donor sperm

Zhang Qingjian , Song Ge , Zhong Xiaoying , Jiang Ronghua , Liu Xiaoling , Zheng Weiwei , Zhu Xiaoli , Li Minru , Zhan Zehu , Cai Xiaolin , Chen Qiao

Key Laboratory of Male Reproduction and Genetics of National Health Commission, Reproductive Center of Guangdong Province Family Planning Science and Technology Research Institute, Guangzhou 510600, China

Corresponding author: Song Ge, Email: songgepp@126.com, Tel: +86-20-87622440 , Fax: +86-20-87777331

【Abstract】 Objective To analyze the effects of various factors on the clinical outcome of artificial insemination with donor sperm (AID) under natural cycles. **Methods** A total of 16 458 natural cycles with donor sperm were analyzed from January 2011 to December 2018 in Reproductive Center of Guangdong Province Family Planning Science and Technology Research Institute. The relationship between the clinical outcome and the factors such as the women's character, donor sperm quality and cycle related factors with χ^2 and multiple factor generalized estimating equation. **Results** Many factors such as women's age ≤ 30 years ($OR=1.865$, $P<0.001$), the woman's age from 31 to 35 years ($OR=1.215$, $P<0.001$), duration of infertility ≤ 5 ($OR=1.139$, $P=0.007$), day 3 luteinizing hormone (LH) level >8.10 IU/L ($OR=1.309$, $P=0.022$), day 3 estrogen level ≤ 77.10 pmol/L ($OR=1.301$, $P=0.012$), day 3 estrogen level from 77.11 pmol/L to 293.60 pmol/L ($OR=1.099$, $P=0.044$), one dominant follicle per cycle ($OR=1.473$, $P=0.038$), cervical mucus score ≥ 10 ($OR=1.256$, $P=0.026$), A type endometrium ($OR=1.114$, $P=0.005$), urinary LH strong positive ($OR=1.171$, $P=0.002$), sperm activity ratio more than 54% after thawing ($OR=1.142$, $P=0.002$), progressively motile sperm number $\geq 35 \times 10^6$ after thawing ($OR=1.217$, $P=0.001$) and double inseminations per cycle ($OR=1.376$, $P=0.001$) significantly affected the pregnancy rates of AID women under natural cycles. **Conclusion** Many factors such as the woman's age, duration of infertility, day 3 LH level, day 3 estrogen level, dominant follicle number per cycle, cervical mucus score, endometrial type, sperm activity ratio after thawing, progressively motile sperm number and insemination times per cycle can affect the women's pregnancy rate under AID natural cycles.

【Key words】 Artificial insemination with donor sperm； Pregnancy； Generalized estimating equation

Fund program： Guangdong Provincial Medical Research Foundation (A2014195 , B2018235)； Guangdong Province Family Planning Science and Technology Research Institute Research Foundation (S2018010)

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冻融周期单囊胚移植临床结局的影响因素研究

张亚楠 谢娟珂 陈圆辉 张翠莲

河南省人民医院，河南省生殖医院，河南省生殖医学工程国际联合实验室，郑州大学人民医院，河南大学人民医院 450000

通信作者：谢娟珂，Email：xiejuanke@126.com，电话：+86-13643716622

【摘要】 目的 分析在冻融单囊胚移植周期中影响临床结局的相关因素。**方法** 回顾性分析 2011 年 1 月至 2018 年 4 月期间于河南省人民医院生殖中心行冻融周期单囊胚移植患者的临床资料，分别比较囊胚体外发育时间、受精方式、囊胚形态学评分等参数对临床结局的影响，并采用二分类 logistic 回归分析筛选影响因素。**结果** 第 5 日 (D5) 囊胚组的生化妊娠率、临床妊娠率与活产率均显著高于第 6 日 (D6) 囊胚组 ($P<0.05$)，但两组间的异位妊娠率、流产率及早期流产率差异无统计学意义 ($P>0.05$)。比较同等级别评分的 D5/D6 囊胚的临床结局，得到上述类似结果。体外受精 (IVF) 及卵胞质内单精子显微注射 (ICSI) 周期来源的囊胚，其临床结局差异无统计学意义 ($P>0.05$)。比较不同扩张状态的 D5 囊胚，4 期、5 期较 3 期、6 期囊胚的生化妊娠率、临床妊娠率及活产率高，早期流产率低，但差异均无统计学意义 ($P>0.05$)。选取移植 4 期 D5 囊胚的患者进行比较，不同组间的生化妊娠率、临床妊娠率及活产率分别随内细胞团 (ICM)、滋养层细胞 (TE) 评分的下降而降低，但差异均无统计学意义 ($P>0.05$)。经 logistic 回归分析后，年龄、囊胚体外发育时间与临床妊娠率及活产率呈负相关，囊胚扩张状态与临床妊娠率呈正相关，囊胚 ICM 及 TE 评级与活产率呈负相关。**结论** 患者的年龄、囊胚体外发育时间、囊胚质量是冻融单囊胚移植周期妊娠结局的影响因素。

【关键词】 冻融胚胎移植周期；单囊胚移植；囊胚形态学评分；临床妊娠率；活产率

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Analysis of the factors influencing clinical outcome in single frozen-thawed blastocyst transfer cycles

Zhang Yanan, Xie Juanke, Chen Yuanhui, Zhang Cuilian

Henan Provincial People's Hospital, Henan Provincial Reproductive Hospital, Henan Joint International Research Laboratory of Reproductive Bioengineering, People's Hospital of Zhengzhou University, People's Hospital of Henan University, Zhengzhou 450000, China
Corresponding author: Xie Juanke, Email: xiejuanke@126.com, Tel: +86-13643716622

