

• 实验研究 •

抗神经生长因子抗体用于改善子宫腺肌病 小鼠宫腔内环境的研究

李雁 叶瑶 徐步芳 张爱军

(上海交通大学医学院附属瑞金医院生殖医学中心, 上海, 200025)

【摘要】目的: 探讨抗神经生长因子抗体(anti-NGF)对改善子宫腺肌病(AM)小鼠宫腔内环境的作用。方法: 将15只雌性ICR小鼠随机分为AM治疗组(A组)、AM溶剂对照组(B组)及正常对照组(C组), A、B组使用口服他莫昔芬法建立AM小鼠模型。A组小鼠腹腔注射anti-NGF, B组以等体积的生理盐水替代, C组不作任何处理。3组小鼠于动情前期处死取双子宫称量后检测缓激肽受体1(BKR-1)、神经激肽1受体(NK-1R)、同源框基因转录因子A10(HOXA10)及芳香化酶(aromatase)基因与蛋白的表达。结果: A组子宫相对重量同B组, 且均明显高于C组($P<0.05$); A组BKR-1基因及蛋白和NK-1R基因水平较B组明显降低($P<0.05$), 与C组比较无统计学差异($P>0.05$); A组HOXA10基因及蛋白水平较B组明显增高($P<0.05$), 与C组比较无统计学差异($P>0.05$); A组芳香化酶基因及蛋白水平较B组减低($P<0.05$), 但仍高于C组($P<0.05$)。结论: anti-NGF可显著缓解AM模型小鼠子宫炎症, 改善内膜容受性、抑制芳香化酶表达, 但短期使用不能抑制病灶增殖。

关键词: 子宫腺肌病(AM); 抗神经生长因子抗体(anti-NGF); 治疗; 炎症; 宫腔内环境

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通讯作者: 张爱军; Tel: +86-21-64370045;

E-mail: ggenesis@126.com

Improving internal environment of mouse uteri with adenomyosis by administration of anti-NGF

Yan LI, Yao YE, Bu-fang XU, Ai-jun ZHANG

(Reproductive Center, Ruijin Hospital, Shanghai Jiao Tong University Medical College, Shanghai, 200025)

【ABSTRACT】 Objective: To explore the effect of anti-nerve growth factor (anti-NGF) on the uteri of adenomyosis (AM) mice. **Methods:** A total of 15 healthy and clean ICR mice were divided into 3 groups which were AM treatment group (group A), AM placebo group (group B) and normal control group (group C) with 5 mice per group. ICR mice with AM (group A and group B) were induced by orally administration of tamoxifen. The mice in group A were intraperitoneal injected with rabbit anti-NGF antibody. The mice in three groups were killed at preoestrus and bilateral uteri were taken. The levels of mRNA and protein for bradykinin receptor 1 (BKR-1), neurokinin1 receptor (NK-1R), homeobox A10 (HOXA10) and aromatase were examined. **Results:** The uterine weight of group A and group B was significantly greater than that in group C ($P<0.05$), but there was no significant difference between group A and group B. The mRNA and protein level of BKR-1 and the mRNA level of NK-1R in group A were lower than those in group B ($P<0.05$) and had no significant difference with group C. The mRNA and protein levels of HOXA10 in group A were higher than those in group B ($P<0.05$) and had no difference with group C. The aromatase mRNA and protein levels of group A were lower than those in group B ($P<0.05$), but were higher than those in group C ($P<0.05$). **Conclusion:** Anti-NGF can significantly relieve inflammation in uteri of AM moden mice. It may play a role in improving endometrium receptivity, inhibiting the local estrogen synthesis. However, it plays no role in inhibiting the proliferation of AM lesions for short-term using.

Key words: adenomyosis (AM); anti-nerve growth factor (anti-NGF); therapy; inflammation; uterine internal

PPAR γ 激动剂对多囊卵巢综合征患者颗粒细胞中细胞色素P450芳香化酶调控机制的研究

王碧君 郭艺红 王笑 张惠红 郝梦梦 李婧

(郑州大学第一附属医院生殖中心, 郑州, 450052)

【摘要】目的: 探讨多囊卵巢综合征(PCOS)患者颗粒细胞中Smad2蛋白是否参与过氧化物酶体增殖物激活受体(PPAR γ)对细胞色素P450芳香化酶(P450arom)的调控作用。方法: 选择雄激素正常的PCOS患者10例(NA-PCOS组, A组)、伴高雄血症的PCOS患者10例(HA-PCOS组, B组)、输卵管因素致不孕患者10例(对照组, C组); 测定各组患者的基础血清性激素水平; 提取各组患者颗粒细胞, 分别给予不同浓度罗格列酮(RSG)进行干预并加入雄烯二酮培养, 用RT-PCR测定PPAR γ 、P450arom mRNA表达, Western blotting测定Smad2、p-Smad2蛋白的表达。结果: ① C组的P450arom mRNA相对表达量(0.823 ± 0.094)显著高于A组(0.537 ± 0.059)和B组(0.322 ± 0.035), PPAR γ mRNA表达量(0.176 ± 0.025)显著低于A组(0.381 ± 0.045)和B组(0.587 ± 0.068), 差异均有统计学意义($P < 0.05$)。② 随着RSG浓度的增加(0 nmol/L、1 nmol/L、10 nmol/L), A、B、C组P450arom mRNA表达水平、p-Smad2蛋白水平均下降, 其中B组的变化最明显($P < 0.05$)。结论: PPAR γ 激动剂可能影响TGF- β /Smads信号途径, 通过阻碍Smad2蛋白磷酸化从抑制P450arom的表达。

关键词: 多囊卵巢综合征(PCOS); 超家族过氧化物酶体增殖物激活受体(PPAR γ); 细胞色素P450芳香化酶(P450arom); TGF- β /Smads 信号途径

