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多囊卵巢综合征的临床复杂性及认识历程

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回溯几十年来对多囊卵巢综合征(polycystic ovary syndrome, PCOS)的认知和探究, 我们发现随着研究的深入, 其临床表现和病理病因都出乎预料的疑难和复杂。目前的研究显示, PCOS 对机体的影响广泛, 涉及多个系统方面。临床表现复杂多样, 不同患者之间甚至同一患者不同年龄段之间的临床表现有很大的差异。这使我们在认识疾病的第一步——准确诊断——遇到了很大的困难和挑战。

即使在今天, PCOS 仍像谜一样困扰着我们, 同时也吸引着我们不断地去研究探索。也许我们就像“盲人摸象”一样, 不同的表现也许只是因为观察的角度不同, 但是我们坚信, 经过我们的共同努力, 随着证据的不断积累, 我们终究有一天会证实“它原来是一头大象”或者“它根本不是大象”。“
临床研究

甲磺酸溴隐亭辅助克罗米芬诱导多囊卵巢综合征不孕患者排卵的随机、开放、对照临床研究

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【摘要】目的 研究多巴胺激动剂溴隐亭(BCT)联合克罗米芬(CC)对多囊卵巢综合征(PCOS)合并不孕患者促排卵助孕的疗效。方法 本研究为随机、开放、对照试验, 在上海 2 家医院共收集 PCOS 合并不孕患者 100 例, 随机分为对照组和试验组。对照组在月经周期 3~7 d 给予 CC 50 mg/d, 试验组在此基础上同时全周期给予 BCT 2.5 mg/d, 两组均治疗 1 个周期。在月经第 3 日, hCG 注射日、hCG 注射第 7 日抽血化验激素水平, 包括促卵泡激素(FSH)、促黄体生成素(LH)、催乳素(PRL)、雌二醇(E2)、总睾酮(T)、孕激素(P), 并行阴道超声测定子宫内膜厚度、卵泡大小, 数量。结果 两组的基础激素水平无统计学差异。对照组和试验组的促排卵成功率分别为 72.0% 和 75.4%(P=0.05), 试验组的持续妊娠率(18.4%)明显高于对照组(8.0%)。hCG 注射日的 FSH、E2、P 水平无统计学差异, LH 水平有所降低, PRL 和 T 显著降低(分别为 P<0.00, P=0.00); hCG 注射第 7 日的 E2、P 水平无统计学差异, PRL 显著下降, 试验组的子宫内膜厚度[(10.20±1.92) mm]明显高于对照组[(9.22±1.88) mm](P=0.01)。结论 BCT 联合 CC 可以提高 PCOS 患者的促排卵助孕成功率, 降低 PRL、LH、T 水平并增加子宫内膜厚度。提示多巴胺激动剂 BCT 可能通过降低垂体激素及雄激素水平、降低子宫内膜血管阻力并增加内膜血供改善 PCOS 不孕患者的助孕结局。

【关键词】 甲磺酸溴隐亭(BCT); 克罗米芬(CC); 多囊卵巢综合征(PCOS); 不孕; 诱导排卵
【基金项目】 上海市科委项目(KXSH021311)
Induction of ovulation with clomiphene combined with bromocriptine in polycystic ovary syndrome patients with infertility: a prospective, randomized, controlled clinical trial  
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【Abstract】Objective  To compare the effects of bromocriptine (BCT) combined with clomiphene citrate (CC) on the outcome of ovulation-induction in patients with polycystic ovary syndrome (PCOS). Methods  A prospective, randomized, controlled clinical trial was performed on 100 PCOS patients with infertility. Patients were randomly divided into two groups, control group received 50 mg CC from day 3 to day 7, test group (CC+ BCT) was given 50 mg of CC from day 3 to day 7 along with 2.5 mg of BCT daily for full cycle. Both the groups were treated for one cycle. Results  The outcomes were measured by the hormonal status, follicular size, endometrial thickness, ovulation rate, and pregnancy outcomes. The baseline level of hormones between the two groups was not different before treatment. After intervention, the rate of ovulation in CC group was 72.0% and in CC+ BCT group was 75.4% (P>0.05), the rate of ongoing pregnancy in CC+ BCT group (18.4%) was higher than that in CC group (8.0%). On hCG injection day, there were no statistically significant differences between two groups regarding to levels of follicle-stimulating hormone (FSH), estradiol (E2) and progesterone (P), but prolactin (PRL) and testosterone (T) was significantly decreased (respectively P=0.000, P=0.004), and LH level was also decreased but with no statistical significance (P=0.094). On hCG injection day 7, levels of P and E2 were not different between the two groups (respectively P=0.901, P=0.192), but PRL level was decreased (P=0.000) and the endometrial thickness was increased significantly (P=0.017). Conclusion  Our results showed that BCT plus CC can improve the outcome of ovulation-induction of PCOS patients, reducing levels of PRL, LH and T, and increasing the endometrial thickness of embryo implantation time. It can be concluded that use of BCT with CC improve the outcome of ovulation-induction more than use of CC alone for infertile PCOS patients, which may be brought about through dopamine agonists efficacy in reducing LH and PRL levels, vascular resistance and increasing uterine blood supply to the uterus.  
【Key words】 Bromocriptine (BCT); Clomiphene (CC); Polycystic ovary syndrome (PCOS); Infertility; Ovulation induction  
Fund program: Project of Shanghai Association for Science and Technology (KXSH021311)
GnRHa联合低剂量hCG扳机在高反应多囊卵巢综合征患者体外受精中的应用

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【摘要】目的 探讨多囊卵巢综合征(PCOS)高反应患者行体外受精/卵胞质内单精子显微注射(DVF/ICSI)治疗使用低剂量联合扳机的安全性和有效性。方法 回顾性队列分析2014年1月1日—2015年12月31日期间在本院生殖医学中心采用促性腺激素释放激素拮抗剂(GnRH-A)方案进行控制性促排卵行IVF/ICSI助孕的PCOS患者(n=364)的临床资料, 分为低剂量联合扳机组(GnRH-A+低剂量hCG, A组, n=127)和标准扳机组(hCG, B组, n=237)。分析比较因卵巢高反应采用不同扳机方案患者的临床资料。结果 患者一般情况和促排卵治疗用药组间均无统计学差异(P>0.05)。A组患者hCG扳机卵泡数2 PN[(19 193.9±7 837.5) pmol/L]及获卵数(29 ± 9)均显著高于B组患者(15 786.8±7 104.1) pmol/L, P<0.05; 24 ± 6, P<0.05]。A组患者I CSI授精率、M2卵比率及双原核(2PN)胚胎率均无统计学差异(P>0.05)。A组患者减胎数(14 ± 6)显著多于B组患者(12 ± 5, P<0.05), 中重度卵巢过度刺激综合征(OHSS)发生率无统计学差异(P>0.05)。冰冻移植周期A组患者胚胎复苏率(62.3%)显著低于B组(77.0%, P<0.05)。两组患者的移植胚胎数、临床妊娠率、着床率、流产率及活产率均无统计学差异(P>0.05)。结论 对于高反应PCOS患者使用拮抗剂方案基础上,应用减量联合扳机并全部胚胎冻存, 不增加重度OHSS发生率, 冰冻胚胎移植周期也得到了满意的治疗结局。