【Abstract】 Objective To investigate the factors influencing clinical outcome in single frozen-thawed blastocyst transfer cycles. **Methods** The clinical data of 1748 frozen-thawed single blastocyst transfer cycles were studied retrospectively in Reproductive Medical Center of Henan Provincial People's Hospital from January 2011 to April 2018. The effects of the development speed of blastocysts, the different fertilization methods and morphological scoring of blastocyst on the pregnancy outcome were observed. Clinical pregnancy rate, biochemical pregnancy rate, early abortion rate and live birth rate were compared among different groups. Logistic regression analysis was performed to determine the correlation between these parameters and clinical pregnancy rate and live birth rate. **Results** The biochemical pregnancy rate, the clinical pregnancy rate and the live birth rate of day 5 (D5) frozen-thawed single blastocyst transfer were significantly higher than those of day 6 (D6) ($P<0.05$), while the ectopic pregnancy rate, the abortion rate and the early abortion rate had no significant difference ($P>0.05$). Coincident results were obtained by comparing the clinical outcomes of D5/D6 blastocysts with the same score. The clinical outcome of the blastocyst of different fertilization methods had no significant differences ($P>0.05$). According to the status of blastocoele

expansion and hatching, blastocysts were divided into stages 3–6. Compared with the stage 3 and stage 6 groups, the stage 4 and stage 5 groups of D5 frozen-thawed single blastocyst transfer showed a higher biochemical pregnancy rate, clinical pregnancy rate, live birth rate and a lower early abortion rate, but there were no statistically significant differences ($P>0.05$). In the stage 4 group of D5 frozen-thawed single blastocyst transfer cycles, there was a tendency of lower biochemical pregnancy rate, clinical pregnancy rate and live birth rate with lower inner cell mass (ICM) or trophoctoderm (TE) score but without statistically significant differences ($P>0.05$). It was found that the age of patients and the development speed of blastocysts were negatively related to the clinical pregnancy rate and pregnancy live birth rate, while the degree of blastocoele expansion and hatching was positively related to the clinical pregnancy rate, and ICM and TE score were negatively related to the live birth rate. **Conclusion** The age of patients, the development speed of blastocysts and blastocyst quality could be the factors influencing clinical outcome in single frozen-thawed blastocyst transfer cycles.

【Key words】 Frozen-thawed embryo transfer ; Single blastocyst transfer ; Morphological scoring ; Clinical pregnancy rate ; Live birth rate

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凝血功能与炎症标志物在妊娠期肝内胆汁淤积症中的变化分析

孙晓彤¹ 郭因² 曲涛¹ 李春明¹ 何西彦¹ 杨彩芳³ 鲁蕃² 杨莉莉²

¹ 甘肃省人民医院, 兰州 730000 ; ² 甘肃中医药大学, 兰州 730000 ; ³ 陇南市第一人民医院 746000

通信作者 : 孙晓彤, Email : sxt13919101217@163.com, 电话 : +86-931-8281045

【摘要】 目的 探索血小板参数、凝血指标及血小板/淋巴细胞比值(platelet and lymphocyte ratio, PLR)值、中性粒细胞/淋巴细胞比值(neutrophil and lymphocyte ratio, NLR)对妊娠期肝内胆汁淤积症(intrahepatic cholestasis of pregnancy, ICP)孕妇的凝血障碍及围产儿结局的影响。方法 回顾性分析 2017 年 1 月至 2018 年 12 月期间在甘肃省人民医院分娩的 106 例 ICP 患者(ICP 组)和 138 例正常孕妇(对照组)的凝血酶原时间(prothrombin time, PT)、活化部分凝血活酶时间(activated partial thromboplastin time, APTT)、纤维蛋白原(fibrinogen, FIB)、D-二聚体(D-dimer, D-D)、血小板计数、平均血小板体积(mean platelet volume, MPV)、血小板分布宽度(platelet distribution width, PDW)、白细胞(white blood cell, WBC)数、PLR、NLR 以及产后出血量及围产儿结局在两组之间的差异;进一步根据血清胆汁酸(total bile acid, TBA)水平是否 $\geq 40 \mu\text{mol/L}$ 将

ICP 组分为轻度 ICP 亚组和重度 ICP 亚组, 分析差异指标在两亚组之间的变化情况。结果 与对照组相比较, MPV($t=4.929$, $P<0.001$)、FIB($t=3.509$, $P<0.001$)、D-D($t=7.834$, $P<0.001$)及 NLR($t=4.098$, $P<0.001$)在 ICP 组中是显著升高的, 差异均有统计学意义。血小板计数($t=4.367$, $P<0.001$)和 PLR($t=2.448$, $P=0.015$)在 ICP 孕妇中是显著降低的, 差异均有统计学意义; ICP 组产后出血量($t=10.003$, $P<0.001$)、胎儿窘迫发生率($\chi^2=17.194$, $P<0.001$)、早产率($\chi^2=13.938$, $P<0.001$)和转入新生儿监护室率 (NICU) ($\chi^2=29.736$, $P<0.001$)均高于对照组, 差异有统计学意义; ICP 组 Apgar 评分($t=3.234$, $P=0.001$)、新生儿出生体质量($t=6.509$, $P<0.001$)均低于对照组, 差异有统计学意义; 将 ICP 组分为重度 ICP 亚组和轻度 ICP 亚组进一步分析显示, 两亚组在 MPV($t=2.376$, $P=0.019$)、FIB($t=2.174$, $P=0.032$)、D-D($t=3.074$, $P=0.003$)、WBC($t=2.021$, $P=0.046$)、中性粒细胞计数($t=2.131$, $P=0.035$)、NLR($t=2.864$, $P=0.005$)等方面差异均有统计学意义; 而且产后出血量($t=3.257$, $P=0.002$)、早产儿发生率($\chi^2=4.025$, $P=0.045$)、出生体质量($t=3.126$, $P=0.002$)、转入 NICU 率($\chi^2=5.518$, $P=0.019$)在两组间差异有统计学意义。结论 ICP 孕妇体内存在异常凝血及纤溶状态, 易导致产后出血, 不良围生结局发生率高, 应当引起临床高度重视。早期通过对 ICP 孕妇的凝血功能和炎症标志物的分析, 评估 ICP 孕妇的妊娠结局, 具有重要的积极意义。