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通讯作者: 郭艺红; Tel: +86-13613863710; Fax: +86-371-66964992;
E-mail: 13613863710@163.com

Regulatory mechanism of PPAR γ agonist to P450arom in the ovarian granulosa cells with PCOS

Bi-jun WANG, Yi-hong GUO, Xiao WANG, Hui-hong ZHANG,
Meng-meng HAO, Jing LI

(Department of Reproductive Medicine, the First Affiliated Hospital of Zhengzhou University, Zhengzhou, 450052)

【ABSTRACT】 Objective: To investigate the regulation of PPAR γ to P450arom in the ovarian granulosa cells of patients with polycystic ovary syndrome (PCOS). **Methods:** A total of 30 patients were included, with 10 patients in NA-PCOS (PCOS with normal androgen) group (group A), 10 patients in HA-PCOS (PCOS with hyperandrogenism) group (group B) and 10 patients in control group (group C). Blood samples were collected. Granulosa cells of each patient were divided into three groups after being added different concentrations of rosiglitazone (RSG), mRNA expression of PPAR γ and P450arom was measured by RT-PCR, and Smad2 and p-Smad2 protein levels were measured by Western blotting. **Results:** 1) P450arom mRNA expression in group C (0.823 ± 0.094) was significantly higher than that of PCOS groups (0.537 ± 0.059 , 0.322 ± 0.035) ($P < 0.05$), PPAR γ mRNA expression in PCOS groups (0.381 ± 0.045 , 0.587 ± 0.068) was significantly higher than that in the control (0.176 ± 0.025) ($P < 0.05$). 2) With the RSG concentration adding, the expression levels of P450arom mRNA and p-Smad2 protein were both decreased as the increasing expression of PPAR γ mRNA [$\chi\omicron\mu\pi\alpha\epsilon\delta\omega\iota\pi\eta\tau\eta\epsilon\chi\omicron\nu\pi\omega\lambda(0\nu\mu\omicron\lambda\lambda)$, $P < 0.05$], and group B changed the most ($P < 0.05$). **Conclusion:** PPAR γ may affect transforming growth factor- β (TGF- β) Smads signaling pathways and hinder Smad2 proteins phosphorylation to inhibit the expression of P450arom.

Key words: polycystic ovary syndrome (PCOS); peroxisome proliferator-activated receptor gamma (PPAR γ); cytochrome P450 (P450arom); TGF- β /Smads signal pathway

血管紧张素(Ang) II、Ang-(1-7)对人卵巢黄素化颗粒细胞的增殖及分泌功能的影响

陈丽华¹ 刘洁² 李晓冬²

(1. 河北北方学院附属第一医院, 张家口, 075000)

(2. 河北医科大学第二医院, 石家庄, 050000)

【摘要】目的: 了解血管紧张素(Ang) II、Ang-(1-7)对人卵巢黄素化颗粒细胞的增殖及分泌功能的影响。方法: 提取行体外受精/卵胞质内单精子注射-胚胎移植(IVF/ICSI-ET)患者卵泡液中的颗粒细胞, 经过提纯后随机分为实验组与对照组。实验组根据添加的药物分为Ang II组与Ang-(1-7)组。分别向Ang II组/Ang-(1-7)组的颗粒细胞培养液中加入 10^{-10} ~ 10^{-5} mmol/L浓度的Ang II/Ang-(1-7), 对照组的颗粒细胞培养液中不添加药物, 各组分别作用24 h、48 h、72 h, 用四甲基偶氮唑蓝盐比色法(MTT法)测定颗粒细胞的吸光度(D)值; 向Ang II组/Ang-(1-7)组的颗粒细胞培养液中分别加入 10^{-6} mmol/L浓度的Ang II/Ang-(1-7), 对照组的培养液中不添加药物, 收集培养0~24 h、24~48 h、48~72 h的上清液, 化学发光分析法(CL)测定黄素化颗粒细胞上清液中雌二醇(E₂)、孕酮(P)水平。结果: 不同浓度的Ang II、Ang-(1-7)分别作用颗粒细胞后, 其D值均较对照组低, 并随着浓度增加D值逐渐降低; 随着时间延长, 各组D值逐渐升高。 10^{-6} mmol/L浓度的Ang II、Ang-(1-7)分别作用于颗粒细胞后, 其上清液中E₂的浓度均较对照组高, P浓度与对照组无统计学差异, 随着时间延长, 各组的E₂和P含量逐渐增加。结论: Ang II及Ang-(1-7)对人卵巢黄素化颗粒细胞生长起抑制作用, 其抑制作用随浓度增加逐渐增强。Ang II、Ang-(1-7)能够增强人卵巢黄素化颗粒细胞分泌雌激素的作用, 但对孕激素的分泌没有影响。提示Ang II、Ang-(1-7)在人卵巢黄素化颗粒细胞的增殖及激素分泌中起一定作用, 两者可能参与了人类的卵泡闭锁、优势卵泡发育、成熟以及排卵等生理过程。

关键词: 血管紧张素(Ang) II; 血管紧张素 1-7[Ang-(1-7)]; 人卵巢黄素化颗粒细胞; 细胞增殖; 雌二醇(E₂); 孕酮(P)

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通讯作者: 李晓冬; Tel/Fax: +86-13933160139;

E-mail: 709866384@qq.com

Effects of angiotensin (Ang) II, Ang-(1-7) on the proliferation and secretory function of human luteinized granulosa cells

Li-hua CHEN¹, Jie LIU², Xiao-dong LI²

(1. The First Affiliated Hospital of Hebei North University, Zhangjiakou, 075000)