【关键词】 多囊卵巢综合征(PCOS); 促性腺激素释放激素拮抗剂(GnRH-A); 控制性卵巢刺激(COS); 促性腺激素释放激素激动剂(GnRHa)扳机; 联合扳机
GnRHa combined with low dose hCG trigger in in vitro fertilization treatment of polycystic ovary syndrome high responders  

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Abstract  
Objective  
To investigate the effectiveness and safety of low dose human chorionic gonadotropin (hCG) dual trigger in polycystic ovary syndrome (PCOS) high-responders who underwent in vitro fertilization/ intracytoplasmic sperm injection (IVF/ICSI).

Methods  
This was a retrospective cohort study. There were 364 infertile patients with PCOS high-responders accepted IVF/ICSI treatment in Reproductive Medical Center of Peking University, between Jan. 1st 2014 and Dec. 31st 2015, with GnRH antagonist flexible protocol. The patients were divided into two groups depending on different trigger protocols. Group A was low dose hCG dual trigger group (n=127), while group B was standard trigger group (n=237). The general characteristics and treatment outcomes were compared between two groups.

Results  
There were no significant differences between the two groups refer to general characteristics, and Gn used dosage (P>0.05). The serum E2 level on hCG trigger day [(19 193.9 ± 7 837.5) pmol/L] and mean number of oocyte retrieved (29 ± 9) in group A were significantly higher than those in group B [(15 786.8 ± 7 104.1) pmol/L, P<0.05; 24 ± 6, P<0.05]. The ICSI rate, MII oocyte rate and 2 pronuclear (2PN) embryo rate were comparable of two groups (P>0.05). The number of frozen embryos were significantly higher in group A (14 ± 6) than that in group B (12 ± 5, P<0.05). The severe ovarian hyperstimulation syndrome (OHSS) rate was comparable in two groups (P>0.05). In frozen-thawed cycles, the embryo survival rate was significantly lower in group A (62.3%) than in group B (77.0%, P<0.05). The number of transferred embryos, clinical pregnancy rate, implantation rate, miscarriage rate and live birth rate were comparable in the two groups (P>0.05).

Conclusion  
For high responders of PCOS patients, besides of GnRH antagonist protocol, using low dose hCG dual trigger and freeze all protocol, will not increase the incidence of OHSS. Furthermore, the frozen-thawed cycles will get satisfied treatment outcomes.

Key words  
Polycystic ovary syndrome (PCOS); GnRH antagonist; Controlled ovarian stimulation (COS); GnRH agonist trigger; Dual trigger
多囊卵巢综合征患者体外受精 / 卵胞质内单精子注射 - 胚胎移植后自然流产相关高危因素的多元回归分析

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【摘要】目的 通过了解多囊卵巢综合征(polycystic ovary syndrome, PCOS)患者行体外受精 / 卵胞质内
单精子注射 - 胚胎移植(IVF/ICSI-ET)助孕后自然流产的发生率及其危险因素,探讨PCOS患者IVF-ET后
流产的相关危险因素,以为临床改善PCOS患者助孕结局提供理论依据。方法 回顾性分析因输卵管因素和
/或男方因素行IVF/ICSI-ET助孕的PCOS患者共2 231例(IVF组, 对照组为条件匹配的因输卵管因素进
行助孕的非PCOS患者共2 231例, 分析其自然流产率和染色体核型异常率。将PCOS组分为自然流产
组和持续妊娠组, 利用多元回归分析方法探索PCOS自然流产发生的高危因素。结果PCOS组的自然流
产率(24.15%)较对照组高(12.75%), 差异有显著统计学意义 (P<0.001)。在流产的患者中, PCOS 组的染色体
核型异常率(36.05%, 31/86)较对照组低(55.56%, 50/90), 差异有统计学意义 (P=0.009)。在PCOS 患者中, 自然
流产组的年龄、体质量指数(body mass index, BMI)、HOMA 指数水平显著高于持续妊娠组 (P<0.05); 以
Logistic 回归分析, 年龄、HOMA 指数及BMI 与自然流产的发生密切相关, 周期类型、移植胚胎数及移
植胚胎数、空腹血糖、空腹胰岛素及基础性激素等组间均无统计学差异 (P>0.05)。结论 与非PCOS
患者相比, PCOS 患者的流产率高。染色体核型异常不是PCOS 患者高流产率的主要因素。年龄、BMI 及
HOMA 指数是PCOS患者在IVF/ICSI-ET助孕后发生自然流产的危险因素。

【关键词】 多囊卵巢综合征(PCOS); 自然流产; 高危因素

【基金项目】国家重大研发项目(2017YFC1001600); 国家自然科学基金(81471507)
Logistic regression analysis of risk factors associated with spontaneous abortion after in vitro fertilization/intracytoplasmic sperm injection-embryo transfer in polycystic ovary syndrome patients  

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Abstract  
Objective To analyze spontaneous abortion rate and its associated risk factors in patients with polycystic ovary syndrome (PCOS) after in vitro fertilization/intracytoplasmic sperm injection-embryo transfer (IVF/ICSI-ET).  
Methods This was a retrospective cohort study of patients undergoing IVF/ICSI treatment. A total of 2,231 patients with PCOS were included. For comparison, we enrolled 2,231 patients with tubular factors as control group. Spontaneous abortion rate and chromosomal abnormality rate were compared between the two groups. Furthermore, clinical data were compared between patients of spontaneous abortion and those of ongoing-pregnancy using univariate and multivariate analysis for risk factors of spontaneous abortion in PCOS patients.  
Results Patients in PCOS group had significantly higher spontaneous abortion rate (24.15%) than control group (12.75%, P<0.001). Chromosomal abnormality rate was significantly lower in PCOS group (36.05%, 31/86) than in control group (55.56%, 50/90, P=0.009). In PCOS group, patients of spontaneous abortion had older age, higher body mass index (BMI) and homeostasis model assessment for insulin resistance (HOMA-IR) than those of ongoing pregnancy. All the differences reached statistically significant. The further Logistic regression analysis confirmed that the age, BMI and HOMA-IR were risk factors of spontaneous abortion in PCOS patients. There were no significant differences in the type of cycles, the quality of embryos transferred, the number of embryos transferred, fasting blood glucose, fasting insulin, etc.  
Conclusion Compared with non-PCOS patients, PCOS patients had higher rate of miscarriage, but chromosomal abnormality was not a major factor for the high rate of miscarriage in PCOS patients. Age, BMI and HOMA-IR were risk factors for spontaneous abortion after IVF/ICSI-ET in PCOS patients.  