【关键词】 妊娠期肝内胆汁淤积症; 产后出血; 妊娠结局; 凝血; 中性粒细胞和淋巴细胞比值; 血小板和淋巴细胞比值

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Analysis of the changes of coagulation function and inflammation markers in intrahepatic cholestasis during pregnancy

Sun Xiaotong¹, Guo Nan², Qu Tao¹, Li Chunming¹, He Xiyan¹, Yang Caifang³, Lu Fan², Yang Lili²

¹ Gansu Provincial Hospital, Lanzhou 730000, China; ² Gansu University of Traditional Chinese Medicine, Lanzhou 730000, China; ³ Longnan First People's Hospital, Longnan 746000, China

Corresponding author: Sun Xiaotong, Email: sxt13919101217@163.com, Tel: +86-931-8281045

【Abstract】 Objective To explore the effects of platelet parameters, coagulation indexes, platelet and lymphocyte ratio (PLR) values, neutrophil and lymphocyte ratio (NLR) values on coagulation disorders and perinatal outcomes in pregnant women with intrahepatic cholestasis of pregnancy (ICP). **Methods** A retrospective analysis of prothrombin time (PT) and activated partial thromboplastin time (activated partial) of 106 ICP patients (ICP group) and 138 normal pregnant women (control group) delivered from Gansu Provincial People's Hospital from January 2017 to December 2018 was performed. Activated partial thromboplastin time (APTT), fibrinogen (FIB), D-dimer (D-D), platelet count, mean platelet volume (MPV), platelet distribution red blood cell distribution width (RDW), number of white blood cell (WBC), PLR, NLR, and postpartum hemorrhage and perinatal outcomes were compared between the two groups. Further based on whether serum bile acid (TBA) was $\geq 40 \mu\text{mol/L}$, the patients in ICP group were divided into mild ICP subgroup and severe ICP subgroup, and the changes in the difference indicators were analyzed between the two subgroups. **Results** Compared with control group, MPV ($t=4.929$, $P<0.001$), FIB ($t=3.509$, $P<0.001$), D-D ($t=7.834$, $P<0.001$) and NLR ($t=4.098$, $P<0.001$) were significantly increased in ICP group ($P<0.05$). Platelet count ($t=4.367$, $P<0.001$) and PLR ($t=2.448$, $P=0.015$) were significantly decreased in ICP pregnant women. The incidence of postpartum hemorrhage ($t=10.003$, $P<0.001$), fetal distress ($\chi^2=17.194$, $P<0.001$), preterm birth rate ($\chi^2=13.938$, $P<0.001$) and transfer into neonatal intensive care unit (NICU) ($\chi^2=29.736$, $P<0.001$) in ICP group was higher than that in control group. Apgar score ($t=3.234$, $P=0.001$) and neonatal birth weight ($t=6.509$, $P<0.001$) in ICP group were lower than those in control group. Further analysis of ICP components for severe ICP and mild ICP revealed significant differences in MPV ($t=2.376$, $P=0.019$), FIB ($t=2.174$, $P=0.032$), D-D ($t=3.074$, $P=0.003$), WBC ($t=2.021$, $P=0.046$), neutrophil count ($t=2.131$, $P=0.035$), NLR ($t=2.864$, $P=0.005$), etc. Postpartum hemorrhage ($t=3.257$, $P=0.002$), the preterm birth rate ($\chi^2=4.025$, $P=0.045$), birth weight ($t=3.126$, $P=0.002$), and transfer rate to the NICU ($\chi^2=5.518$, $P=0.019$) were also significantly different between the two groups. **Conclusion** ICP pregnant women have abnormal coagulation and fibrinolysis, which may lead to postpartum hemorrhage. The incidence of poor perinatal outcomes is high, which should be highly valued by the clinic. It is of great significance to evaluate the pregnancy outcome of pregnant women with ICP by analyzing the coagulation function and inflammatory markers of ICP pregnant women.

【Key words】 Intrahepatic cholestasis of pregnancy ; Postpartum hemorrhage ; Pregnancy outcome ; Blood coagulation ; Neutrophil and lymphocyte ratio ; Platelet and lymphocyte ratio

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不孕症夫妇生育压力、主观幸福感和生育生活质量的差异性及心理弹性的中介作用

蔡艳娜 董悦芝 周飞京 白睿敏 李亚南 朱艳红

郑州大学第一附属医院 450052

通信作者 : 朱艳红 , Email : zhuyanhongit@126.com , 电话 : +86-15093356961

【摘要】 目的 探索不孕症夫妇在生育压力、主观幸福感和生育生活质量方面的差异性及心理弹性的中介作用。方法 采用横断面研究和方便抽样法抽取 2017 年 4 月至 2018 年 4 月期间在郑州大学第一附属医院生殖中心门诊接受初诊的不孕症夫妇。采用心理弹性量表 (CD-RISC) 、生育压力量表 (FPI) 、主观幸福感量表 (SWBS) 和生育生活质量量表 (FertiQoL) 对纳入的 230 例不孕症夫妇进行调查。结果 不孕症夫妇在心理弹性 ($P=0.034$) 、生育压力 ($P<0.001$) 和生育生活质量 ($P=0.005$) 方面差异具有统计学意义, 主观幸福感差异无统计学意义 ($P>0.05$) 。不孕症女方的心理弹性在生育压力与主观幸福感和生育生活质量的中介作用拟合度理想 [$\chi^2/df=1.437$, 拟合优度指数 (GFI) =0.936 , 修正的拟合优度指数 (AGFI) =0.909 , 近似误差均方根 (RMSEA) =0.043] , 且中介作用显著。不孕症男方心理弹性在生育压力与主观幸福感和生育生活质量的中介作用拟合度良好 [$\chi^2/df=2.011$, GFI=0.93 , 增值拟合指数 (IFI) =0.918 , 标准化拟合指数 (CFI) =0.917 , RMSEA=0.067] , 但心理弹性在生育压力与生育生活质量中有中介作用, 在生育压力与主观幸福感中无中介作用。结论 不孕症夫妇的生育压力和生育生活质量存在差异。心理弹性在不孕症夫妇的生育压力与生育生活质量中存在中介作用。