(2. The Second Hospital of Hebei Medical University, Shijiazhuang, 050000)

【ABSTRACT】 Objective: To investigate the effects of angiotensin (Ang) II, Ang-(1-7) on the proliferation and secretory function of human luteinized granulosa cells. **Methods:** The granulosa cells in the follicular fluid were extracted from the patients undergoing IVF/ICSI-ET cycles, and were randomly divided into experimental group and control group after purification. According to adding different drugs, the experimental group was divided into Ang II group and Ang-(1-7) group. Granulosa cells of Ang II group were interfered with the Ang II of 10^{-10} – 10^{-5} mmol/L dose, granulosa cells of Ang-(1-7) group were interfered with the Ang-(1-7) of 10^{-10} – 10^{-5} mmol/L dose. The control was interfered without drug. All of the groups were cultured by 24 h, 48 h and 72 h, respectively, *D* values were determined by MTT method; Ang II group and Ang-(1-7) group were interfered with Ang II and Ang-(1-7) of 10^{-6} mmol/L dose respectively, the control was interfered without drug. All of the groups were cultured and the supernatant was collected by 24 h, 48 h and 72 h. The estradiol (E_2) and progesterone (P) levels in the culture medium were detected by chemiluminescence method. **Results:** Compared with control group, all the *D* values of granulosa cells interfered with Ang II, Ang-(1-7) in different doses and at different time were lower ($P < 0.05$), and the *D* values gradually reduced with the increase of concentrations, the *D* values of all groups were increased as time went by. Compared with control group, the E_2 levels of Ang II group and Ang-(1-7) group were higher which interfered with Ang II and Ang-(1-7) of 10^{-6} mmol/L, respectively at the different time, but the P levels of Ang II group, Ang-(1-7) group and control group had no obvious difference. As time went by, the E_2 , P levels of all the groups were increased. **Conclusion:** Both of Ang II and Ang-(1-7) restrained the growth of the granulosa cells, and the effect was enhanced with increased dose. Both Ang II and Ang-(1-7) promoted ovarian granulosa cells estrogen secretion, but it had no significant effect on P secretion. It prompted that Ang II and Ang-(1-7) played an important role in proliferation and hormone secretion of human ovarian granulosa cells, and both of them might participate in the human physiological processes of follicular atresia, advantages, mature follicle development and ovulation.

Key words: angiotensin (Ang) II; angiotensin1-7 [Ang-(1-7)]; granulosa cell; cell proliferation; estradiol (E_2); progesterone (P)

乙酸阴道热敏凝胶剂流变性和体外释药行为的研究

田芳¹ 王玉柱¹ 黄超¹ 职瑞娜^{1,2} 丁训诚¹ 李卫华¹

(1. 国家人口和计划生育委员会计划生育药具重点实验室, 上海市计划生育科学研究所, 上海, 200032)

(2. 复旦大学公共卫生学院, 上海, 200032)

【摘要】目的: 乙酸阴道热敏原位凝胶剂(Acetic Acid vaginal thermosensitive *in situ* gel, Ace-Acid TISG)作为一种候选阴道外用避孕药, 具有温度敏感性的特点, 本文旨在考察在不同温度下的流变性质、凝胶溶蚀以及体外释放特性。方法: 冷法制备 Ace-Acid TISG, 采用 Kinexus Pro 高级旋转流变仪测定相转变温度, 胶凝温度以及不同温度下相变过程中的流变参数; 无膜溶出法检测凝胶的溶蚀行为; 电位滴定法测定乙酸的体外释放度。结果: Ace-Acid TISG 相转变温度为 25 ℃, 胶凝温度为 30 ℃; 低温下为流体, 粘弹性很低, 相角很高; 温度升高, 粘弹性呈指数增长, 相角降低。乙酸体外释放速率与凝胶溶蚀速率呈现良好的线性关系, 两者遵循零级动力学方程。结论: 本凝胶制剂具有良好的热敏感性和体外释放性, 符合阴道即用型凝胶的要求, 有望在临床中获得应用。

关键词: 乙酸; 热敏原位凝胶; 胶凝温度; 相转变; 凝胶溶蚀; 体外释放

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通讯作者: 李卫华; Tel/Fax: +86-21-64437475;

E-mail: iamliwehua@yahoo.com

Rheological characteristics and *in vivo* release of acetic acid vaginal thermosensitive *in situ* gel

Fang TIAN¹, Yu-zhu WANG¹, Chao HUANG¹, Rui-na ZHI^{1,2},

Xun-cheng DING¹, Wei-hua LI¹

(1. State Key Labs of Family Planning Devices, Shanghai Institute of Planned Parenthood Research, Shanghai, 200032)

(2. School of Public Health, Fudan University, Shanghai, 200032)

【ABSTRACT】 Objective: Acetic Acid vaginal thermosensitive *in situ* gel (Ace-Acid TISG) is expected to be used as vaginal topical contraceptive candidate and characterized to be thermosensitive. We aimed to detect the rheological properties at different temperatures, the gel dissolution and *in vitro*. **Methods:** Ace-Acid TISG was prepared using the cold method. The phase transition temperature (PTT), gelling temperature and the different rheological parameters were detected using Kinexus Pro Advanced rotation rheometer during the phase transition. The dissolution behavior was measured by the membraneless dissolution test. *In vitro* release was tested by the potentiometric titration method. **Results:** The PTT and the GT of Ace-Acid TISG were 25 °C and 30 °C, respectively. When the temperature was below 25 °C, Ace-Acid TISG was fluid, its viscoelasticity was very low and phase angle (δ) was 80°–90°; as the temperature increasing, its viscoelasticity showed exponential growing, δ decreases (30°–40°). It showed the typical linear relationship between the *in vitro* release rate and gel dissolution rate of acetic acid, and followed zero-order kinetics. **Conclusion:** Ace-Acid TISG is the thermosensitive gel. It can meet the requirements for vaginal topical use and is expected to be applied in clinical practice.