Key words Polycystic ovary syndrome (PCOS); Spontaneous abortion; Risk factors  
Fund program: National Key R&D Plan (2017YFC1001600); National Natural Science Foundation of China (81471507)
临床研究

伴有高雄激素血症的多囊卵巢综合征患者患有II型糖尿病和肥胖的风险升高

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【摘要】目的 评估鹿特丹标准的多囊卵巢综合征(PCOS)患者中，高雄激素血症对代谢紊乱的影响。
方法 收集符合2003年鹿特丹诊断标准的883名PCOS患者的临床资料，按照不同的PCOS诊断标准和是否合并高雄激素血症，分组比较患肥胖和糖代谢异常的发生率，并用717名正常育龄女性作为对照。
结果 共有719例(81.4%)PCOS患者伴有高雄激素血症。鹿特丹PCOS、美国国立卫生研究院(NIH)-PCOS和雄激素过多协会(AES)-PCOS(又称作高雄激素血症的PCOS)患者肥胖的发生率分别为42.0%、45.3%和44.8%，II型糖尿病的发生率分别为29.9%、24.2%和11.0%。而雄激素水平正常的PCOS的肥胖发生率为29.9%。II型糖尿病的发生率为0.7%。对照组II型糖尿病的发生率为1.0%。与正常雄激素患者相比，伴有高雄激素血症的PCOS患者中，肥胖、II型糖尿病、黑棘皮症和糖蛋白家族史的发生率均明显升高。
结论 高雄激素血症是II型糖尿病(OR=5.7, P=0.028)及肥胖(OR=1.7, P=0.005)的独立危险因素。

【关键词】 高雄激素血症(HA); II型糖尿病; 肥胖; 多囊卵巢综合征(PCOS)

基金项目: 国家自然科学基金面上项目(81471425, 81771545); 广东省自然科学基金(2015A030313091); 广东省公益研究与能力建设专项资金(2014A020213006); 2016年高校基本科研业务费中山大学青年教师重点培育项目
Hyperandrogenic women with polycystic ovary syndrome have higher risks for type 2 diabetes and obesity

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【Abstract】Objective To evaluate the effect of hyperandrogenism (HA) on obesity and the disturbance of carbohydrate metabolism among patients with polycystic ovary syndrome (PCOS) diagnosed by the Rotterdam criteria.

Methods The incidences of obesity and abnormal glucose disorders were compared among a cohort of 883 women with PCOS diagnosed by the Rotterdam criteria, according to different diagnostic criteria including Rotterdam (Rott), National Institutes of Health (NIH) and Androgen Excess Society (AES) criteria, and whether accompany with HA, with 717 premenopausal normal controls identified from the general population as the control. Results A total of 719 (81.4%) patients were classified with PCOS and HA, which is also as AES criteria. The incidence of obesity of the Rott-PCOS, NIH-PCOS and AES-PCOS was 42.0%, 45.3% and 44.8%, respectively. And the incidence of type-2 diabetes mellitus (2-DM) was 4.2%, 4.9% and 4.9%, respectively. Nevertheless, the incidence of obesity in PCOS group with normal androgens was 29.9%, and that of 2-DM was 0.7%. The incidence of 2-DM in control group was 1.0%. Women with HA exhibited higher incidences of obesity, 2-DM, acanthosis nigricans and genetic history of diabetes, compared with those with normal androgen levels. HA was independently associated with the risk for 2-DM (OR=5.7, \( P=0.028 \)) and obesity (\( OR=1.7, \ P=0.005 \)).

Conclusion HA is associated with increased risks for 2-DM and obesity among women with PCOS and should be considered at first-line management of HA and infertility due to PCOS.

【Key words】Hyperandrogenism (HA); Type 2 diabetes; Obesity; Polycystic ovary syndrome (PCOS)

Fund program: National Natural Science Foundation of China (81471425, 81771545); the Natural Science Foundation of Guangdong Province (2015A030313091); the Science Technology Research Project of Guangdong Province (2014A020213006); the Key Project of Fundamental Research Funds for the Central Universities
临床研究

达英-35 联合二甲双胍治疗多囊卵巢综合征合并子宫内膜不典型增生及早期子宫内膜样腺癌

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【摘要】目的 探讨达英-35 联合二甲双胍治疗多囊卵巢综合征(PCOS)患者合并子宫内膜不典型增生或早期子宫内膜样腺癌转化的疗效及安全性。 方法 43 例 PCOS 合并子宫内膜病变的患者全部采用相同治疗方法, 月经周期或孕激素撤药出血第 5 日起, 口服避孕达英-35(每日含雌酮 2 mg 和炔雌醇 0.035 mg, 1 片/d, 连服 21 d, 周期性使用; 同时口服二甲双胍 500 mg/片, 每日 2 次, 每次服 2~3 次服, 连续服用, 治疗 3~6 个月, 同时对肥胖的患者予以饮食控制及适当运动的指导。治疗期间每月随访超声了解子宫内膜厚度及盆腔核磁共振是否存在子宫肌层浸润改变, 每 3 个月行子宫内膜诊刮或宫腔镜下诊刮, 了解内膜转化情况。治疗前、后行胰岛素释放试验, 肝、肾功能、血脂检查。 结果 43 例 PCOS 合并子宫内膜病变患者中 30 例为子宫内膜不典型增生(EAH)患者(其中 9 例曾采用高效孕激素转化失败), 13 例为早期子宫内膜样腺癌 (EEC) 患者。在给予达英-35 联合二甲双胍治疗 3~9 个月后, 经宫腔镜下腔长度及病理证实的 43 例 PCOS 合并子宫内膜病变的患者的内膜病变均完全转化。随访 6~18 个月, 2 例 EAH 患者复发, 该 2 例患者在转化成功后都没有继续使用孕激素保护子宫内膜; 2 例 EEC 患者复发。随访过程检查到该 2 例患者出现卵巢肿瘤, 1 例为卵巢囊肿, 另 1 例为卵巢囊肿样肿瘤。妊娠结局: 9 例(5 例 EEC, 4 例 EAH)已足月分娩均获活婴, 另有 2 例目前仍在妊娠中, 其中 5 例为自然受孕, 6 例为体外受精—胚胎移植 (IVF-ET) 受孕。结论 达英-35 是一类具有抗雌激素活性的含低剂量雌激素的口服避孕药, 与二甲双胍联用对可使 PCOS 患者的子宫内膜病变(EAH 和 EEC) 得到完全转化, 即使对那些应用高剂量孕激素药物仍转化失败的患者同样有效。