【关键词】 不孕症夫妇 ; 生育压力 ; 主观幸福感 ; 心理弹性 ; 生育生活质量 ; 结构方程模型

Differences in the infertility stress, subjective well-being and fertility quality of life among infertile couples and mediating role of psychological resilience

Cai Yanna , Dong Yuezhi , Zhou Feijing , Bai Ruimin , Li Yanan , Zhu Yanhong
The First Affiliated Hospital of Zhengzhou University, Zhengzhou 450052, China

Corresponding author: Zhu Yanhong, Email: zhuyan hongit@126.com, Tel: +86-15093356961

【Abstract】 Objective To explore the differences in the infertility stress, subjective well-being and fertility quality of life among infertile couples and mediating role of psychological resilience. **Methods** A cross-sectional study and convenient sampling method were used to recruit the new diagnosed as infertility couples from April 2017 to April 2018 in the Reproductive Center of the First Affiliated Hospital of Zhengzhou University. The Resilience Scale (CD-RISC), the Fertility Problem Inventory (FPI), the Subjective Well-being Scale (SWBS) and the Fertility Quality of Life Questionnaire (FertiQoL) were used to investigate the 230 infertile couples. **Results** Infertility couples had statistical differences in psychological resilience ($P=0.034$), infertility stress ($P<0.001$), and fertility quality of life ($P=0.005$), and there was no statistically significant difference in subjective well-being. The fitting degree of structural equation model of infertility stress and subjective well-being and fertility quality of life among infertility women was relatively ideal [$\chi^2/df=1.437$, goodness of fit index (GFI)=0.936, adjusted goodness of fit index (AGFI)=0.909, root mean square error of approximation (RMSEA)=0.043], and the mediating effects of psychological resilience on subjective well-being and fertility quality of life was significant. The fitting degree of structural equation model of infertility stress and subjective well-being and fertility quality of life among infertility men was relatively ideal [$\chi^2/df=2.011$, GFI=0.93, incremental fit index (IFI)=0.918, comparative fit index (CFI)=0.917, RMSEA=0.067], and psychological resilience had a mediating effect on fertility quality of life, but had no mediating effect on subjective well-being. **Conclusion** There are differences in infertility stress and fertility quality of life among infertile couples. psychological resilience has a mediating effect on the infertility stress and fertility quality of life among infertile couples.

【Key words】 Infertility couple ; Infertility stress ; Subjective well-being ; Psychological resilience ; Fertility quality of life ; Structural equation model

·流行病学研究·

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三氯生暴露对早发性卵巢功能不全的影响

祝文婷 毛愉婵 金帆

浙江大学医学院附属妇产科医院生殖医学中心, 杭州 310006

通信作者：金帆, Email : jinfan@zju.edu.cn, 电话 : +86-571-87013871

【摘要】 目的 评估环境三氯生(2,4,4'-三氯-2'-羟基二苯醚)暴露与早发性卵巢功能不全(POI)发病的关联性。**方法** 本研究为病例对照研究, 2014年3月至2015年12月从浙江、上海和山东三个省份的三家生殖中心门诊招募确诊的POI患者45名(POI组)和525名因男方不孕或输卵管性不孕前来就诊的患者, 依据中心、年龄(± 1 岁)、体质指数(BMI)(± 2 kg/m²)按照1:2的比例给POI患者在男方或输卵管性因素所致不孕的患者库中匹配对照90名(对照组), 检测其尿液标本中的三氯生水平, 用多元回归分析模型研究三氯生暴露与POI发病和基础内分泌激素之间的关联性。**结果** 88.9%的尿液标本中检测出三氯生, 浓度为1.37(0.56,3.50) ng/mg肌酐。尿中三氯生浓度与女性POI发病呈正向关联(调整后 $OR=1.31$;95% $CI=1.00\sim 1.70$), 且有剂量反应效应。三氯生浓度与卵泡刺激素(FSH)水平之间呈正向关联(调整后 $\beta=2.89$;95% $CI=0.06\sim 5.71$)。**结论** 三氯生暴露可能与POI的发病风险之间有关联, 但需要大样本的研究人群进一步进行验证。

【关键词】 三氯生； 早发性卵巢功能不全； 卵泡刺激素

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Effects of triclosan exposure on premature ovarian insufficiency in humans

Zhu Wenting , Mao Yuchan , Jin Fan

Medical Center for Human Reproduction, Women's Hospital, Zhejiang University School of Medicine, Hangzhou 310006, China

Corresponding author: Jin Fan, Email: jinfan@zju.edu.cn, Tel: +86-571-87013871

【Abstract】 Objective To investigate the potential effects of triclosan (TCS) on premature ovarian insufficiency (POI) in women. **Methods** A total of 45 POI patients and 525 women who sought fertility treatment for male factors or tubal obstruction were recruited from three reproductive centers in three provinces of China from March 2014 to December 2015. Totally 90 women who sought fertility treatment for male factors or tubal obstruction were center-age-body mass index (BMI) matched controls. TCS concentrations were quantified in urine samples. Baseline reproductive hormones were measured on the 2nd-3rd day of menstruation. **Results** TCS was detected in 88.9% of women [1.37(0.56, 3.50) ng/mg creatinine]. TCS concentrations were associated with increased risk of POI (adjust $OR=1.31$; 95% $CI=1.00-1.70$). We also divided TCS concentration into quartiles *in priori* and there tended to be a dose-response pattern. TCS concentrations were also positively associated with the levels of follicle-stimulating hormone (FSH) (adjust $\beta=2.89$; 95% $CI=0.061-5.710$). **Conclusion** TCS concentrations may associate with increased risk of POI, but a large study population is needed for further verification.