Key words: acetic acid; thermosensitive *in situ* gel; phase transition; gelation temperature; gel dissolution; *in vitro* release

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通讯作者: 李卫华; Tel/Fax: +86-21-64437475;
E-mail: iamliwehua@yahoo.com

含铜宫内节育器中吲哚美辛体外释放规律的研究

邹凤平 吉蓉 丁彪 姚天平

(上海市医疗器械检测所, 上海, 201318)

【摘要】目的: 测定含铜宫内节育器(CuIUD)中吲哚美辛(IMC)在体外模拟宫腔液中的释放规律。方法: 以体外模拟宫腔液作为提取介质, 在 37 ± 0.5 °C条件下静态释放IMC, 然后通过高效液相色谱(HPLC)检测IMC的释放量。结果: IMC释放试验的前期释放量有较大(2.2~2.5 mg)的药物突释现象, 释放率占载药量的10%, 中期IMC的日均释放量逐渐变得缓慢, 后期IMC的日均释放量趋于稳定。整个周期的释放量为7~12 mg, 释放率占载药量的36%~49%。结论: 建立了HPLC测定IMC在模拟宫腔液释放量的方法, 且IMC体外累积释放率呈幂函数释放规律, 每日释放量呈逐日下降趋势。

关键词: 含铜宫内节育器(CuIUD); 高效液相色谱法; 吲哚美辛释放量

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通讯作者: 姚天平; Tel/Fax: +86-21-3801990*1421;
E-mail: ytp_2013@163.com

Study on *in vitro* release behavior of indomethacin used for CuIUD

Feng-ping ZOU, Rong JI, Biao DING, Tian-ping YAO

(Shanghai Testing & Inspection Institute for Medical Devices, Shanghai, 201318)

【ABSTRACT】 Objective: To evaluate the release behavior of indomethacin (IMC) *in vitro* used for CuIUD. **Methods:** Four kinds of CuIUDs soaked in simulated uterine fluid, the concentration of IMC was analyzed by high performance liquid chromatography (HPLC). **Results:** IMC was released profusely from indomethacin rubber in initial term (2.2–2.5 mg), the releasing degree was 10%, then the daily release degree of IMC was slowly in medium term. In the following days, the trend of release level was even and steady. Releasing amount of IMC was 7–12 mg during the whole experiment, the releasing degree was 36%–49%. **Conclusion:** The HPLC method was established for the determination of IMC releasing content in simulated uterine fluid, and the accumulating release behavior of IMC follows the power function rule and the daily releasing trend is decreasing gradually.

Key words: CuIUD; high performance liquid chromatography (HPLC); release degree of indomethacin (IMC)

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通讯作者: 姚天平; Tel/Fax: +86-21-3801990*1421;

E-mail: ytp_2013@163.com

• 临床研究 •

孕激素抑制LH峰在控制性卵巢 刺激过程中的疗效观察

朱秀娴^{1,2*} 章晓乐^{1,3*} 傅永伦¹

(1. 上海交通大学医学院附属第九人民医院辅助生殖科, 上海, 200011)

(2. 上海交通大学医学院九院临床医学院, 上海, 200011)

(3. 上海中医药大学附属曙光医院妇产科, 上海, 201203)

【摘要】目的: 探讨在控制性卵巢刺激(COS)过程中应用孕激素抑制黄体生成素(LH)峰的临床效果。方法: 回顾性分析83例行体外受精/卵胞质内单精子注射-冻融胚胎移植(IVF/ICSI-FET)患者的资料, 所有患者均采用孕激素联合促性腺激素方案, 83个取卵周期共完成了92个FET周期, 统计分析促排卵过程中的激素变化、胚胎实验室情况及妊娠结局。结果: 在促排卵过程中, LH持续低水平, 基础、中期(月经第9~11日)、诱发排卵当日LH水平分别为 3.85 ± 2.03 IU/L、 3.64 ± 2.01 IU/L、 2.62 ± 1.77 IU/L, 未监测到LH峰。hMG的用药剂量为 1964.76 ± 468.73 IU, 孕激素(商品名: 安琪坦)的用药剂量为 2.05 ± 0.34 g。平均获卵数为 10.9 ± 6.1 , 每个取卵周期平均冷冻 5.0 ± 2.5 个胚胎。FET后临床妊娠率为52.17%(48/92), 胚胎种植率为39.34%(72/183), 流产率为10.42%(5/48)。结论: 孕激素能够有效抑制LH峰, 孕激素联合Gn促排卵方案为基于FET的促排卵技术提供了新的备选方案。

关键词: 孕激素; 黄体生成素(LH)峰; 安琪坦; 控制性卵巢刺激(COS); 冻融胚胎移植(FET)

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通讯作者: 傅永伦; Tel/Fax: +86-21-53078108;

E-mail: fuyonglunivf@163.com

*: 为共同第一作者

Effect of progesterone used to prevent LH surges in controlled ovarian stimulation

Xiu-xian ZHU^{1,2*}, Xiao-le ZHANG^{1,3*}, Yong-lun FU¹

(1. Department of Assisted Reproduction, Shanghai Ninth People's Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, 200011)

(2. Shanghai Jiao Tong University School of Medicine, Shanghai, 200011)

(3. Department of Gynaecology, Shuguang Hospital Affiliated to Shanghai University of Traditional Chinese Medicine, Shanghai, 201203)