【关键词】 多囊卵巢综合征 (PCOS); 子宫内膜不典型增生 (EAH); 早期子宫内膜样腺癌 (EEC); 达英-35 联合二甲双胍
Diane-35 combined with metformin in the treatment of polycystic ovary syndrome patients with atypical endometrial hyperplasia and early endometrial adenocarcinoma  

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Abstract
Objective To explore the clinical efficacy and safety Diane-35 and metformin combined treatment for endometrial atypical hyperplasia (EAH) and early endometrial carcinoma (EEC) in polycystic ovary syndrome (PCOS) patients. Methods PCOS patients with endometrium lesion were re-cruited. All patients were treated with Diane-35 (1 tablet per day, for 21 d per month) plus metformin (1 000 mg, qd) for 6 months. Endometrial biopsies for pathological evaluation before, during and after treatment were conducted. Other clinical parameters included body weight (BW), body mass index (BMI), follicle-stimulating hormone (FSH), luteinizing hormone (LH), total testosterone (TT), sex hormone-binding globulin (SHBG), free androgen index (FAI), insulin area under curve (IAUC), homeostasis model assessment of insulin resistance (HOMA-IR) were detected as well. After successful conversion of endometrial lesions, we continued to give patients with Dydrogesterone (10 mg/d, for 14 d per month) and metformin. Results Totally 43 PCOS patients with endometrium lesion (30 EAH and 13 EEC) were re-cruited. After 6-month treatment, the endometrium in all PCOS patients was confirmed by pathological evaluation to be reversed to normal epithelia with Diane-35 plus metformin treatment. By the end of 6-month treatment, mean BMI, TT, FAI, HOMA-IR were decreased respectively ($P<0.05$), while SHBG were increased ($P<0.05$). The complete response (CR) rate was 100%. During 6–18 months of follow-up, 2 EAH patients relapsed, and both of whom did not continue to use progesterone therapy monthly; 2 EEC relapsed, who had complicated with ovary tumor. Conclusion Diane 35, a low-dose oral contraceptives with anti-androgen activity, when used in combination with metformin can completely revert the EEC and EAH to normal endometrial cell in PCOS patients, even in those who have been failure to high-dose progestin treatment before. Diane-35 with metformin combination treatment may be a good choice for the EAH and EEC in PCOS patients, which enables these patients to preserve the fertility.

Key words Polycystic ovary syndrome (PCOS); Endometrial atypical hyperplasia (EAH); Early endometrial carcinoma (EEC); Diane-35 combined with metformin
临床研究

多囊卵巢综合征患者高尔基体磷酸化蛋白3表达与颗粒细胞凋亡和促排卵结局的相关性

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DOI: 10.3760/cma.j.issn.2096-2916.2017.12.007

【摘要】目的探讨多囊卵巢综合征(PCOS)患者控制性超促排卵(COH)周期卵巢颗粒细胞高尔基体磷酸化蛋白3(GOLPH3)的表达与颗粒细胞凋亡和COH结果的关系。方法选择因输卵管因素或男方因素首次接受体外受精/胚胎移植(IVF/ICSI-ET)助孕治疗的PCOS患者70例和同期非PCOS患者70例作为对照组。应用免疫细胞化学(ICC)和Real-time PCR技术检测颗粒细胞GOLPH3、Bcl-2、Bax、Caspase-3蛋白和mRNA的表达,并行相关性分析。结果①GOLPH3在卵巢颗粒细胞胞质中呈阳性表达,PCOS患者颗粒细胞 GOLPH3 和Bcl-2 的表达低于对照组(P<0.05), Bax 和Caspase-3 的表达均高于对照组(P<0.05); ②PCOS患者卵巢颗粒细胞GOLPH3 mRNA、Bcl-2 mRNA表达水平低于对照组(P<0.05), Bax mRNA、Caspase-3 mRNA 表达水平均高于对照组(P<0.05); ③PCOS患者中临床妊娠亚组颗粒细胞 GOLPH3 蛋白和mRNA 的表达水平高于未妊娠亚组(P<0.05); ④相关性分析显示: GOLPH3蛋白表达与闭经相关因子Bcl-2呈正相关(P<0.001), 与促凋亡相关因子Bax、Caspase-3呈负相关(P<0.001), 与COH 结局[获卵数、双原核(2PN)受精数、卵裂数、优质胚胎数、优质囊胚数、可利用胚胎数]呈正相关;颗粒细胞GOLPH3 mRNA表达水平与优质胚胎数呈正相关; 多元线性回归分析提示GOLPH3表达与Bcl-2表达, 可利用胚胎数呈正相关, 与Bax表达呈负相关。结论COH周期PCOS患者颗粒细胞GOLPH3表达水平下降可能促进颗粒细胞凋亡, 影响卵母细胞质量, 进而影响胚胎发育潜能。

【关键词】高尔基体磷酸化蛋白3(GOLPH3); 多囊卵巢综合征(PCOS); 颗粒细胞; 细胞凋亡

基金项目:福建省临床重点专科建设项目(闽卫科教2012149)
Relationship of Golgi phosphoprotein-3 expression with granulosa cells apoptosis and controlled ovarian hyperstimulation outcomes patients with polycystic ovary syndrome  

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Abstract

Objective  To explore the effect of Golgi phosphoprotein-3 (GOLPH3) in granulosa cells of patients with polycystic ovary syndrome (PCOS) during controlled ovarian hyperstimulation (COH) cycles on granulosa cells apoptosis and COH outcomes.

Methods  Seventy eligible in vitro fertilization/intracytoplasmic sperm injection-embryo transfer (IVF/ICSI-ET) cases with PCOS owing to the tubal or male factors and 70 corresponding IVF/ICSI-ET cases with non-PCOS were included. Immunocytochemistry and Real-time PCR were used to detect the protein and mRNA expression of GOLPH3, Bcl-2, Bax and Caspase-3 in granulosa cells of the two groups, respectively. Meanwhile, the correlations of GOLPH3 expression with cells apoptosis factors (Bcl-2, Bax and Caspase-3) and COH outcomes were analyzed.