【Key words】 Triclosan ; Premature ovarian insufficiency ; Follicle-stimulating hormone

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金凤丸联合长效促性腺激素释放激素激动剂在冻融胚胎移植中的应用

张丹¹ 周寒² 郭影³ 张信贤² 郝桂敏¹ 崔娜¹ 姜蕾¹ 杨爱敏¹ 王玮¹

¹河北医科大学第二医院, 石家庄 050000 ; ²石家庄市第四医院 050000 ; ³邢台不孕不育专科医院 054000

张丹现工作于沧州市中心医院 061000

通信作者：王玮, Email : wangwei_ivf@163.com , 电话 : +86-13832177339

【摘要】 目的 探讨金凤丸联合长效促性腺激素释放激素激动剂 (GnRH-a) 在冻融胚胎移植 (FET) 中的应用价值。 **方法** 回顾分析 2017 年 1 月 1 日至 2017 年 12 月 31 日期间于河北医

科大学第二医院生殖医学科行 FET 的 220 例患者的临床资料, 根据是否联合应用金凤丸准备内膜分为金凤丸联合长效 GnRH-a 组(试验组, $n=102$)和单纯 GnRH-a 组(对照组, $n=118$)。比较两组患者的一般资料及胚胎复苏率、移植胚胎数、胚胎种植率、临床妊娠率、子宫内膜增殖时间、子宫内膜转化日血清雌二醇水平及子宫内膜转化日子宫内膜厚度。结果 试验组患者与对照组患者相比, 其子宫内膜增殖时间较短 $[(14.03\pm 3.39) \text{ d} \text{ 比 } (16.40\pm 1.45) \text{ d}]$ 、子宫内膜转化日血清雌二醇水平较高 $[(347.67\pm 26.78) \text{ ng/L} \text{ 比 } (259.57\pm 24.78) \text{ ng/L}]$ 、子宫内膜转化日子宫内膜较厚 $[(11.89\pm 1.57) \text{ mm} \text{ 比 } (9.69\pm 0.85) \text{ mm}]$, 差异均有统计学意义($P<0.001$); 试验组胚胎种植率及临床妊娠率均较高(32.66%比 31.70%; 53.92%比 50.85%), 但差异均无统计学意义($P>0.05$)。患者年龄、不孕年限、原发不孕比例、抗苗勒管激素 (AMH)、窦卵泡计数 (AFC)、体质量指数 (BMI)、解冻次数、胚胎复苏率、移植胚胎数、多胎妊娠率组间比较, 差异均无统计学意义 ($P>0.05$)。结论 金凤丸联合长效 GnRH-a 可以改善 FET 的妊娠结局。

【关键词】 金凤丸; 促性腺激素释放激素激动剂; 冻融胚胎移植; 人工周期

Application of Jinfeng pill combined with long-acting gonadotropin-releasing hormone agonist for frozen-thawed embryo transfer

Zhang Dan¹, Zhou Han², Guo Ying³, Zhang Xinxian², Hao Guimin¹, Cui Na¹, Jiang Lei¹, Yang Aimin¹, Wang Wei¹

¹ The Second Hospital of Hebei Medical University, Shijiazhuang 050000, China ; ² The Forth Hospital of Shijiazhuang, Shijiazhuang 050000, China ; ³ Xingtai Infertility Specialist Hospital, Xingtai 054000, China

Zhang Dan is now working in Cangzhou Central Hospital, Cangzhou 061000, China

Corresponding author: Wang Wei, Email: wangwei_ivf@163.com, Tel: +86-13832177339

【Abstract】 **Objective** To investigate the application value of Jinfeng pill combined with long-acting gonadotropin-releasing hormone agonist (GnRH-a) in frozen-thawed embryo transfer (FET). **Methods** A retrospective analysis of 220 cases of FET in the Department of Reproductive Medicine, the Second Hospital of Hebei Medical University during January 1, 2017 and December 31, 2017 was performed. All cases were divided into Jinfeng pill combined with long-acting GnRH-a group (experimental group, $n=102$) and long-acting GnRH-a group (control group, $n=118$) according to whether the endometrium was prepared in combination with Jinfeng pill or not. The general data, embryo resuscitation rate, number of transplanted embryos, embryo implantation rate, clinical pregnancy rate, endometrial proliferation time, serum estradiol level on the day of endometrial transformation and endometrial thickness on the day of endometrial transformation were compared between the two groups. **Results** Compared with control group, the experimental group had a shorter endometrial proliferation time $[(14.03\pm 3.39) \text{ d} \text{ vs. } (16.40\pm 1.45) \text{ d}, P<0.001]$, and the serum estradiol level was higher $[(347.67\pm 26.78) \text{ ng/L} \text{ vs. } (259.57\pm 24.78) \text{ ng/L}, P<0.001]$. The endometrium on the endometrial transformation was thicker $[(11.89\pm 1.57) \text{ mm} \text{ vs. } (9.69\pm 0.85) \text{ mm}, P<0.001]$, the difference was statistically significant. The embryo implantation rate and the clinical pregnancy rate in experimental group were higher than those in control group (32.66% vs. 31.70%; 53.92% vs. 50.85%), but the difference was not statistically significant ($P>0.05$). There were no significant differences in age, infertility duration, primary infertility ratio, anti-Müllerian hormone (AMH), antral follicle count (AFC), body mass index (BMI), number of thawing, embryo resuscitation rate, number of transplanted embryos, and multiple pregnancy rates between the two groups ($P>0.05$). **Conclusion** Jinfeng pill combined with long-effect GnRH-a can improve the pregnancy outcome of FET.