*: Equally contributed to the research

【ABSTRACT】Objective: To explore whether progesterone (P) can be used clinically to prevent LH surges in controlled ovarian stimulation (COS) for IVF cycle with the subsequent frozen-thawed embryo transfer (FET). **Methods:** A total of 83 patients undergoing COS in a gonadotropin (Gn) and P (trade name: Utrogestan[®]) protocol were analyzed. After COS, 92 FET cycles had been finished. The changes of hormones during COS, the embryo information and the pregnancy outcomes were analyzed. **Results:** The LH levels on day 3, day 9–11 and the trigger day were 3.85 ± 2.03 IU/L, 3.64 ± 2.01 IU/L, 2.62 ± 1.77 IU/L, respectively, and premature LH surges were not detected. The dose of Gn was 1964.76 ± 468.73 IU, and the dose of progesterone was 2.05 ± 0.34 g. The number of oocytes retrieved was 10.9 ± 6.1 and the number of cryopreserved embryos was 5.0 ± 2.5 . After FET, the clinical pregnancy rate was 52.17% (48/92), the implantation rate was 39.34% (72/183), and the abortion rate was 10.42% (5/48). **Conclusion:** The usage of progesterone is an effective method to inhibit the premature LH surges, and the Gn and P protocol is a novel protocol in combination with FET.

Key words: progesterone (P); LH surge; Utrogestan[®]; controlled ovarian stimulation (COS); frozen-thawed embryo transfer (FET)

通讯作者: 傅永伦; Tel/Fax: +86-21-53078108;

E-mail: fuyonglunivf@163.com

*: 为共同第一作者

GnRH激动剂长效剂型和短效剂型 在长方案中的应用比较

宋娟¹ 龚斐^{1,2} 罗克利^{1,2} 张顺吉²

(1. 中南大学湘雅医学院生殖与干细胞工程研究所, 长沙, 410000)
(2. 中信湘雅生殖与遗传专科医院, 长沙, 410000)

【摘要】目的: 探讨比较 GnRH激动剂(GnRH-a)长效剂型和短效剂型在长方案中的临床应用效果。方法: 将IVF-ET/ICSI治疗的长方案患者按照GnRH-a的不同剂型分为长效组(A组)和短效组(B组), 比较A、B组间垂体降调节效果、促排卵过程及妊娠结局。结果: A组促性腺激素(Gn)总量、Gn使用天数、hCG注射日P、P/E₂、子宫内膜厚度、平均获卵数、受精率及中、重度卵巢过度刺激综合征(OHSS)发生率高于B组, 差异有统计学意义($P < 0.05$); B组hCG注射日LH、E₂、OHSS取消率、优质胚胎率、流产率较A组高, 差异有统计学意义($P < 0.05$)。移植胚胎数、移植妊娠率、着床率、宫外孕率比较组间无显著差异。结论: 在控制性超促排卵(COH)长方案中应用GnRH-a长、短效2种剂型均可获得较满意的垂体降调节效果, 虽各有利弊, 但并不影响妊娠结局。

关键词: GnRH激动剂(GnRH-a); 长方案; 垂体降调节; 妊娠结局

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通讯作者: 龚斐; Tel: +86-18674860305;
E-mail: lj_0305@126.com

Application of long and short acting GnRH agonists in the long protocol

Juan SONG¹, Fei GONG^{1,2}, Ke-li LUO^{1,2}, Shun-ji ZHANG²

(1. Xiangya School of Medicine, CSU, Changsha, 410000)

(2. Reproductive & Genetic Hospital CITIC-Xiangya, Changsha, 410000)

【ABSTRACT】 Objective: To compare the clinical effect of long and short acting GnRH agonists (GnRH-a) in the long protocol. **Methods:** Patients in IVF-ET treatment with long protocol were divided into the long acting group (group A) and short acting group (group B). The pituitary down regulation effect, ovulation and pregnancy outcome of two groups were compared. **Results:** In group A, total Gn doses, Gn stimulation days, hCG level, P, P/E₂, and endometrial thickness, average oocyte number, the fertilization rate and the incidence of moderate and severe OHSS were significantly higher than those of group B ($P<0.05$); hCG, LH, E₂ levels, the OHSS cancellation rate, the good-quality embryo rate, the abortion rate of group B were higher than those in group A ($P<0.05$). The number of transferred embryos, the pregnancy rate, the implantation rate and ectopic pregnancy rate between the two groups were not significantly different. **Conclusion:** The application of two forms of GnRH-a in controlled ovarian hyperstimulation (COH) can get satisfactory pituitary down regulation effect, although each has advantages and disadvantages, it does not affect the outcome of pregnancy.

Key words: GnRH agonist (GnRH-a); long protocol; pituitary down regulation; pregnancy outcome

卵巢功能正常患者高孕激素状态下促排卵的内分泌特征及IVF/ICSI临床结局的研究

叶静^{1,2} 陈秋菊¹ 匡延平¹

(1. 上海交通大学医学院附属第九人民医院辅助生殖科, 上海, 200011)

(2. 上海交通大学医学院九院临床医学院, 上海, 200011)

【摘要】目的: 探讨高孕激素状态下促排卵方案在临床应用中的价值。方法: 将因输卵管因素或男方因素或不明原因行 IVF/ICSI 治疗的不孕症患者分成高孕激素状态下促排卵组(A组, $n=57$)和短方案组(B组, $n=59$), 观察患者的获卵数、成熟卵数、正常受精数、卵裂数、有效胚胎数及促排卵过程中血清 FSH、LH、 E_2 、P、抑制素 A 和 B 的水平及后续冻融胚胎移植(FET)周期的妊娠结局。结果: 高孕激素促排卵组患者的获卵数 10.8 ± 5.4 个, 与短方案组相比无统计学差异 ($P>0.05$), 获卵数、成熟卵数、受精数、卵裂数, 有效胚胎数与短方案组相似 ($P>0.05$), 后续的 FET 周期中, 临床妊娠率和胚胎种植率比短方案组稍高 (47.9%, 42.1% vs 40.9%, 31.9%), 但均无统计学差异 ($P>0.05$)。高孕激素促排卵过程中 LH 水平逐渐下降, 诱发排卵日的 LH 水平在 1.3 ± 0.9 IU/L, 无一例发生自发 LH 峰。结论: 高孕激素状态下促排卵组可以获得具有发育潜能的胚胎, 还可以有效控制早发 LH 峰。高孕激素状态下促排卵方案可作为一种新的促排卵方案应用于临床实践, 但是其广泛推广应用还有待多中心的联合研究。