Results  1) GOLPH3 protein was detected in the cytoplasm of granulosa cells in two groups. The expressions of GOLPH3 and Bcl-2 protein in PCOS group were lower than those in control group (P<0.05), while the expressions of Bax and Caspase-3 protein were higher than those in control group (P<0.05). 2) GOLPH3 mRNA and Bcl-2 mRNA in PCOS group were lower than those in control group (P<0.05). However, Bax mRNA and Caspase-3 mRNA were higher than those in control group (P<0.05). 3) Both the protein and mRNA levels of GOLPH3 expression in pregnant PCOS group were higher than those in non-pregnant PCOS group (P<0.05). 4) The expression of GOLPH3 protein in granulosa cells was strongly positively correlated with inhibit apoptosis factor Bcl-2 protein (P<0.001), and negatively correlated with pro-apoptosis factors Bax and Caspase-3 protein (P<0.001), meanwhile, presented positive correlation with COH outcomes, including the number of retrieved oocytes, two pronucleus (2PN) fertilizations, cleavages, high-quality embryos, high-quality blastocysts and available embryos. GOLPH3 mRNA was positively correlated with the number of high-quality embryos. Multivariate linear analysis discovered that GOLPH3 expression levels were positively associated with Bcl-2 level and the number of available embryos, while were negatively associated with Bax level.

Conclusion  Down-expression of GOLPH3 in granulosa cells of PCOS patients during COH period may be associated with the quality of oocytes and the unfavorable embryo developmental potential via promoting granulosa apoptosis.

Key words  Golgi phosphoprotein-3 (GOLPH3); Polycystic ovary syndrome (PCOS); Granulosa cells (GC); Apoptosis

Fund program: The Key Clinical Specialty Discipline Construction Program of Fujian (2012149)
【摘要】目的 探讨颗粒细胞中胚胎干细胞因子Nanog、Oct4、Sox2与多囊卵巢综合征(PCOS)发生的关系。方法 选择接受体外受精/卵胞质内单精子注射-胚胎移植术(IVF/ICSI-ET)治疗的PCOS患者40例,同期输卵管因素或男方因素不孕患者40例作为对照组。利用Real time-PCR技术检测颗粒细胞中Nanog、Oct4、Sox2以及抗苗勒氏管激素(AMH) mRNA的表达水平,并用Western blotting分析蛋白表达水平与PCOS发生的关系。结果 PCOS组体质量指数(BMI)(26.44 ± 3.46) kg/m²、黄体生成素(LH)(7.56 ± 0.98) IU/L、LH/卵泡刺澈素(FSH)(1.06 ± 0.15)及获卵数(28.7 ± 3.9)较对照组(22.43 ± 3.17) kg/m²、(4.26 ± 0.34) IU/L、0.57 ± 0.04、15.1 ± 2.0]有显著升高(P均<0.05)。Real time-PCR结果显示,PCOS组胚胎干细胞因子Nanog(0.60 ± 0.09)和Oct4(0.85 ± 0.14) mRNA表达水平显著高于对照组(1.65 ± 1.59 ± 0.17)](P<0.05), AMH转录水平(1.28 ± 0.11)显著高于对照组(0.89 ± 0.07)(P<0.05)。Logistic回归分析结果显示, Nanog是PCOS发生的危险因素(OR=26.577, P=0.002)。且Nanog与BMI、获卵数及AMH呈显著负相关(r=-0.415, P=0.023; r=-0.415, P=0.022; r=-0.373, P=0.043)。与Oct4呈显著正相关(r=0.684, P<0.01)。Western blotting结果显示,与对照组比较,PCOS组Nanog蛋白表达降低,AMH蛋白表达水平增高。结论 PCOS卵巢颗粒细胞中胚胎干细胞因子Nanog以及AMH的异常表达可能参与了PCOS的发生并影响卵母细胞的发育与成熟,为PCOS的临床治疗提供理论依据。

【关键词】 胚胎干细胞因子; 多囊卵巢综合征(PCOS); Nanog; 抗苗勒氏管激素(AMH)

【基金项目】 山西省回国留学人员科研资助项目(2012-100); 山西省人才引进与开发专项资金; 国家卫生和计划生育委员会资助项目(201402004)
Correlation of expressions of embryonic stem cell factor Nanog, Oct4, Sox2 with clinical characteristic of polycystic ovary syndrome  

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**Abstract**  
Objective To explore the relationship of expressions of embryonic stem cell factor Nanog, Oct4, Sox2 in granulosa cells with polycystic ovary syndrome (PCOS).  
Methods Totally 40 PCOS patients and 40 infertile cases due to tubal factors and/or male infertility who underwent in vitro fertilization/intracytoplasmic sperm injection-embryo transfer (IVF/ICSI-ET) at the same period were recruited as experimental group and control group, respectively. Real-time PCR was used to detect the expression levels of Nanog, Oct4, Sox2 and anti-Müllerian hormone (AMH) mRNA in granulosa cells. Logistic regression analysis was carried out on the pathogenesis of PCOS.  
Results Body mass index (BMI) [(26.44 ± 3.46) kg/m²], lutenizing hormone (LH) [(7.56 ± 0.98) IU/L], LH/follicular stimulating hormone (FSH) (1.06 ± 0.15) levels and the number of retrieved oocytes (28.7 ± 3.9) were significantly increased in PCOS group compared with control group [(22.43 ± 3.17) kg/m², (4.26 ± 0.34) IU/L, 0.57 ± 0.04, 15.1 ± 2.0] (P<0.05). However, the mRNA levels of Nanog (0.60 ± 0.09) and Oct4 (0.85 ± 0.14) in PCOS group were significantly lower than those in control group (1.65 ± 0.17, 1.59 ± 0.17) (P<0.05) and the mRNA level of AMH (1.28 ± 0.11) was higher than that in control group (0.89 ± 0.07) (P<0.05). Logistic regression analysis showed Nanog was a risk factor of PCOS, and the Nanog mRNA level was negatively associated with BMI, number of retrieved oocytes and AMH (r₁=0.415, P=0.023; r₂=0.415, P=0.022; r₃=0.373, P=0.043, respectively), and positively correlated with Oct4 (r=0.684, P<0.01). Western blotting results showed that the Nanog level decreased in PCOS group compared with control group. While, the AMH level increased.  
Conclusion The abnormal expression levels of Nanog and AMH in granulosa cells may be associated with the morbidity of PCOS and development and mature of oocyte. It will provide theoretical basis for treatment of PCOS.