【Key words】 Jinfeng pill ; Gonadotropin-releasing hormone agonist ; Frozen-thawed embryo transfer ; Artificial cycle

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体外受精-胚胎移植后原发腹腔妊娠的 3 例 临床病例报道

谢言信 丁淼 邱绮 赵雅男 潘萍 李予 张清学

中山大学孙逸仙纪念医院妇产科, 广州 510000

通信作者：张清学, Email: zhangqingxue666@aliyun.com, 电话: +86-20-81332233

【摘要】 目的 探讨体外受精-胚胎移植 (IVF-ET) 后发生原发性腹腔妊娠的临床诊断及治疗方案。方法 本文报道 3 例中山大学孙逸仙纪念医院收治的 IVF-ET 后原发性腹腔妊娠病例, 并对其诊治进行了讨论。结果 3 例腹腔妊娠均在术前通过经阴道 B 超诊断, 行腹腔镜下腹腔妊娠物切除, 术后人绒毛膜促性腺激素(hCG)水平下降良好。目前 1 例已通过解冻胚胎移植并获得活产, 1 例自然妊娠后获得活产。结论 IVF-ET 术后的原发性腹腔妊娠是极其罕见的异位妊娠, 严密监测 hCG 水平及 B 超有助于早期诊断, 腹腔镜探查并腹腔妊娠物切除是有效的治疗方法。腹腔妊娠的早期诊断及治疗可改善预后。

【关键词】 受精, 体外; 胚胎移植; 腹腔妊娠; 腹腔镜

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Clinical diagnosis and treatment analysis of 3 cases with primary abdominal pregnancy after *in vitro* fertilization and embryo transfer

Xie Yanxin, Ding Miao, Qiu Qi, Zhao Yanan, Pan Ping, Li Yu, Zhang Qingxue

Department of Obstetrics and Gynecology, Sun Yat-Sen Memorial Hospital, Sun Yat-Sen University, Guangzhou 510000, China

Corresponding author: Zhang Qingxue, Email: zhangqingxue666@aliyun.com, Tel: +86-20-81332233

【Abstract】 Objective To investigate the clinical diagnosis and treatment of primary abdominal pregnancy after *in vitro* fertilization and embryo transfer (IVF-ET). **Methods** This paper reports 3 cases of primary abdominal pregnancy after IVF-ET in Sun Yat-Sen Memorial Hospital of Sun Yat-Sen University, and discusses the diagnosis and treatment. **Results** All 3 cases of abdominal pregnancy were diagnosed by transvaginal B-ultrasound before operation. Laparoscopic resection of the abdominal cavity pregnancy gas was performed, and the level of postoperative human chorionic hormone (hCG) decreased. **Conclusion** Primary abdominal pregnancy after IVF-ET is a rare ectopic pregnancy. Close monitoring of hCG level and B-ultrasound are helpful for early diagnosis. Laparoscopic exploration and abdominal pregnancy resection are effective treatments. Early diagnosis and treatment of abdominal pregnancy can improve the prognosis.

【Key words】 Fertilization *in vitro*; Embryo transfer; Abdominal pregnancy; Laparoscopy

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不同人群冻融胚胎移植周期内膜准备方案的选择

梁靓 李蓉

北京大学第三医院妇产科生殖医学中心 100191

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

【摘要】 冻融胚胎移植因增加促排卵周期的累积妊娠率而被广泛应用，其成功率的影响因素包括胚胎质量、子宫内膜容受性和内膜与胚胎的同步性。内膜准备方案是影响内膜容受性和内膜与胚胎同步性的重要因素，是获得最佳妊娠结局的关键。冻融胚胎移植周期内膜准备方案有：自然周期、改良自然周期、激素替代周期、降调节激素替代周期和促排卵周期，需针对不同人群的特点进行选择。本文综述国内外关于不同人群内膜准备方案的最新研究进展。

【关键词】 冻融胚胎移植；内膜准备；子宫内膜容受性

Selection of endometrial preparation for frozen-thawed embryo transfer cycles in different populations

Liang Liang, Li Rong

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

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

【Abstract】 Frozen-thawed embryo transfer (FET) is widely used to improve the cumulative pregnancy rate of ovulation induction cycle. The factors that affect success rate of FET include embryo quality, endometrial receptivity and the synchronization between both of them. Endometrial preparation protocol is a significant factor which can impact endometrial receptivity and the synchronization of endometrium and embryo. The endometrial preparation of FET cycle includes natural cycle, modified natural cycle, hormone replacement cycle, downregulation hormone replacement cycle and ovulation induction cycle. We should choose the optimal means of preparing the endometrium according to the characteristics of patients. In this review, selection of endometrial preparation for FET cycles in different populations is summarized through the existing literature and research.

【Key words】 Frozen-thawed embryo transfer；Endometrial preparation；Endometrial receptivity

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抗苗勒管激素水平在子宫内膜异位症患者中的研究进展

李清¹ 马建婷²

¹ 宁波大学医学院 315211 ; ² 余姚市人民医院 315400

通信作者: 马建婷, Email: mjt9977@126.com, 电话: +86-13805802310

【摘要】 子宫内膜异位症是生育期女性的常见病,腹腔镜手术是治疗子宫内膜异位症的金标准术式。子宫内膜异位症疾病本身可引起卵巢储备功能减退,手术操作可能导致卵巢储备功能进一步下降,甚至卵巢早衰。临床上对卵巢储备功能评估的指标有基础内分泌激素、窦卵泡计数、抑制素 B、抗苗勒管激素的检测等,其中抗苗勒管激素的检测不受月经周期的影响,可作为评估卵巢储备功能的较好指标。本文就抗苗勒管激素水平在子宫内膜异位症中变化的相关研究进展进行综述。

【关键词】 子宫内膜异位症; 抗苗勒管激素; 卵巢储备功能

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Advances in anti-Müllerian hormone levels in the patients with endometriosis