关键词: 促排卵; IVF/ICSI; 临床结局

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通讯作者: 匡延平; Tel/Fax: +86-21-53078108;
E-mail: kuangyanp@126.com

Endocrine characteristic and the clinical outcomes of IVF/ICSI treatment in women with normal ovarian reserve during progestin-primed ovarian stimulation

Jing YE^{1,2}, Qiu-ju CHEN¹, Yan-ping KUANG¹

(1. Reproductive Medicine Department of Shanghai Ninth People's Hospital Affiliated Shanghai Jiao Tong University School of Medicine, Shanghai, 200011)

(2. Shanghai Jiao Tong University School of Medicine, Shanghai, 200011)

【ABSTRACT】 Objective: To analyze the endocrine characteristics and the clinical outcomes of IVF/ICSI treatment during progestin-primed ovarian stimulation, and to explore the value of clinical application of progestin-primed ovarian stimulation. **Methods:** A prospective study including 116 patients with normal ovarian reserve was performed, the patients were divided into two groups. In group A ($n=57$), hMG and medroxyprogesterone acetate (MPA) were administered simultaneously beginning on menstrual cycle day 3/4, that is progestin-primed ovarian stimulation. In group B ($n=59$), the short protocol was performed. The levels of FSH, LH, E₂, P, inhibin A and inhibin B were measured during the ovarian stimulation to investigate the endocrine characteristic of progestin-primed ovarian stimulation. The number of oocytes retrieved, the number of mature oocytes, the number of fertilization and the number of cleavage, the clinical pregnancy rates and the implantation rates in the subsequent FET cycles were compared between the two groups. **Results:** The number of oocytes retrieved in group A was similar to group B ($P>0.05$). No differences were found in the number of mature oocytes, the number of fertilization and the number of cleavage between the two groups. No statistically significant differences were found in the clinical pregnancy rates and the implantation rates in frozen-thawed embryo transfer (FET) cycles. LH values gradually decreased during progestin-primed ovarian stimulation and no patients experienced premature LH surge. **Conclusion:** The embryos originating from the progestin-primed ovarian stimulation have a similar developmental potential compared with the control. Progestin-primed ovarian stimulation provides an effective method to control premature LH surge during the ovarian stimulation. Progestin-primed ovarian stimulation can be used as a new kind of ovarian stimulation scheme applied in clinical practice to control premature LH surge during the ovarian stimulation, but its widespread application has yet to need more centers join this research.

Key words: ovarian stimulation; IVF/ICSI; clinical outcomes

谷胱甘肽S-转移酶基因多态性与男性特发性少弱精子不育症患者精液参数相关性研究

唐开发¹ 王鹏飞¹ 徐绍源² 丁上书²

刘睿哲² 王新阳² 孙发¹ 邢俊平²

(1. 贵州医科大学附属医院泌尿外科, 贵阳, 550004)

(2. 西安交通大学医学院第一附属医院泌尿外科, 西安, 710061)

【摘要】目的: 探讨谷胱甘肽S-转移酶(glutathione S-transferase, GST)M1、T1及P1基因多态性与男性特发性少弱精子不育症患者精液参数的相关性。方法: 收集246例男性特发性少弱精子不育症患者的全血及精液。采用聚合酶链反应(polymerase chain reaction, PCR)、聚合酶链反应-限制性片段长度多态性(polymerase chain reaction-restriction fragment length polymorphism, PCR-RFLP)方法分别对GSTM1、T1和P1基因进行分型; 计算机精液辅助分析(computer-aided semen analysis system, CASA)系统对精液常规参数及精子运动参数进行检测。结果: GSTM1及T1基因缺失型特发性少弱精子不育症患者精子浓度等常规参数及平均曲线运动速度(curvilinear velocity, VCL)等运动参数与野生型组有显著差异($P < 0.05$)。另外, 经Logistic回归分析GSTM1及T1基因缺失型与精子常规参数及运动参数呈负性相关。结论: GSTM1、T1基因缺失型与特发性少弱精子男性不育精液参数存在负相关。而GSTP1基因多态性与特发性少弱精子男性不育精液参数无明显相关性。

关键词: 男性不育症; 谷胱甘肽S-转移酶(GST); 多态性; 精液分析

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通讯作者: 邢俊平; E-mail: xingjpcn@gmail.com

孙发; E-mail: sfguizhou@163.com

Correlation between glutathione S-transferase polymorphisms and semen parameters in male infertile patients with idiopathic oligoasthenospermia

Kai-fa TANG¹, Peng-fei WANG¹, Shao-yuan XU², Shang-shu DING²,
Rui-zhe LIU², Xin-yang WANG², Fa SUN¹, Jun-ping XING²

(1. Department of Urology, the Affiliated Hospital of Guizhou Medical University, Guiyang, 550004)

(2. Department of Urology, the First Affiliated Hospital of Medical college of Xi'an Jiaotong University, Xi'an, 710061)