【Key words】 Embryonic stem cell factor; Polycystic ovary syndrome (PCOS); Nanog; Anti-Müllerian hormone (AMH)

Fund program: Research Project Supported by Shanxi Scholarship Council of China (2012-100); Special Fund or Talent Introduction and Development of Shanxi Province; Research Fund of National Health and Family Planning Commission of China (201402004)
循证医学

多囊卵巢综合征诊断的潜在新指标——
抗苗勒管激素: 一项 Meta 分析

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【摘要】目的 探讨抗苗勒管激素(AMH)对多囊卵巢综合征(P COS)患者的诊断价值。方法 系统检索 1950 年 1 月—2017 年 5 月间国内外电子文献数据库关于血清 AMH 水平评价 PCOS 诊断效能的相关数据。按照纳入标准及排除标准收集文献, 根据 QUADAS 标准评价纳入文献的质量, 并采用 Meta-Disc 1.4 软件按合并受试者工作特征(SROC)曲线, 合并诊断效率对 AMH 在 PCOS 患者的诊断效能进行 Meta 分析。结果 本研究共纳入 28 篇文献, 其中 24 篇为研究 AMH 作为单独指标的诊断效率, 4 篇为研究 AMH 替代 2003 年鹿特丹诊断标准中“多囊卵巢”指标的诊断效率。结果显示, AMH 作为单独指标及取代“多囊卵巢”诊断以年龄 PCOS 的敏感度分别为 0.77 和 0.85, 特异度为 0.84 和 0.98, 其诊断信度比为 1497 和 343.18。此外, SROC 曲线图显示, AMH 单独诊断及联合诊断 PCOS 的曲线下面积分别为 0.864 0 和 0.985 8, Q 指数为 0.794 6 和 0.948 8, 两者比较具有统计学差异(Z=4.21, P<0.01)。结论 血清 AMH 水平对 PCOS 的诊断具有良好的临床应用价值, AMH 替代鹿特丹诊断标准中“多囊卵巢”指标与其余指标联合具有较高的诊断效能, 值得临床推广应用。

【关键词】多囊卵巢综合征(PCOS); 抗苗勒管激素(AMH); Meta 分析; 诊断试验
A potential diagnostic marker for patients with polycystic ovary syndrome–anti-Müllerian hormone: a Meta analysis  
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【Abstract】Objective To evaluate the diagnostic value of serum anti-Müllerian hormone (AMH) in patients with polycystic ovary syndrome (PCOS).
Methods All literatures in English and Chinese for differential diagnosis of PCOS by serum AMH were collected from January 1950 to May 2017. Data were extracted and assessed according to established criteria and QUADAS standard. Sensitivity, specificity and diagnostic odds ratio were pooled with Meta-Disc1.4 software. Summary receiver operating characteristics (SROC) curve analysis was used to evaluate the diagnostic value of serum AMH.
Results Twenty-eight studies were included in the Meta-analysis. The sensitivity, specificity and diagnostic odds ratio of serum AMH alone in the diagnosis of PCOS were 0.77, 0.84 and 14.97. As the AMH was substitution of polycystic ovary morphology (PCOM) and combined with either oligo/amenorrhea or hyperandrogenism data, the sensitivity, specificity and diagnostic odds ratio of serum AMH were 0.85, 0.98 and 343.18, respectively. Moreover, concerning the area under curve (AUC) of AMH level by SROC, the AUC was 0.864 0 in single serum AMH and 0.985 8 in AMH combined with aforementioned clinical features, which was significantly different (Z=4.21, P<0.01).
Conclusion AMH might be a potential diagnostic value for PCOS patients. Moreover, AMH replaced PCOM and combined with aforementioned clinical features was a more accurate diagnostic marker.

【Key words】Polycystic ovary syndrome (PCOS); Anti-Müllerian hormone (AMH); Meta-analysis; Diagnostic test
循证医学

维生素 D 与多囊卵巢综合征代谢及内分泌水平的 Meta 分析

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【摘要】目的 评价多囊卵巢综合征 (PCOS) 女性代谢及内分泌水平与维生素 D 水平的关系。方法 在中、英文主流数据库中检索维生素 D 与 PCOS 相关的临床研究, 截止到 2017 年 5 月。筛选文献、提取数据、
评估文献质量, 应用 RevMan5.3 软件进行分析。结果 纳入 30 篇文献, Meta 分析结果表明: PCOS 女性维生素 D 水平显著降低 (SMD: -1.16, 95% CI=-1.84~0.49, I²=98%); 维生素 D 水平与体质量指数 (BMI)、空腹血糖、空腹胰岛素、胰岛素抵抗指数、β 细胞功能指数、游离雄激素指数、甲状腺素呈负相关, 与高密度脂蛋白、性激素结合球蛋白呈正相关; 与安慰剂相比, 维生素 D 能提高血钙水平 (SMD=0.81, 95% CI=0.40~1.22, I²=0%) 及维生素 D 水平 (SMD=2.79, 95% CI=2.02~3.55, I²=46%), 但不能改善其他代谢及内分泌指标。结论 PCOS 患者维生素 D 水平显著降低, 维生素 D 水平与 PCOS 代谢及内分泌指标呈相关性, 维生素 D 治疗 PCOS 并不能显著改善其代谢及内分泌水平。

【关键词】 维生素 D; 多囊卵巢综合征 (PCOS); 内分泌代谢障碍; Meta 分析
Vitamin D and metabolic/endocrinological levels among women with polycystic ovary syndrome: a Meta-analysis
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【Abstract】Objective To assess the relationship between serum vitamin D level and metabolic/endocrine disorders in women with polycystic ovary syndrome (PCOS). Methods The clinical studies about vitamin D and PCOS were undertaken through popular English and Chinese databases until May 2017. Two authors independently screened studies, extracted data and evaluated study quality. Data analyses were conducted by RevMan5.3. Results Thirty studies were included. Meta-analysis showed vitamin D level of PCOS women was lower (SMD=−1.16, 95% CI=−1.84—−0.49, I²=98%); Negative correlations between vitamin D and body mass index (BMI), fasting plasma glucose, fasting insulin, homeostatic model assessment-insulin resistance, homeostatic model assessment-beta cell function, free androgen index, parathyroid hormone were found. Positive correlations between vitamin D and high-density lipoprotein, sex hormone binding globulin were found. Compared with placebo, vitamin D could improve serum calcium level (SMD=0.81, 95% CI=0.40—1.22, I²=0%) and vitamin D level (SMD=2.79, 95% CI=2.02—3.55, I²=46%) but not other metabolic and endocrinological parameters. Conclusion Vitamin D level in women with PCOS is much lower. Vitamin D level is related to metabolic and endocrinological parameters among PCOS women. Vitamin D is not an effective treatment to improve metabolic and endocrinological levels among PCOS women.