Li Qing¹, Ma Jianting²

¹ Medical School of Ningbo University, Ningbo 315211, China ; ² Yuyao People's Hospital, Yuyao 315400, China

Corresponding author: Ma Jianting, Email: mjt9977@126.com, Tel: +86-13805802310

【Abstract】 Endometriosis is a common disease of female in the reproductive stage. Laparoscopic surgery is the gold standard for treatment of endometriosis. Endometriosis may lead to a decline in the reserve function of ovary, and surgery may also cause the ovarian reserve function to decline, even cause ovarian early failure. The indexes for evaluating the ovarian reserve function include the basic endocrine hormone, antral follicle count, inhibin B, and anti-Müllerian hormone, and the anti-Müllerian hormone is not affected by the menstrual cycle, so it can be a good index for evaluating the reserve function of ovary. In this paper, we summarized the research and development of the changes of anti-Müllerian hormone under laparoscopic surgery about endometriosis.

【Key words】 Endometriosis ; Anti-Müllerian hormone ; Ovarian reserve function

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·综述·

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子宫内膜异位症患者卵泡液蛋白质组学研究进展

马英杰¹ 孙振高² 王欣磊³ 张祎³ 李丽¹ 高丹丹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, 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: sunzhengao77@163.com, 电话: +86-13708938621

【摘要】 子宫内膜异位症是一种影响育龄妇女并可能导致不孕的慢性妇科疾病。随着医学技术的进步, 关于子宫内膜异位症的研究日益增多, 但目前可用于评估该疾病的技术方法缺乏敏感度、特异度和准确性, 因此在诊断和治疗方面仍然面临困难。蛋白质组学不仅可以从生理、病理学角度研究疾病, 而且对于认识疾病发展过程中所涉及的不同蛋白质及其变化有重要的意义。卵泡液是人体中由卵母细胞、颗粒细胞和卵泡膜细胞等产生的含有多种蛋白质的一种重要分泌物, 因此本综述从对卵泡液中蛋白质组学的研究来概述子宫内膜异位症的研究进展。

【关键词】 子宫内膜异位症; 卵泡液; 蛋白质组学

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Progress in proteomics of follicular fluid in endometriosis patients

Ma Yingjie¹, Sun Zhengao², Wang Xinlei³, Zhang Yi³, Li Li¹, Gao Dandan³

¹ The First Clinical College, Shandong University of Chinese Medicine, Jinan 250014, China; ² The Affiliated Hospital of Shandong University of Chinese Medicine, Jinan 250014, China; ³ Institute of Traditional Chinese Medicine, Shandong University of Chinese Medicine, Jinan 250014, China
Corresponding author: Sun Zhengao, Email: sunzhengao77@163.com, Tel: +86-13708938621

【Abstract】 Endometriosis is a chronic gynecological disease that affects women of childbearing age and may lead to infertility. With the progress of medical technology, there are more and more studies on endometriosis, but the technical methods that can be used to evaluate the disease are lack of sensitivity, specificity and accuracy, so they still face difficulties in diagnosis and treatment. Proteomics can not only study diseases from the perspective of physiology and pathology, but also play an important role in understanding the different proteins involved in the development of diseases and their changes. Follicular fluid is an important secretion containing many kinds of proteins produced by oocytes, granulosa cells and theca cells in human body. Therefore, this review summarizes the research progress of endometriosis from the study of proteomics in follicular fluid.

【Key words】 Endometriosis; Follicular fluid; Proteomics

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·综述·

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炎性衰老影响子宫内膜容受性的机制研究进展

赵晓丽 宋佳怡 夏天

天津中医药大学第一附属医院生殖中心 300193

通信作者：夏天,Email : xiatian76@163.com , 电话 : +86-15822238896

【摘要】 女性年龄是决定生育力的重要因素,随着年龄增长,女性生殖能力逐渐下降。子宫内膜容受性下降是女性年龄相关性生殖功能下降的主要原因之一。机体在衰老过程中,由衰老细胞分泌的一系列促炎因子介导一种慢性、低度、系统性、非可控性的炎症状态,称为炎性衰老。外周循环以及子宫局部的促炎因子例如白细胞介素(IL)-1 β 、IL-6、白血病抑制因子(LIF)、肿瘤坏死因子 α (TNF- α)等的积累,与雌孕激素协同作用,通过调控同源框A10(HOXA10)、整合素 $\alpha\beta$ 3、黏蛋白1(MUC1)、基质金属蛋白酶(MMPs)等子宫内膜容受性标志性分子的表达和功能,损伤子宫内膜稳态,导致女性年龄相关性子宫内膜容受性下降。本文从子宫内膜容受性的形态学标志物、细胞生长发育,以及子宫内膜容受性标志分子MMPs、LIF、MUC1、肝素结合性表皮生长因子(HB-EGF)、整合素 $\alpha\beta$ 3、HOXA10等多个方面对炎性衰老影响子宫内膜容受性的分子机制作一综述。

【关键词】 子宫内膜容受性; 炎性衰老; 子宫内膜; 植入

Progress in the study of the effect of inflammaging on endometrial receptivity

Zhao Xiaoli, Song Jiayi, Xia Tian

Reproductive Center of First Teaching Hospital of Tianjin University of Traditional Chinese Medicine, Tianjin 300193, China

Corresponding author: Xia Tian, Email: xiatian76@163.com, Tel: +86-15822238896

【Abstract】 Female age is one of the most important factors determining fecundity, which gradually declines with natural aging. The decrease of endometrial receptivity is the major cause for age-related decline of fecundity. In the progress of aging, senescent cells secrete inflammatory factors inducing a chronic, low-degree, systemic, uncontrolled inflammatory state, termed "inflammaging". Accumulated inflammatory mediators such as interleukin-1 β (IL-1 β), interleukin-6 (IL-6), leukemia inhibitory factor (LIF) and tumor necrosis factor- α (TNF- α) in peripheral circulation and local uterus, together with estrogen and progesterone, lead to the abnormal expression and function of markers of endometrial receptivity such as homeobox A10 (HOXA10), integrin $\alpha\beta$ 3, mucoprotein (MUC1) and matrix metalloproteinase (MMP). This disturbs the endometrial homeostasis and contributes significantly to the age-related decline of endometrial receptivity. In this paper, we reviewed the molecular mechanisms of the effect of inflammaging on endometrial receptivity with the focus on the development of pinopodes, which is a morphological marker of endometrial receptivity and the involvement of other markers including MMPs, LIF, MUC1, heparin-binding epidermal growth factor (HB-EGF), integrin $\alpha\beta$ 3 and HOXA10.