【ABSTRACT】 Objective: To investigate the relationship between glutathione S-transferase enzyme (GST) gene *M1*, *T1* and *P1* gene polymorphism and semen parameters of infertile idiopathic patients with oligoasthenospermia. **Methods:** The study included 246 infertile idiopathic patients with oligoasthenospermia. Polymerase chain reaction (PCR) and polymerase chain reaction restriction fragment length polymorphism (polymerase chain reaction-restriction fragment length polymorphism, PCR-RFLP) methods were used to identify *GSTM1*, *T1* and *P1* genotype, respectively. Computer assisted semen analysis (computer-aided semen analysis system, CASA) system was used to analyze the semen parameters. **Results:** The sperm concentration, vitality, motility, curvilinear velocity (VCL), straight line velocity (VSL), path velocity (VAP), straightness (STR), linearity (LIN), wobble (WOB) and beat cross frequency (BCF) in *GSTM1* and *T1* gene deletion group were lower and amplitude of lateral head displacement (ALH) was higher compared with these in wild type group in patients with idiopathic oligoasthenospermia infertility ($P < 0.01$). There were negative relations between *GSTM1*(-) and *GSTT1*(-) gene types and idiopathic oligoasthenospermia infertile patients on sperm concentration, motility, vitality VSL and other parameters according Logistic regression analysis. The STR and ALH in *GSTP1* (A/G+G/G) were lower and ALH was higher compared with these in wild type group in patients with idiopathic oligoasthenospermia ($P < 0.05$). **Conclusion:** There are negative correlations between *GSTM1* and *T1* gene deletion genotype and semen parameters in infertile patients with idiopathic oligoasthenospermia. However, there are little correlations between *GSTP1* polymorphisms and semen parameters.

Key words: male infertility; glutathione S-transferase (GST); polymorphism; semen analysis

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通讯作者: 邢俊平; E-mail: xingjpcn@gmail.com

孙发; E-mail: sfguizhou@163.com

· 综述 ·

骨形态发生蛋白 15(BMP15)/生长分化因子 9(GDF9)在卵巢功能及女性生育过程中的作用

余雁 周丽 全进毅

(杭州市妇产科医院, 杭州, 310000)

【摘要】人类卵巢功能的调节机制极其复杂,是由多个卵巢内旁分泌信号整合的中枢神经系统、垂体及卵巢之间进行复杂对话的过程。卵子来源的骨形态发生蛋白 15(BMP15)及生长分化因子 9(GDF9)是近年来新发现的卵巢内旁分泌调节机制相关调节分子,已逐渐成为卵巢功能维持及卵子发生调节的研究热点。BMP15/GDF9在女性生育中的主要的生物学功能包括:①促进卵泡生长及成熟(从不依赖于促性腺激素的原始卵泡期开始);②调节颗粒细胞对促卵泡生成素(FSH)作用的敏感性,决定卵泡排出的比例;③预防颗粒细胞凋亡;④促进卵泡的发育潜能。BMP15/GDF9异常将导致 Turner 综合征、卵巢功能不全,还可能与 PCOS, 异卵双胞胎有关;而卵泡液中 BMP15 水平是预测卵巢低反应患者 IVF 结局的一个潜在指标。

关键词: 女性生育力;骨形成蛋白 15(BMP15);生长分化因子 9(GDF9);原发性卵巢功能不足;多囊卵巢综合征(PCOS)

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通讯作者: 全进毅; Tel: +86-13588818180;
E-mail: yuyanhangzhou@163.com

Role of bone morphogenetic protein 15/growth and differentiation factor 9 in ovarian function and female fertility

Yan YU, Li ZHOU, Jin-yi TONG

(Hangzhou Maternity Hospital, Hangzhou, 310000)

【ABSTRACT】 Ovarian folliculogenesis is finely tuned by a complex endocrine dialog between the central nervous system, the pituitary and the ovary. The network of signals exchanged between the oocyte and the surrounding granulosa cells (GCs) is far from being fully understood, but in recent years several of these signals have been discovered, thus opening previously unpredicted insights on this extraordinary biological process. The oocyte-derived bone morphogenetic protein 15 (BMP15) and growth and differentiation factor 9 (GDF9) are recently known as the critical signals in the ovary paracrine regulation mechanism, and have been a hot area of research for the regulation of ovarian function and oogenesis. The biological actions of BMP15/GDF9 include: 1) the promotion of follicle growth and maturation starting from the primary gonadotrophin-independent phases of folliculogenesis; 2) the regulation of follicular granulosa cell (GC) sensitivity to FSH action and the determination of ovulation quota; 3) the prevention of GC apoptosis and 4) the promotion of oocyte developmental competence. Abnormal expression of BMP15/GDF9 will lead to Turner syndrome and premature ovary failure (POF), and will be related to polycystic ovary syndrome (PCOS) and fraternal twins. BMP15 in follicular fluid maybe become a potential predictor for IVF outcomes of poor ovarian response patients.

Key words: female fertility; bone morphogenetic protein 15 (BMP15); growth and differentiation factor 9 (GDF9); primary ovarian insufficiency; polycystic ovary syndrome (PCOS)

染色体易位-胚胎植入前诊断的研究进展

范俊梅^{1,2} Cram David¹ 刘忠宇¹ 李娜³ 姚元庆¹

(1. 中国人民解放军总医院妇产科, 北京, 100853)

(2. 山西省妇幼保健院生殖医学中心, 太原, 030013)

(3. 第四军医大学唐都医院妇产科, 西安, 710038)