【Key words】Vitamin D; Polycystic ovary syndrome (PCOS); Endocrinological and metabolic disorder; Meta analysis
前列腺特异抗原在多囊卵巢综合征诊断中的意义

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【摘要】雄激素升高是诊断多囊卵巢综合征（polycystic ovary syndrome, PCOS）的重要指标，但是自1935年Stein-leventhal提出这一疾病至今，尚缺乏对雄激素血症客观可靠的检测方法。目前研究表明前列腺特异抗原(prostate specific antigen, PSA)与PCOS患者的雄激素水平密切相关，PSA 有可能成为PCOS 诊断潜在的新指标。本文对国内外有关PSA 在PCOS 诊断中的价值进行综述。

【关键词】多囊卵巢综合征（PCOS）；前列腺特异抗原；雄激素过多症；血清标志物
【基金项目】国家重点研发计划(2017YFC1001004); 国家自然科学基金面上项目(81471428)
Diagnostic value of prostate specific antigen in women with polycystic ovary syndrome  
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【Abstract】Hyperandrogenism is an important indicator for diagnosis of polycystic ovary syndrome (PCOS). However, since Stein-Leventhal identified this condition in 1935, there has not been any objective or reliable test of hyperandrogenism. Prostate specific antigen (PSA) is closely associated with androgen levels in patients with PCOS. Therefore PSA may be a potential marker to diagnose PCOS. In this paper, the value of PSA in PCOS diagnosis is reviewed.

【Key words】Polycystic ovary syndrome (PCOS); Prostate specific antigen; Hyperandrogenism; Serum biomarkers

Fund program: National Key Research and Development Plan (2017YFC1001004); National Nature Science Foundation of China (81471428)
肌醇在多囊卵巢综合征中的治疗临床应用现状

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【摘要】多囊卵巢综合征(polycystic ovary syndrome, PCOS)是最常见的妇科内分泌疾病之一, 以高雄激素、持续无排卵和胰岛素抵抗(IR)为特征, 是导致女性不孕的主要原因之一。肌肉肌醇(MI)和D-手性肌醇(DCI)为两种肌醇异构体, 可通过改善IR, 降低雄激素和改善代谢, 以及降低氧化应激对PCOS有治疗作用。然而, 使用大剂量的DCI对卵子质量反而有不利影响。近年来, 越来越多的研究表明, MI和DCI联合应用, 以40：1的生理剂量比例治疗PCOS效果更为显著。现对肌醇在PCOS中的治疗作用及其机制作一综述。

【关键词】多囊卵巢综合征(PCOS); 肌醇; 治疗
Therapeutic effect and mechanism of the inositol in polycystic ovary syndrome  
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【Abstract】Polycystic ovary syndrome (PCOS) is the most common endocrine disorder and is one of the leading cause of female infertility, characterized by hyperandrogenism, chronic anovulation and insulin resistance (IR). Myo-inositol (MI) and D-chiro-inositol (DCI) which are two inositol isomers have been proven to be effective in PCOS treatment, by improving the IR, androgen and metabolism, reducing oxidative stress (OS) damage. However, only using large dose of DCI have an adverse effect on oocyte quality. In recent years, more and more studies have shown that the combined administration of MI and DCI in the physiological plasma ratio (40 : 1), could be have more remarkable effect. Here we review the role and mechanism of inositol in PCOS.

【Key words】Polycystic ovary syndrome (PCOS); Inositol; Treatment
·综述·

饮食改善肥胖多囊卵巢综合征患者体内慢性炎症作用的研究进展

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【摘要】多囊卵巢综合征(PCOS)是典型的生殖障碍性疾病, 主要表现为月经稀发、雄激素过多症或高雄激素血症(HA), 卵巢多囊样改变。有关PCOS的发病机制尚无定论, 但目前认为PCOS患者体内的慢性炎症状态是发病机制之一。肥胖诱发的炎症可能会引发一系列事件导致胰岛素抵抗(IR)、血脂异常增加、卵巢雄激素生成增多, 最终导致PCOS患者发生生殖障碍。近年流行病学数据表明, 饮食中的某些成分可能会促进生殖健康, 尤其是与炎症有关的女性生殖疾病, 如PCOS。本文根据流行病学和基础研究所得, 简要概述慢性炎症在肥胖PCOS患者生殖障碍中的作用, 为未来饮食干预肥胖PCOS患者的生殖结局提供依据。

【关键词】炎症; 肥胖; 多囊卵巢综合征(PCOS); 饮食
Research progress of diet improving chronic inflammation in obese and polycystic ovary syndrome infertility patients  Yang Yuan, Zhang Xuehong

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【Abstract】 Polycystic ovary syndrome (PCOS) is a typical reproductive disorder characterized by menstrual irregularities, hyperandrogenism and polycystic ovaries. The pathogenesis of PCOS has not been determined, but it is currently believed that the chronic inflammatory state in patients with PCOS is one of the pathogenesis. Obesity-induced inflammation can lead to insulin resistance (IR), blood lipids abnormal increasing, hyperandrogen, and finally resulted in the occurrence of reproductive disorders in patients with PCOS. Recent epidemiological data show that certain diet ingredients may affect reproductive health, particularly in women with inflammation, such as PCOS. This article is based on epidemiology and research to overview the role of chronic inflammation in the reproductive dysfunction of obese PCOS patients and the function of diet for obesity PCOS patients in reproductive outcomes.