【Key words】 Endometrial receptivity; Inflammaging; Endometrium; Implantation

·综述·

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肿瘤坏死因子- α 抑制剂在自身免疫疾病合并妊娠中的应用

李佳钊 刘倩 侯悦 金大中 乔宠

中国医科大学附属盛京医院妇产科，沈阳 110022

通信作者：乔宠，Email：qiaochong2002@163.com

【摘要】 自身免疫疾病是机体对自身抗原产生免疫反应，导致自身组织损伤的慢性炎性疾病。自身免疫异常能够影响女性生育能力和妊娠结局，妊娠也能够影响自身免疫疾病的病情，故孕前、妊娠期及产后控制疾病状态十分重要。肿瘤坏死因子- α 在多种自身免疫疾病的发病及进展中发挥重要作用，肿瘤坏死因子- α 抑制剂被应用于自身免疫疾病的治疗。本文就肿瘤坏死因子- α 抑制剂在自身免疫疾病合并妊娠中的临床应用进行综述。

【关键词】 肿瘤坏死因子- α ；抑制剂；自身免疫疾病；妊娠

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Application of tumor necrosis factor- α inhibitor in pregnancy with autoimmune disease

Li Jiapo, Liu Qian, Hou Yue, Jin Dazhong, Qiao Chong

Shengjing Hospital of China Medical University, Department of Obstetrics and Gynaecology, Shenyang 110022, China

Corresponding author: Qiao Chong, Email: qiaochong2002@163.com

【Abstract】 Autoimmune disease is a chronic inflammatory disease in which the body produces immune response to its own antigen, leading to tissue damage. Autoimmune abnormalities can affect women's fertility and pregnancy outcomes. Pregnancy can also affect the condition of autoimmune diseases. Therefore, it is very important to control disease status before pregnancy, during pregnancy and after childbirth. Tumor necrosis factor- α (TNF- α) plays an important role in the pathogenesis and progress of various autoimmune diseases. TNF- α inhibitors have been used in the treatment of autoimmune diseases. This article reviews the clinical application of TNF- α inhibitors in pregnancy with autoimmune diseases.

【Key words】 Tumor necrosis factor-alpha; Inhibitor; Autoimmune disease; Pregnancy

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2018 SOGC 多囊卵巢综合征诱导排卵实践指南(No. 362)解读

张巧利 贾婵维 周丽颖 刘艳君 余兰 徐潇雨 王树玉

首都医科大学附属北京妇产医院生殖医学中心 100026

通信作者：王树玉，Email：yushu572000@126.com，电话：+86-10-85960837

【摘要】 多囊卵巢综合征（PCOS）是临床常见的妇科内分泌紊乱性疾病，是引起育龄期女性无排卵性不孕的主要原因。2018 年加拿大妇产科医师协会（SOGC）针对 PCOS 患者制定了诱导排卵的临床实践指南，推荐生活方式干预，雌激素受体拮抗剂枸橼酸氯米芬（CC）和选择性芳香化酶抑制剂来曲唑（LE）为一线治疗，促性腺激素（Gn）为二线治疗，体外受精为三线治疗。胰岛素抵抗者可服用胰岛素增敏剂二甲双胍；CC 或 LE 抵抗者，如果存在腹腔镜手术的其他指征可行腹腔镜卵巢打孔术。指南提出在临床实践过程中应遵循个体化和渐进性原则对 PCOS 患者进行规范诱导排卵。

【关键词】 多囊卵巢综合征；诱导排卵；胰岛素抵抗；生活方式干预；受精，体外

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Interpretation to SOGC clinical practice guideline: No. 362-Ovulation Induction in Polycystic Ovary Syndrome

Zhang Qiaoli, Jia Chanwei, Zhou Liying, Liu Yanjun, Yu Lan, Xu Xiaoyu, Wang Shuyu

Department of Human Reproductive Medicine, Beijing Obstetrics and Gynecology Hospital, Capital Medical University, Beijing 100026, China

Corresponding author: Wang Shuyu, Email: yushu572000@126.com, Tel: +86-10-85960837

【Abstract】 Polycystic ovary syndrome (PCOS), a common clinical endocrine disorder, is the main cause of anovulatory infertility in women of childbearing age. The clinical practice guideline for ovulation induction in PCOS patients has been supported by the Society of Obstetricians and Gynaecologists of Canada (SOGC) in 2018. First line management of infertility once a diagnosis of PCOS is made should include weight loss and lifestyle modifications. Subsequently, first line medical therapy for ovulation induction should include selective estrogen receptor modulator—clomiphene citrate (CC) and aromatase inhibitor—letrozole (LE). The gonadotropins (Gn) should be considered as the second-line medical therapy, and *in vitro* fertilization treatment should be the third-line medical therapy. Insulin resistant patients can take the insulin sensitizer—metformin. When there are other indications for laparoscopy, laparoscopic ovarian drilling (LOD) may be considered in cases of CC or LE resistant PCOS. The clinical preventive action, that individual and progressive principles should be followed to normalize ovulation induction in PCOS patients.

【Key words】 Polycystic ovary syndrome；Ovulation induction；Insulin resistance；Lifestyle modifications；Fertilization *in vitro*

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