【摘要】 染色体易位携带者有较高的发生不良妊娠结局的风险, 主要源自高概率的非均衡配子。对于染色体易位的携带者, 进行胚胎植入前遗传学诊断(preimplantation genetic diagnosis, PGD)可以改善妊娠结局。目前, 临床应用的非平衡易位诊断的方法主要有比较基因组杂交微阵列(comparative genomic hybridization array, array CGH)、单核苷酸多态性微阵列(single nucleotide polymorphism array, SNP array)和二代测序(next generation sequencing, NGS); 荧光原位杂交(fluorescence *in situ* hybridization, FISH), 能够区分平衡易位和正常胚胎, 可能实现的技术有NGS。此外, 平衡易位的诊断是否有必要开展尚存在争议。

关键词: 染色体易位; 植入前遗传学诊断(PGD); 配子类型; 诊断方法; 生育能力

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通讯作者: 姚元庆; Tel/Fax: +86-10-66938043;

E-mail: yqyao@126.com

Chromosome translocations: the dynamics of embryos preimplantation genetic diagnosis

Jun-mei FAN^{1,2}, Cram David¹, Zhong-yu LIU¹, Na LI³, Yuan-qing YAO¹

(1. Department of Obstetrics and Gynecology, Chinese PLA General Hospital, Beijing, 100853)

(2. Department of Reproductive Center, Shanxi Maternal and Child Health Care Hospital, Taiyuan, 030013)

(3. Department of Obstetrics and Gynecology, Tangdu Hospital, the Fourth Military Medical University, Xi'an, 710038)

【ABSTRACT】 Chromosome translocation is closely related to high risk adverse pregnancy outcome which results from high percent unbalanced gametes. Preimplantation genetic diagnosis (PGD) is an effective way to improve pregnant outcome for those couple. Currently, comparative genomic hybridization array (array CGH), single nucleotide polymorphism array (SNP array) and next generation sequencing (NGS) are applied in unbalanced chromosome translocation diagnosis in PGD, and fluorescence *in situ* hybridization (FISH) for balanced. NGS might be feasible in future for balanced chromosome translocation diagnosis in PGD. Meanwhile, there are some controversies on the issues whether it is necessary to launch balanced translocation diagnosis.

Key words: chromosome translocation; preimplantation genetic diagnosis; gamete type; diagnosing method; reproduction

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通讯作者: 姚元庆; Tel/Fax: +86-10-66938043;

E-mail: yqyao@126.com

青春期多囊卵巢综合征治疗研究进展

刘颖华¹ 侯丽辉² 李妍² 高金金¹

(1. 黑龙江中医药大学, 哈尔滨, 150040)

(2. 黑龙江中医药大学附属第一医院妇产科, 哈尔滨, 150040)

【摘要】 多囊卵巢综合征(PCOS)是育龄期最常见的内分泌疾病,始于青春期。目前,青春期PCOS的诊断尚未明确,成人的诊断标准不完全适合于青春期,生活方式调整常为其一线干预措施,但有越来越多的研究显示胰岛素增敏剂、避孕药、抗雄激素药物及中医疗法对青春期PCOS亦有明显的改善作用。

关键词: 青春期; 多囊卵巢综合征(PCOS); 治疗; 诊断

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通讯作者: 侯丽辉; Tel/Fax: +86-451-82124304;

E-mail: houlihui2007@sina.com

Treatment of polycystic ovary syndrome in adolescence

Ying-hua LIU¹, Li-hui HOU², Yan LI², Jin-jin GAO¹

(1. Heilongjiang University of Chinese Medicine, Harbin, 150040)

(2. Department of Obstetrics and Gynecology, the First Affiliated Hospital, Heilongjiang University of Chinese Medicine, Harbin, 150040)

【ABSTRACT】 Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders in women of reproductive age, begins in adolescence. Currently, the diagnosis of adolescents with PCOS is a challenge and it does not apply for the diagnosis criteria of adults. Lifestyle therapy is the first-line therapy, but more and more studies show that insulin-sensitizing drugs, oral contraceptive pills, anti-androgens, traditional chinese medicine are effective for adolescents with PCOS. The paper provides an overview on the treatments of adolescents with PCOS.

Key words: adolescents; polycystic ovary syndrome (PCOS); treatment; diagnosis

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通讯作者: 侯丽辉; Tel/Fax: +86-451-82124304;

E-mail: houlihui2007@sina.com

B超在辅助生育技术中的主要应用

周久力 纪亚忠

(同济医院生殖医学中心, 上海, 200065)

【摘要】 B型超声是辅助生殖技术(ART)中的重要辅助检查方法, 常用于监测卵泡发育, 评价卵巢储备功能、预测排卵、诊断排卵障碍, 评估子宫内膜容受性, 为调整促排卵方案及内膜用药剂量提供重要依据; 同时应用与明确输卵管病变、评价卵巢储备功能、诊断排卵障碍、评估子宫内膜的容受性、引导卵巢穿刺取卵术、胚胎移植(ET)及多胎妊娠选择性减胎等相关手术, 对提高临床妊娠率起着重要作用。

关键词: B超; 辅助生殖技术(ART); 卵泡; 子宫内膜; 输卵管; 手术

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通讯作者: 纪亚忠; Tel: +86-13386273692;

E-mail: jiyazhong@hotmail.com

Main application of B-mode ultrasonography in assisted reproductive technology

Jiu-li ZHOU, Ya-zhong JI

(The Reproductive Medical Center of Tongji Hospital, Shanghai, 200065)

【ABSTRACT】 As an important adjuvant examination method in assisted reproductive technology (ART), B-mode ultrasonography is often applied to monitor the development of follicles, evaluate ovarian reserve function and endometrial receptivity, predict ovulation and diagnose ovulation failure, examine diseases of the fallopian tube, to provide an important basis on ovulation stimulation protocols, and it can also guide relevant surgeries, which plays a significant role in improving the clinical pregnancy rate.

Key words: B-mode ultrasonography; assisted reproductive technology (ART); follicle; endometrium; fallopian tube; surgery