【Key words】 Inflammation; Obesity; Polycystic ovary syndrome (PCOS); Diet
多囊卵巢综合征患者生活方式的调整与减重治疗

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【摘要】 多囊卵巢综合征(PCOS)是育龄期女性最常见的内分泌及代谢紊乱性疾病之一。生活方式调整包括饮食控制、运动和行为干预, 改善超重或者肥胖 PCOS 患者的代谢和内分泌异常; 被推荐为 PCOS 患者的一线治疗。当生活方式干预联合减重药物治疗时, 可对超重/肥胖 PCOS 患者的内分泌异常改善发挥更有效的作用。奥利司他、二甲双胍和胰岛素等药物用于 PCOS 患者人群, 可有效减轻体质量改善 PCOS 临床症状。但目前仅有奥利司他获批为减肥适应证药物。此外减重手术也是肥胖 PCOS 女性的有效治疗手段。本文对生活方式调整和减重药物对 PCOS 的代谢和内分泌影响的相关研究进行综述。

【基金项目】 多囊卵巢综合征(PCOS); 生活方式干预; 减重治疗; 奥利司他

基金项目: 首都特色应用研究及成果推广(Z161100000516143); 首都卫生发展科研专项项目(2016-2-2113); 北京市医院管理局临床技术创新项目(XMLX201710); 北京市卫生系统高层次卫生技术人才(学科带头人)项目(2014-2-016)
Lifestyle intervention and anti-obesity therapies in patients with polycystic ovary syndrome

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【Abstract】Polycystic ovary syndrome (PCOS) is a common endocrine and metabolic disorder in women of reproductive age. Lifestyle interventions, including diet, exercise and behavioral modification, improving the metabolic abnormalities of overweight and obese patients with PCOS, are recommended as first-line treatment. Lifestyle interventions combined with anti-obesity products, may exert more effects improving endocrine abnormalities of overweight/obese PCOS patients. Anti-obesity products include orlistat, metformin, and inositol can be effective in decreasing weight or improving PCOS manifestations. However, only orlistat is approved for obesity treatment. Moreover, bariatric surgery is efficient in achieving significant weight loss for obese PCOS women. In the paper, we reviewed and summarized the recently related studies.

【Key words】Polycystic ovary syndrome (PCOS); Lifestyle intervention; Anti-obesity therapies; Orlistat

Fund program: Capital Characteristic Clinic Project of China (Z16110000516143); Beijing Capital Foundation for Medical Science Development and Research (2016-2-2113); Clinical Technique Innovation Project of Beijing Municipal Administration of Hopsitals (XMLX201710); Beijing Municipality Health Technology High-level Talent (2014-2-016)
免疫紊乱与多囊卵巢综合征

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【摘要】多囊卵巢综合征(PCOS)是育龄期妇女最常见的生殖内分泌疾病, 以生殖和代谢异常为主要特征。临床上PCOS患者出现的高雄激素血症、胰岛素抵抗(IR)及低黄体酮均引起机体免疫系统异常活化, 导致机体免疫功能紊乱, 进而加剧生殖和代谢异常。本文综述了近年来免疫与PCOS关系的研究进展, 从免疫学角度探讨PCOS的发病机理。

【关键词】多囊卵巢综合征(PCOS); 慢性炎症; 代谢; 自身免疫
Role of the immune dysfunction in pathology of polycystic ovary syndrome  
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【Abstract】Polycystic ovary syndrome (PCOS) is the most common reproductive endocrinopathy affecting females during reproductive age. Reproductive and metabolic disorder are the main features of the syndrome. Clinically, hyperandrogenism, insulin resistance and low level of progesterone in PCOS can cause over-stimulation of immune system that results in immune disorders. Perturbations in immune system further aggravate the reproductive and metabolic syndrome. Here, we reviewed the current understanding of immune-PCOS interactions and expected to explore the pathogenesis of PCOS.

【Key words】Polycystic ovary syndrome (PCOS); Chronic inflammation; Metabolism; Autoimmune
多囊卵巢综合征与脂肪分布的研究进展

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【摘要】多囊卵巢综合征(polycystic ovary syndrome, PCOS)是育龄期女性最常见的生殖内分泌疾病，超重和/或肥胖可加重PCOS女性的代谢状况及生殖障碍情况。肥胖症及内脏脂肪堆积与慢性低度炎症状态相关，PCOS患者机体处于一种慢性炎症状态，炎症可诱导胰岛素抵抗(insulin resistance, IR)，IR可导致高雄激素血症(IR)及雄激素增多；与此同时，IR加重机体的炎症反应状态，两者互相作用，相互影响，形成恶性循环。性激素影响体脂分布，PCOS患者中约50%~60%的患者常表现为男性体脂分布，出现腹部脂肪积聚的表现。IR、炎症反应和腹型肥胖之间存在因果关系。腹型肥胖可能导致IR和炎症反应，IR和炎症反应的增加也会导致腹型肥胖。一般将脂肪细胞分为白色脂肪细胞和棕色脂肪细胞。白色脂肪组织(white adipose tissue, WAT)主要分布在身体的皮下和内脏，与炎症、IR和II型糖尿病(type 2 diabetes mellitus, T2DM)强烈相关。棕色脂肪组织(brown adipose tissue, BAT)可以增加能量消耗并产生热量，主要在肩胛间、周围和主动脉区蓄积。棕色脂肪可改善PCOS的能量消耗及糖代谢状况，降低相关性激素水平，有助于改善PCOS患者的月经周期及排卵情况。

【关键词】多囊卵巢综合征(PCOS); 内脏脂肪(VAT); 皮下脂肪(SAT); 白色脂肪组织(WAT); 棕色脂肪组织(BAT)
Research progress on polycystic ovary syndrome and fat distribution  
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Abstract  Polycystic ovary syndrome (PCOS) is the most common reproductive endocrine disease in women. Overweight/obesity can aggravate the metabolic status and reproductive disorders of PCOS women. Obesity and visceral fat accumulation are associated with chronic hypo-inflammatory status, PCOS patients are in a chronic inflammatory state. Inflammation can lead to insulin resistance (IR), and IR will lead to hyperandrogenism and increased androgen. IR and inflammation interact with each other, becoming a vicious cycle. Sex hormones affect the body fat distribution, PCOS patients in about 50% to 60% often manifested as male body fat distribution, the emergence of abdominal fat accumulation. IR, inflammatory response and abdominal obesity have the relationship between each other. Abdominal obesity may lead to IR and inflammatory response, IR and increased inflammatory response can also lead to abdominal obesity. Traditionally, adiposities are divided into white adiposities and brown adiposities. White adipose tissue (WAT) mainly distributed in the subcutaneous and viscera of the body, and strongly correlated with inflammation, IR and type 2 diabetes mellitus (T2DM). Brown adipose tissue (BAT) can increase energy consumption and generate heat, mainly in the scapular, surrounding and aortic deposits. BAT can improve the energy consumption of PCOS and glucose metabolism, reduce the level of related hormones, help to improve the menstrual cycle of PCOS patients and ovulation.

Key words  Polycystic ovary syndrome (PCOS); Visceral adipose tissue (VAT); Subcutaneous adipose tissue (SAT); White adipose tissue (WAT); Brown adipose tissue (BAT)